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Management of patients with cardiac implantable electronic devices (CIED) undergoing radiotherapy
A consensus document from Associazione Italiana Aritmologia e Cardiostimolazione (AIAC), Associazione Italiana Radioterapia Oncologica (AIRO), Associazione Italiana Fisica Medica (AIFM)

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ABSTRACT

The management of patients with a cardiac implanted electronic device (CIED) receiving radiotherapy (RT) is challenging and requires a structured multidisciplinary approach. A consensus document is presented as a result of a multidisciplinary working group involving cardiac electrophysiologists, radiation oncologists and physicists in order to stratify the risk of patients with CIED requiring RT and approaching RT sessions appropriately.
When high radiation doses and beam energy higher than 6 MV are used, CIED malfunctions can occur during treatment. In our document, we reviewed the different types of RT and CIED behavior in the presence of ionizing radiations and electromagnetic interferences, from the cardiologist's, radiation oncologist's and medical physicist's point of view. We also reviewed in vitro and in vivo literature data and other national published guidelines on this issue so far. On the basis of literature data and consensus of experts, a detailed approach based on risk stratification and appropriate management of RT patients with CIEDs is suggested, with important implications for clinical practice.

1. Purpose of the paper

The management of patients with a cardiac implanted electronic device (CIED) receiving radiotherapy (RT) is challenging and requires a structured multidisciplinary approach. The Italian Associations of Arrhythmologists (Associazione Italiana Aritmologia e Cardiostimolazione — AIAC), Radiation Oncologists (Associazione Italiana Radioterapia Oncologica — AIRO) and Medical Physicists (Associazione Italiana Fisica Medica — AIFM) formed a multidisciplinary working group to develop a consensus document for the management of patients with a cardiac implantable electronic device (CIED) undergoing radiotherapy (RT).

In patients with CIEDs, including cardiac pacemakers (PM) and implantable cardioverter-defibrillators (ICD), RT could compromise CIED function and, moreover, CIED could limit RT options.

In the presence of high radiation doses (in Gy) and especially when beam energy >6 MV are used, both software and hardware errors may occur [1]. Malfunctions can be:

1. *transient* (due to electromagnetic interference and occurring only during radiation exposure)

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2. *reset to back-up setting*, which can be reverted by CIED programming
3. *permanent*, requiring CIED substitution.

Electromagnetic interference could lead to

- *inappropriate pacing inhibition*, particularly dangerous, even if brief, in pacing-dependent patients (usually defined as patients without intrinsic or escape rhythm >30/min)
- *inappropriate antitachycardia therapies* (including ICD shock) when long enough to be recognized as ventricular fibrillation (>5–10 s).

Awareness among physicians on the topic is unknown, but it is likely to be low. According to published data, up to half of the patients with CIED are not evaluated after RT [2,3] and a close communication between Cardiologists and Radiation Oncologists is often lacking.

A series of guidelines have been published so far, but recommendations regarding the risk stratification, CIED management and treatment planning are quite divergent [1,4,5]. In our document, we created a multidisciplinary group of Cardiologists, Radiation Oncologists and Medical Physicists with the aim to provide a detailed and updated approach to risk stratification with regard to CIED patients undergoing RT, with the result of a document proposing a tailored patient-centered management. In addition, some consideration about new technologies (leadless PM and entirely subcutaneous ICD) are included, adding specific recommendations not included in previous guidelines.

In summary, the aims of this document are to

- increase the awareness of the topic among Cardiologists, Radiation Oncologists and Medical Physicists
- allow a tailored risk assessment for patients with CIEDs requiring RT
- propose a flowchart for safe management of these patients before, during and after RT by close cooperation among Cardiologists (in particular Electrophysiologists), Radiation Oncologists and Medical Physicists.

The management of patients with other devices (Implantable Loop Recorders, spinal cord stimulators, vagal nerve stimulators, etc.) is not discussed in this document.

2. Radiotherapy in patients with CIED: literature data

2.1. Epidemiology

RT is offered in approximately 70% of cancer patients [1] while > 500,000 PMs and 100,000 ICDs are implanted every year in Europe [6]. In a Danish Population-Based Cohort Study [3] the annual rate of RT courses in CIED patients was 4.33 treatments per 100,000 person-years in 2012.

2.2. Implantable devices: types and general characteristics

See Supplementary material 1 and Suppl Table 1.

2.3. Radiation treatments

See Supplementary material 1.

2.4. Characteristics of radiation energy and potential interactions with CIED.

See Supplementary material 1.

2.5. Effects of radiation on implantable devices: in vitro and in vivo data

See Supplementary material 1 and Table 1.

2.6. Operating manuals provided by manufacturers

See Supplementary material 2-7 and Supplementary Table 3.

2.7. Published guidelines

The first recommendations for the management of patients with PMs undergoing RT were developed in 1994 by the American Association of Physicists in Medicine [7]. These were followed by other recommendations for the management of patients with PMs [8,9], PMs and ICDs [10,11] and ICDs only [12], as well as national guidelines, consensus statements or position papers [4,5,13,14], in some cases included within a statement on the perioperative management [15].

Reviewing all published recommendations, it emerged that the risk of malfunctions (or adverse events in the case of malfunctions) is associated both with treatment characteristics (dose at CIED site and energy of radiation) and patient characteristics (type of CIED, PM dependency) and this was the basis for appropriate risk stratification before RT. Combining both the risk of malfunctions and of adverse clinical events, patients can be classified at low, moderate or high risk and this is common to most guidelines.

In our document we adapted the recommendations published so far to the present practice of RT and CIED technology and according to the latest available literature data. These recommendations will need an update in the future according to evolving techniques.

3. Management of the patient

3.1. Before radiotherapy

3.1.1. Identification of the patients, general and oncological assessment

General and oncological evaluation of patients, the choice of intent (curative, adjuvant, neoadjuvant, palliative, ablative), doses, schedules and techniques of treatment are crucial phases before starting RT. Radiation therapy may be used to treat almost every type of solid tumor; the most frequent sites of RT are breast, head and neck, prostate, lung, brain and bone metastases.

Contraindications to RT are pregnancy, inherited hypersensitivity syndromes (such as ataxia-telangiectasia) and non-compliance. The presence of active collagen vascular diseases (such as lupus, scleroderma, Sjogren's syndrome) was considered in the past to be a contraindication for RT because RT might cause connective tissue damages. The data currently available from case series and a few retrospective studies are still insufficient to support a specific contraindication, but a cautious approach for this category of patients seems to be reasonable [16].

The Radiation Oncologist should estimate the cancer risk in terms of total and disease-free survival, benefits and risks of RT-related side effects (including RT-related CIED malfunctions).

During treatment planning procedures, the Radiation Oncologist must consider radiation dose involving Organs-At-Risk (OAR), defined as healthy organ tissues close to the irradiated target. Thus, CIEDs could be considered as OARs during RT planning. The final choice of RT should be discussed with Cardiologists, Medical Physicists and patients.

As shown in Fig. 1 in the phase evaluating a patient for RT and planning of RT, the Radiation Oncologist should:

- Identify CIED patients and inform the referring Cardiologist and/or Electrophysiologist
- Stratify the patient according to the risk of malfunction and the risk of adverse clinical events (together with the Cardiologists and Medical Physicists)
- Evaluate the RT plan and the radiation dose to the device, excluding, whenever possible, the CIED from the treatment fields
- Inform the patient about the risks associated with RT according to his/her class of risk obtaining specific written consent.

Table 1
In vivo published data on radiotherapy and CIEDs.

First author (year)	n. of patients	Tumor site	Device	Total RT dose/fraction	Dose at CIED site	Energy	Effects
Raitt [31] 1994	1	Thyroid	PM	4.8 GyE neutrons	0.9 GyE	n.d.	Uncontrollable increase in pacing frequency (runaway pacemaker, 180/min)
Tsekos [32] 2000	1	Neuroendocrine cancer right arm and axilla	PM	50.4/1.8 Gy	50 Gy (direct radiation)	n.d.	Intermittent decrease in magnetic frequency
Nibhanupudy [33] 2001	1	Left breast	PM	50.40/2 Gy	1.8 Gy	6 MV	No malfunction
Hoecht [34] 2002	3	Pelvic	ICD	< 0.5 Gy/n.m.	<0.5 Gy	n.d.	Reset into fallback mode ($n = 1$), reproduced after ICD replacement malfunction
Frantz [35] 2003	1	Breast	PM	66/2 Gy	50 Gy (direct radiation)	n.d.	Loss of telemetry capabilities
John [36] 2004	1	Breast	ICD	50/2.5 Gy	(direct radiation)	n.d.	Shock impedance >125 Ω (partial exposure of the device after RT)
Thomas [37] 2004	1	Right lung	ICD	56/2 Gy	<0.5 Gy	18 MV	Reset into fallback mode
Ampil [38] 2006	3	Lung	PM	20–60 Gy	n.d.	n.d.	No malfunction
Mitra [39] 2006	1	Right lung and mediastinum	PM	40 Gy	0.7325 Gy	n.d.	No malfunction
Sepe [40] 2007	1	Laryngeal	ICD	60 Gy	2.5 Gy	6 MV	No malfunction
Nemec [41] 2007	1	Left lung	ICD	59.4/1.8 Gy	n.a.	n.d.	Runaway ICD, 175/min; induction of polyform VT, necessitation of CPR
Munshi [42] 2008	1	Breast	PM	50.4/1.8 Gy	4.3 Gy	10 MV	No malfunction
Kapa [43] 2008	8	Head and neck, lung, breast cancer	PM	30–70 Gy	n.a.	n.d.	No malfunction
Oshiro [44] 2008	8	Thorax, abdomen	PM	33–77 GyE (protons)/ 2.2–6-6 Gy	0 Gy or 36.3–77 Gy	155–250 MeV (protons)	Reset into fallback mode (n = 1), modification of programmed stimulatory frequency ($n = 1$)
Lau [45] 2008	1	Prostate cancer	ICD	74/2 Gy	0.004 Gy	23 MV	Reset into fallback mode
Zweng [46] 2009	1	Esophageal cancer	PM	30/3 Gy	0.11 Gy	18 MV	Deviation from programmed stimulatory mode (DDD to AAI) and runaway PM, (185/min)
Gelblum [47] 2009	33	Head and neck, thorax, abdomen, pelvis, legs	ICD	6–86.4/1.8–2 Gy	0.01–2.99 Gy	15 MV	Reset into fallback mode ($n = 2$)
Zaremba [48] 2010	1	Breast cancer	PM	48/2 Gy	2–37 Gy	6–18 MV	Inappropriate warning: "invalid data detected" (no malfunction detected)
Ferrara [49] 2010	37	Head and neck, thorax, abdomen, pelvis	PM	8–79.2 Gy	< 2 Gy ($n = 32$), >2 Gy ($n = 5$)	n.d.	No malfunction
Wadasadawala [9] 2011	8	Head and neck, lung, breast cancer	PM	45–70/1.8–2 Gy	0.14–60 Gy	6–15 MV	No malfunction
Dasgupta [50] 2011	1	Cardiac metastases (right atrium and left ventricle)	PM	37.5/2.5 Gy	0.26 Gy	n.d.	Single episode of ventricular undersensing (epicardial lead)
Soejima [2] 2011	60	Various	PM	20–74 Gy	>2 Gy in 6 pts., >5 Gy in 1 pt	15 MV	Reset into fallback mode ($n = 1$, prostate cancer)
	2	Various	ICD	20–74 Gy	>2 Gy in 6 pts., >5 Gy in 1 pt	15 MV	No malfunction
Menard [51] 2011	5	Breast cancer	ICD	32.5–66/2 Gy	<0.1–0.3 Gy	4–6 MV	No malfunction
Croshaw [52] 2011	8	Breast cancer	PM/ICD	34–38.5 Gy	0.23–1.68 Gy	6	No malfunction
Kirova [53] 2012	1	Sarcoma	PM	30/3 Gy	0.3 Gy	20 MV	No malfunction
Kesek [54] 2012	1	Lung cancer	PM	80 Gy/1.6 Gy bid	25 Gy mean/ 48 Gy max	6 MV	No malfunction
Makkar [55] 2012	50	Various	PM	n.d.	0.9–505.7 cGy	6–16 MV	No malfunction
	19		ICD		4–169 cGy	(in 24 pts) 6–16 MV (in 12 pts)	Partial reset in 2 devices at 16 MV
Elders [56] 2013	15	Head and neck, lung, abdomen, pelvis, legs	ICD	16–70/2–8 Gy	n.a.	6–18 MV	6 malfunctions in 5 RT courses at 10 and 18 MV: invalid data ($n = 2$), reset ($n = 1$), inappropriate tachycardia sensing ($n = 1$), reset ($n = 1$)
Keshtgar [57] 2012	1	Breast cancer	PM	20 Gy IORT	8 cGy	50 kV	No malfunction
Gomez [58] 2013	28	Various	PM	46.8–87.5 Gy	0.13–21 Gy	n.d.	Reset into fallback mode in 2 PMs and in 2 ICDs
	14		ICD				
Dell'Oca [59] 2013	1	Mediastinum	ICD	64 MV	<5 Gy	6	No malfunction
Zaremba [60] 2013	5	Thorax	ICD	37	37	6–18 MV	Converting to backup mode ($n = 1$)
Ampil [61] [102] 2014	2	Head and neck	PM	n.d.		6	No malfunction
Gossman [62] 2014	67	Various	PM	n.d.	<2 Gy in 85%, never exceeding 6.5 Gy	14% > 8 MV	Failure at 0.3 Gy ($n = 1$); increase in sensor rate during RT ($n = 1$); type of device not specified
	40		ICD				
Ahmed [63] 2014	1	Lung	ICD	70 Gy	52.4 Gy	15	No malfunction
Brambatti [30] 2015	207	Various	PM	n.d.	<2Gy in 80.4%, 2-20Gy in 7.4%, >20 Gy in 0.2%	6–18 MV	1 ICD reset (18 MV), 3 PM maximum sensor pacing
	54		ICD				
Zaremba [3] 2015	487	Various	PM	various	n.d.	9	PM: Reset or deprogramming ($n = 9$), increase in atrial pacing threshold ($n = 1$)
	73		ICD				ICD: Reset ($n = 3$), reset and increase in pacing threshold ($n = 1$)

(continued on next page)

Table 1 (*continued*)

First author (year)	n. of patients	Tumor site	Device	Total RT dose/fraction	Dose at CIED site	Energy	Effects
Grant [64] 2015	123 92	Various	PM ICD	n.d.	1.5–20 Gy	6–18 MV	PM: 5 malfunctions (data loss, reset and interferences) with 18 MV, 1 signal interference with 6 MV 11 malfunctions (data loss and reset) with 18 MV, 1 signal interference with 6 MV
Bagur [65] 2017	199	Various	PM	43.3 ± 24.2	n.d.	n.d.	14 patients experienced malfunctions ("mainly" reset into fallback mode)

- Instruct the patient to report any symptom (during and after RT). In particular, the patient should be made aware of the signs of syncope or dizziness as potential signs of latent CIED defects. In this case, patients should seek immediate advice from their cardiologists.

3.2. Cardiological and electrophysiological assessment

An evaluation of the cardiac and arrhythmic profile of the patient, as well as of the CIED assessment should be performed by a cardiologist with appropriate competence in CIED management (Fig. 1).

The risk of CIED malfunctions depends on the RT site, modality and energy while the risk of *adverse clinical events* during RT (not necessarily due to CIED malfunctions) depends both on the CIED and patient characteristics. The following conditions are sources of potential risk (Fig. 1-2):

- PM-dependent patients. The presence of atrial or ventricular stimulation artifacts at baseline ECG does not always mean that the patient is PM-dependent, as this mainly depends on device programming. For example, in patients with Cardiac Resynchronization Therapy (CRT), constant ventricular stimulation is desirable while in single and dual chamber devices it should be avoided whenever possible. *PM-dependency* is defined as the absence of any spontaneous ventricular activity (or the presence of low-rate, clinically not tolerated, spontaneous activity when the CIED is transiently programmed in VVI 30–40/min). In these patients the consequences of a temporary or permanent pacing failure could be devastating. The prevalence of the PM-dependency is significantly variable, ranging from 2.1% to 24% [17–19]. Fluctuation of PM-dependency must be taken into account, as up to 13% of patients with a reliable escape rhythm at a first examination, are pacing-dependent at a second examination and vice versa [19]. PM-dependency is usually due to:
  - o permanent AV block (in sinus rhythm or atrial fibrillation)
  - o ablation of AV node ("ablate and pace") for the management of atrial fibrillation (often in the presence of Cardiac Resynchronization Therapy)
  - o Severe sick sinus syndrome

  Even brief electromagnetic interference (few seconds), leading to asystole, can cause significant clinical adverse events in PM-dependent patients.
  On the contrary, if no PM artifacts are presents, the patient is not PM-dependent by definition (N.B. bipolar pacing can be sometimes difficult to identify).

- Patient with ICDs.
  Electromagnetic interference can lead to *inappropriate ICD shocks* if inappropriately recognized as high-rate ventricular signals when

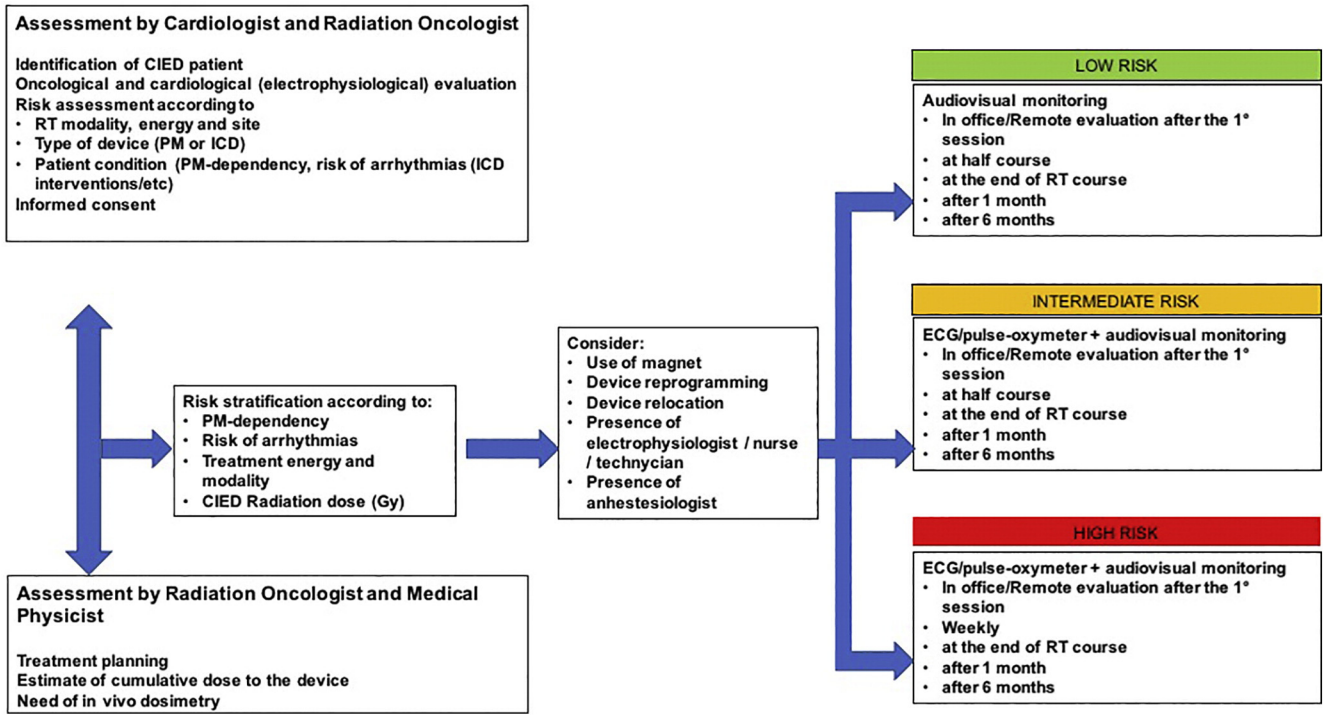

Fig. 1. Flow-chart of patient assessment and follow-up. RM: Remote Monitoring.

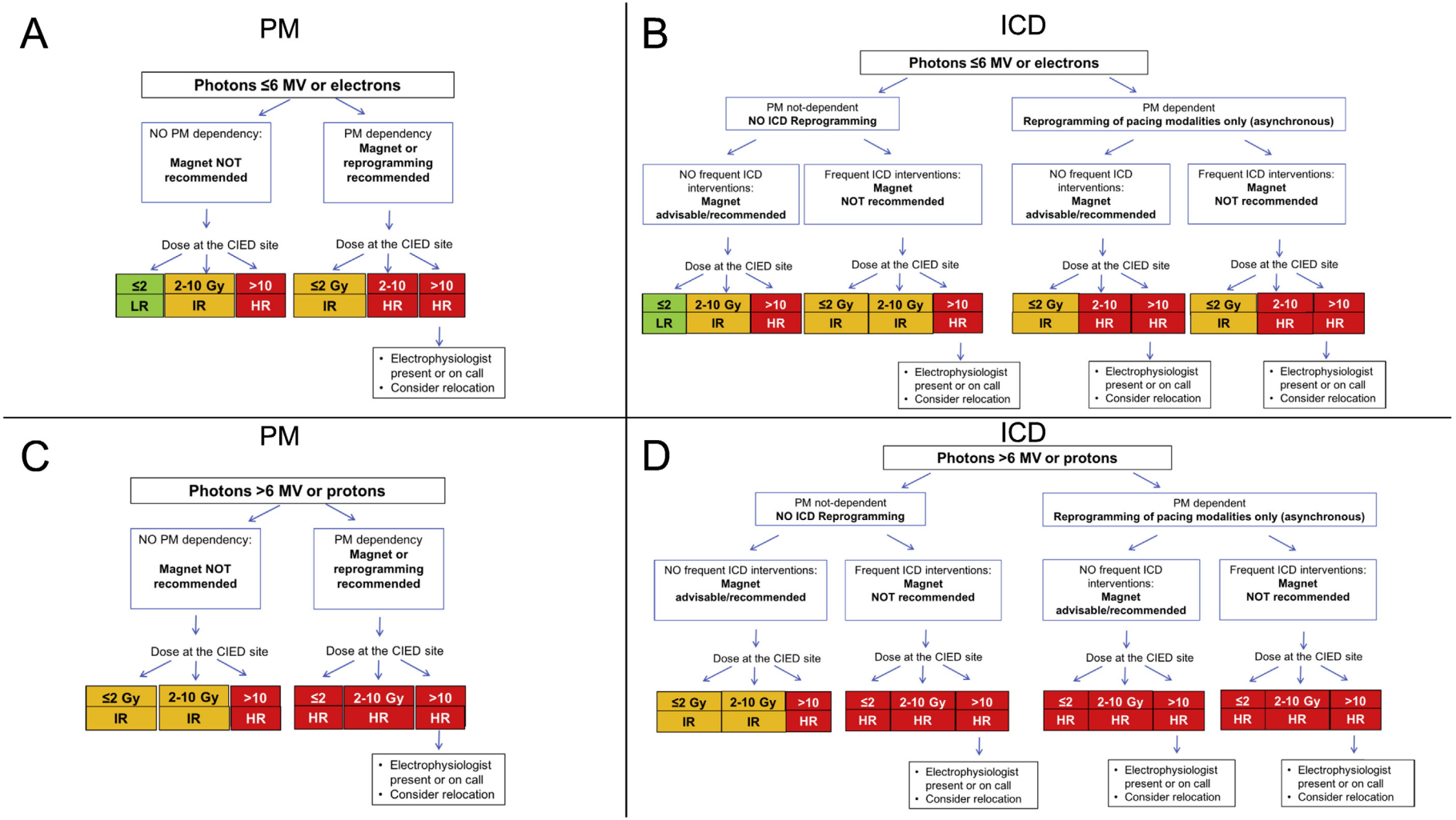

Fig. 2. Risk assessment and patient management. 2A: Low energy radiotherapy (PM); 2B: Low energy radiotherapy (ICD); 2C: High energy radiotherapy (PM); 2D: High energy radiotherapy (ICD); Low Risk (LR); Intermediate Risk (IR); High Risk (HR).

Table 2
Risk stratification.

	Low risk	Intermediate risk	High risk
Pacemaker	Electrons or photons ≤ 6 MV **and** • PM not-dependent • Dose at CIED ≤2 Gy	Electrons or Photons ≤6 MV **and** • PM not-dependent • Dose at CIED 2–10 Gy Protons or Photons >6 MV **and** • PM not-dependent • Dose at CIED ≤10 Gy	Dose at CIED >10 Gy Electrons or photons ≤6 MV **and** • PM dependent • Dose at CIED 2–10 Gy Protons or Photons >6 MV **and** • PM dependent
ICD	Electrons or photons ≤6 MV **and** • PM not-dependent • No frequent ICD interventions • Dose at CIED ≤2 Gy	Electrons or photons ≤6 MV **and** • PM not-dependent • No frequent ICD interventions • Dose at CIED 2–10 Gy Electrons or photons ≤6 MV **and** • PM not-dependent • Frequent ICD interventions • Dose at CIED ≤10 Gy Electrons or photons ≤6 MV **and** • PM dependent • Dose at CIED ≤2 Gy Protons or Photons >6 MV **and** • PM not-dependent • No frequent ICD interventions • Dose at CIED ≤10 Gy	Dose at CIED >10 Gy Electrons or photons ≤6 MV **and** • PM dependent • Dose at CIED >2 Gy Protons or photons >6 MV **and** • PM dependent *or* • Frequent ICD interventions

long enough (usually several seconds). Patients with frequent *appropriate ICD interventions* are more likely to suffer severe ventricular arrhythmias during RT session because of intrinsic arrhythmic risk (not dependent on CIED malfunctions). A definition of "frequent" appropriate ICD interventions cannot be provided and should be left to clinical judgement, but an interval of 6–12 months free from sustained ventricular arrhythmias can be considered appropriate.

A close relationship between Cardiologists involved in PM management (not all cardiologists have the necessary skills to perform PM/ICD evaluation) and Radiation Oncologists is highly recommended and all RT Centers should have a referral PM clinic.

When a patient with a CIED is scheduled for RT, *before starting the treatment* the cardiologist involved should:

- Assess the patient's clinical cardiological history, particularly regarding CIED indications, type and model
- Check the last ambulatory or remote evaluation available; if performed recently (within 3–6 months) a pre-RT re-evaluation is not mandatory.
- Assess (with the Radiation Oncologist) the risk category (according to both the risk of adverse cardiac events and the risk of malfunctions); in particular, evaluate whether (Fig. 1–2 and Table 2):
  - o the patient is PM-dependent
  - o the CIED is an ICD
  - o there is a recent history of frequent ICD appropriate interventions
- Assess the timing of evaluations (ambulatory or remote)
- Assess the status of battery charge
- Evaluate the need for the magnet during sessions
- Because of the risk of upper sensor rate, rate-response functions, whenever present, should be disabled before RT
- Provide any additional information required on the potential risks for the CIED during RT treatment
- If the CIED is localized within the treatment field, consider device relocation (even by just a few centimeters) before RT, mainly to avoid interference with adequate tumor treatment rather than CIED damage; contralateral relocation (involving new CIED implantation with new leads, with or without the old lead extraction) is rarely feasible and is associated with a high risk of procedural and late complications.
- Evaluate (with the Radiation Oncologist) departmental staff potentially involved in patient care (electrophysiologist, nurses, PM technicians, intensive care specialists or anesthesiologist).

3.3. Estimate of the dose to the device: simulation of treatment, treatment planning, CIED dose estimation and recording, use of shields and in vivo dosimetry

Before treatment, patients undergo CT imaging, necessary for the plan. No clinically-evident device malfunctions during CT imaging have been documented [20].

According to all published guidelines, CIEDs should not be included within the RT beam and the cumulated dose should either be estimated or measured during treatment. For a proper evaluation of the dose at the CIED site, a CT scan including the device is recommended when the distance between the device and the target is ≤10 cm and the CIED must be contoured for an appropriate dose estimation. In all other cases, it is not necessary to include the device in CT scan. For dose estimation details see the Supplementary material 1.

In vivo dosimetry is recommended if the dose estimated by the treatment planning system is close to 2 Gy or in the case of short (<3 cm) distance between the CIED and the field edge.

The Medical Physicist should evaluate for each patient the use of shielding (lead, bolus, etc.) that could reduce the dose only for a few selected cases. Dose reduction is higher for the higher energies, but it is also strongly affected by the type and geometry of treatment [21].

The dose due to setup imaging during patient treatment provides an extra dose that should be taken in account for the final accumulated dose estimation to the device.

The cumulated dose must be estimated and/or measured by the Medical Physicist, and reported and communicated to the Radiation Oncologist for classification in the proper risk category [4].

Despite the limited available studies, some practical advice could be proposed:

- A distance of at least 3 cm should be maintained between the device and the periphery of the beam, also when using "non-standard" geometry or non-coplanar beams instead of direct radiation [22].
- Photonic energy ≤6 MV is recommended to avoid the production of secondary neutrons. This value was chosen as the best LINAC energy cut-off for the risk stratification, considering that 7 MV is the threshold for neutron production [23] and 6, 10, 15, and 18 MV are the energy values available with current LINACs.
- With Intensity-Modulated RT (IMRT) and Volumetric-Modulated Arc Therapy (VMAT) there are lower doses near the edge of the treatment field but higher doses far from the treatment field. Modern IMRT/VMAT leads to low scatter radiation to normal tissue close to the tumor and should be the recommended choice for the treatment [24–26].
- Electron therapy is less dangerous due to a 5% neutron production per Gy compared with photon therapy at the same nominal energy [4,13]. Only from 20 MeV electrons upwards is the neutron flux comparable with a 10 MV photon beam [5].
- During proton therapy the incidence of PM malfunction seems to be higher than with photon RT [27,28].
- The leads are generally not sensitive to radiation [4].

For accurate dose evaluation and dose reduction strategy the additional presence of the Medical Physicist during the first session of treatment is recommended.

3.4. Informed consent

All patients undergoing RT should declare the presence or the absence of a CIED (this should be included within the informed consent for all RT).

All patients with CIED undergoing RT should be informed about the potential risks of malfunctions and know how to behave in the event of symptoms potentially due to CIED malfunctions.

4. During radiotherapy

4.1. Required staff and necessary skills

As a general rule, the personnel usually involved during RT sessions (1 radiation oncologist, 1 RT technician and 1 nurse) is sufficient.

At least one Radiation Oncologist and Medical Physicist with knowledge on the specific management of CIED patients undergoing RT should be available [4].

All the staff should receive elementary notions about PM and ICD functioning and specific training for the management of CIED patients.

The presence, during RT sessions, of an electrophysiologist (or a technician/nurse expert in CIED management) for urgent CIED interrogation and programming should be considered necessary only in very selected cases (see Fig. 2) and a "stand by" of the electrophysiologist (availability on call in a few minutes) may be considered. The need for an anesthesiologist depends in general on the patient's clinical status, regardless of the presence of a CIED.

During RT in CIED patients, the following equipment should be available

- A magnet (90–130 Gauss)
- ECG and non-electrocardiographic cardiac monitoring (pulse-oximeter for non-invasive identification of arterial pulse also in the presence of EMI or ECG lead dislodgment)
- Emergency kit (with external defibrillator possibly including pacing facilities)

4.2. Emergency protocol

A written emergency protocol, also approved by the referring PM Clinic, should be available in all RT Centers. All personnel should be able to identify critical CIED complications (asystole, ventricular fibrillation, cardiogenic shock) immediately, initiate basic life support (BLS-D) and alert the Emergency Team.

In the presence of not clinically relevant arrhythmias or minor malfunctions (even suspected) during RT, the PM clinic should be informed and the CIED checked after the session.

In the presence of clinically relevant events (sustained ventricular arrhythmias or arrhythmias with hemodynamic impairment, heart failure, chest pain, severe hypotension, appropriate or inappropriate ICD therapy, PM malfunctions in PM-dependent patients) the session should be immediately interrupted and the PM clinic immediately alerted.

4.2.1. Patient monitoring and use of the magnet

During the session, constant audiovisual monitoring of the patient should always be performed. In moderate and high risk patients, heart rate should be monitored by ECG and non-ECG systems (i.e. a pulse-oximeter).

Use of the magnet. Heavy magnets (90–130 Gauss) have different effects on PMs and ICDs.

- In PM patients, when a magnet is positioned on the CIED pocket, the PM sensing capabilities are disabled, so ventricular or both atrial-ventricular (in dual chamber and CRT PMs) pacing is guaranteed at a fixed rate in asynchronous mode, regardless of the presence of any cardiac or non-cardiac electrical signal. In patients with a PM and no spontaneous ventricular activity, this avoids the risk of oversensing due to EMI potentially leading to asystole.
- In ICD patients, when a magnet is positioned on the CIED pocket only the delivery of antitachycardia therapies is disabled, avoiding the risk of inappropriate shocks due to oversensing of EMI. However, PM functions are not usually modified and in ICD patients who are PM-dependent (typically those treated with AV node ablation) CIED reprogramming to asynchronous mode is necessary to ensure constant ventricular stimulation in the presence of EMI. Even in these patients the use of magnet should be preferred to manual deactivation of antitachycardia therapies [29]

In nearly all devices all previous PM and ICD functions are automatically enabled on removing the magnet from the CIED site.

As discussed earlier, however, the risk of oversensing, although theoretically present, is extremely low, so the use of the magnet can be considered prudential in selected cases but not mandatory in all ICD patients [30]. Indeed, standard use of the magnet is not recommended in the most recent guidelines [5]; in some patients, the risk of ventricular arrhythmias can be overwhelming so magnet positioning could be questionable.

In summary, personalized planning of the strategies to be used during RT is needed and the cardiologist has to clearly define the use of the magnet in every specific case.

4.3. Classification according to the risk class, device management during sessions and frequency of checks during the course of radiotherapy

The classification of the risk class is a multidisciplinary task, taking into account both the risk of malfunctions (depending on the RT characteristics and the target site) and the risk of clinical events in the case of malfunctions, depending on the patient's and device's characteristics (Fig. 1 and Fig. 2 and Table 2).

Although a high risk can be due to several conditions, patients with this type of profile are not common and the vast majority of patients belong to the low risk category.

The presence of an electrophysiologist is rarely necessary during RT sessions, with the exception of high risk patients with frequent ICD interventions and in PM-dependent patients with very high-risk RT protocols.

4.3.1. Frequency of checks

No data support the need for CIED evaluation after every single session, even in high risk patients, when all precautions during RT are taken. However, CIEDs should be periodically interrogated to rule out the presence of malfunctions or spontaneous arrhythmias during the RT course: once every week (in high risk patients) or only one evaluation during the RT course and another at the end of the course are probably sufficient in low and moderate risk patients.

If RM is available, more frequent interrogations can be programmed and performed manually or automatically; in most CIEDs, clinically relevant malfunctions and arrhythmias are automatically notified.

No clinical studies have been published on this specific issue and guidelines suggest different recommendations about the frequency of evaluations during RT. Considering the low risk of clinical events and the increasing role of remote monitoring, we arbitrarily suggest the following frequency of evaluations.

In-office only:

- After the first session
- At mid-course (low and intermediate risk patients) or every week (high risk patients)
- At the end of the course with testing of threshold levels, sensing and stimulation parameters, lead impedance, battery capacity
- Supplementary evaluations in the case of arrhythmias or malfunctions (detected or suspected)

In-office + Remote Monitoring (RM):

- After the first session (RM) and then depending on the CIED characteristics and RM facilities during the course
- At the end of the course with testing of threshold levels, sensing and stimulation parameters, lead impedance, battery capacity
- Supplementary evaluations (RM or in-office) in the case of arrhythmias or malfunctions (detected or suspected)

5. After radiotherapy

Some data suggest the risk of late malfunctions in CIED patients undergoing RT [1,4], but considering the low likelihood of events we arbitrarily recommend as follows:

- Perform a complete in-office evaluation just after the RT course
- Repeat in-office or remote evaluation after 1 month and after 6 months.

6. Management of new implantable devices (entirely subcutaneous ICDs and leadless pacemakers

See Supplementary material 1.

Conflict of interest disclosure

Giuseppe Boriani reported speaker's fees of small amount from Biotronik, Boston Scientific and Medtronic. Barbara Jereczek reported speaker fees from Zeiss, Filippo Alongi reported honoraria for speaker activities and consultancies from Varian (Palo Alto, California, US). The other authors report no relationships that could be construed as a conflict of interest".

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2017.12.061.

References

[1] W. Harms, W. Budach, J. Dunst, et al., DEGRO practical guidelines for radiotherapy of breast cancer VI: therapy of locoregional breast cancer recurrences, Strahlenther. Onkol. 192 (2016) 199–208.
[2] T. Soejima, E. Yoden, Y. NI, et al., Radiation therapy in patients with implanted cardiac pacemakers and implantable cardioverter defibrillators: a prospective survey in Japan, J. Radiat. Res. 52 (2011) 516–521.
[3] T. Zaremba, A.R. Jakobsen, M. Sogaard, et al., Risk of device malfunction in cancer patients with implantable cardiac device undergoing radiotherapy: a population-based cohort study, Pacing Clin. Electrophysiol. 38 (2015) 343–356.
[4] C.W. Hurkmans, J.L. Knegjens, B.S. Oei, et al., 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. 7 (2012) 198.
[5] J.H. Indik, J.R. Gimbel, H. Abe, et al., 2017 HRS expert consensus statement on magnetic resonance imaging and radiation exposure in patients with cardiovascular implantable electronic devices, Heart Rhythm. 14 (2017) e97–e153.
[6] G. Hindricks, J. Camm, B. Merkely, P. Raatikainen, D.O. Arnar, The EHRA White Book 2016 — The Current Status of Cardiac Electrophysiology in ESC Member Countries, 2016.
[7] J.R. Marbach, M.R. Sontag, J. Van Dyk, A.B. Wolbarst, Management of radiation oncology patients with implanted cardiac pacemakers: report of AAPM Task Group No. 34. American Association of Physicists in Medicine, Med. Phys. 21 (1994) 85–90.
[8] S. Sundar, R.P. Symonds, C. Deehan, Radiotherapy to patients with artificial cardiac pacemakers, Cancer Treat. Rev. 31 (2005) 474–486.
[9] T. Wadasadawala, A. Pandey, J.P. Agarwal, et al., Radiation therapy with implanted cardiac pacemaker devices: a clinical and dosimetric analysis of patients and proposed precautions, Clin Oncol (R Coll Radiol). 23 (2011) 79–85.
[10] F. Hudson, D. Coulshed, E. D'Souza, C. Baker, Effect of radiation therapy on the latest generation of pacemakers and implantable cardioverter defibrillators: a systematic review, J Med Imaging Radiat Oncol. 54 (2010) 53–61.
[11] F. Tondato, D.W. Ng, K. Srivathsan, G.T. Altemose, M.Y. Halyard, L.R. Scott, Radiotherapy-induced pacemaker and implantable cardioverter defibrillator malfunction, Expert Rev Med Devices. 6 (2009) 243–249.
[12] M. Langer, E. Orlandi, M. Carrara, P. Previtali, E.A. Haeusler, Management of patients with implantable cardioverter defibrillator needing radiation therapy for cancer, Br. J. Anaesth. 108 (2012) 881–882 (author reply 2).
[13] B. Gauter-Fleckenstein, C.W. Israel, M. Dorenkamp, et al., DEGRO/DGK guideline for radiotherapy in patients with cardiac implantable electronic devices, Strahlenther. Onkol. 191 (2015) 393–404.
[14] Iwgo Cardio-Oncology, Cardio-oncologia, 2015.
[15] M.E. Stone, B. Salter, A. Fischer, Perioperative management of patients with cardiac implantable electronic devices, Br. J. Anaesth. 107 (Suppl. 1) (2011) i16–26.
[16] N. Giaj-Levra, S. Sciascia, A. Fiorentino, et al., Radiotherapy in patients with connective tissue diseases, Lancet Oncol. 17 (2016) e109–17.
[17] J. Lelakowski, J. Majewski, J. Bednarek, B. Malecka, A. Zabek, Pacemaker dependency after pacemaker implantation, Cardiol J. 14 (2007) 83–86.
[18] T. Nagatomo, H. Abe, K. Kikuchi, Y. Nakashima, New onset of pacemaker dependency after permanent pacemaker implantation, Pacing Clin. Electrophysiol. 27 (2004) 475–479.
[19] S. Rosenheck, C. Bondy, A.T. Weiss, M.S. Gotsman, Comparison between patients with and without reliable ventricular escape rhythm in the presence of long standing complete atrioventricular block, Pacing Clin. Electrophysiol. 16 (1993) 272–276.
[20] A.A. Hussein, A. Abutaleb, J. Jeudy, et al., Safety of computed tomography in patients with cardiac rhythm management devices: assessment of the U.S. Food and Drug Administration advisory in clinical practice, J. Am. Coll. Cardiol. 63 (2014) 1769–1775.
[21] A. Bourgouin, N. Varfalvy, L. Archambault, Estimating and reducing dose received by cardiac devices for patients undergoing radiotherapy, J Appl Clin Med Phys. 16 (2015) 5317.
[22] A. Munshi, J.P. Agarwal, K.C. Pandey, Cancer patients with cardiac pacemakers needing radiation treatment: a systematic review, J. Cancer Res. Ther. 9 (2013) 193–198.
[23] T. Isobe, H. Kumada, K. Takada, et al., Effects of secondary neutron beam generated in radiotherapy on electronic medical devices, Progress in Nuclear Sci. Technol. 2 (2011) 524–529.
[24] E.E. Klein, B. Maserang, R. Wood, D. Mansur, Peripheral doses from pediatric IMRT, Med. Phys. 33 (2006) 2525–2531.

[25] S.F. Kry, B. Bednarz, R.M. Howell, et al., AAPM TG 158: measurement and calculation of doses outside the treated volume from external-beam radiation therapy, Med. Phys. 18 (2017) 715–716.
[26] M. Tajstra, E. Gadula-Gacek, P. Buchta, S. Blamek, M. Gasior, J. Kosiuk, Effect of therapeutic ionizing radiation on implantable electronic devices: systematic review and practical guidance, J. Cardiovasc. Electrophysiol. 27 (2016) 1247–1251.
[27] U. Schneider, R. Halg, The impact of neutrons in clinical proton therapy, Front. Oncol. 5 (2015) 235.
[28] T. Ueyama, T. Arimura, T. Ogino, et al., Pacemaker malfunction associated with proton beam therapy: a report of two cases and review of literature—does field-to-generator distance matter? Oxf Med Case Reports 8 (2016).
[29] R.G. Hauser, L. Kallinen, Deaths associated with implantable cardioverter defibrillator failure and deactivation reported in the United States Food and Drug Administration manufacturer and user facility device experience database, Heart Rhythm. 1 (2004) 399–405.
[30] M. Brambatti, R. Mathew, B. Strang, et al., Management of patients with implantable cardioverter-defibrillators and pacemakers who require radiation therapy, Heart Rhythm. 12 (2015) 2148–2154.
[31] M.H. Raitt, G.H. Bardy, Advances in implantable cardioverter-defibrillator therapy, Curr. Opin. Cardiol. 9 (1994) 23–29.
[32] A. Tsekos, F. Momm, M. Brunner, R. Guttenberger, The cardiac pacemaker patient — might the pacer be directly irradiated? Acta Oncol. 39 (2000) 881–883.
[33] J.R. Nibhanupudy, M.A. de Jesus, M. Fujita, A.L. Goldson, Radiation dose monitoring in a breast cancer patient with a pacemaker: a case report, J. Natl. Med. Assoc. 93 (2001) 278–281.
[34] S. Hoecht, P. Rosenthal, D. Sancar, S. Behrens, W. Hinkelbein, U. Hoeller, Implantable cardiac defibrillators may be damaged by radiation therapy, J. Clin. Oncol. 20 (2002) 2212–2213.
[35] S. Frantz, J. Wagner, H. Langenfeld, Radiation-induced pacemaker malfunction, Z. Kardiol. 92 (2003) 415–417.
[36] J. John, G.C. Kaye, Shock coil failure secondary to external irradiation in a patient with implantable cardioverter defibrillator, Pacing Clin. Electrophysiol. 27 (2004) 690–691.
[37] D. Thomas, R. Becker, H.A. Katus, W. Schoels, C.A. Karle, Radiation therapy-induced electrical reset of an implantable cardioverter defibrillator device located outside the irradiation field, J. Electrocardiol. 37 (2004) 73–74.
[38] F.L. Ampil, G. Caldito, Radiotherapy for palliation of lung cancer in patients with compromised hearts, J. Palliat. Med. 9 (2006) 241–242.
[39] D. Mitra, K. Ghosh, P. Gupta, J. Jayanti, A. Dev, P. Sur, Radiation dose monitoring in a lung cancer patient with a pacemaker — a case report, Chest 16 (2006) 875–877.
[40] S. Sepe, P. Schaffer, K. Krimmel, M. Schaffer, Irradiation treatment of laryngeal cancer in a patient with an implantable cardioverter-defibrillator (ICD), Onkologie 30 (2007) 378–380.
[41] J. Nemec, Runaway implantable defibrillator — a rare complication of radiation therapy, Pacing Clin. Electrophysiol. 30 (2007) 716–718.
[42] A. Munshi, T. Wadasadawala, P.K. Sharma, et al., Radiation therapy planning of a breast cancer patient with in situ pacemaker — challenges and lessons, Acta Oncol. 47 (2008) 255–260.
[43] S. Kapa, L. Fong, C.R. Blackwell, M.G. Herman, P.J. Schomberg, D.L. Hayes, Effects of scatter radiation on ICD and CRT function, Pacing Clin. Electrophysiol. 31 (2008) 727–732.
[44] Y. Oshiro, S. Sugahara, M. Noma, et al., Proton beam therapy interference with implanted cardiac pacemakers, Int. J. Radiat. Oncol. Biol. Phys. 72 (2008) 723–727.
[45] D.H. Lau, L. Wilson, M.K. Stiles, et al., Defibrillator reset by radiotherapy, Int. J. Cardiol. 130 (2008) e37–8.
[46] A. Zweng, R. Schuster, R. Hawlicek, H.S. Weber, Life-threatening pacemaker dysfunction associated with therapeutic radiation: a case report, Angiology 60 (2009) 509–512.
[47] D.Y. Gelblum, H. Amols, Implanted cardiac defibrillator care in radiation oncology patient population, Int. J. Radiat. Oncol. Biol. Phys. 73 (2009) 1525–1531.
[48] T. Zaremba, A.M. Thogersen, O. Eschen, S.P. Hjortshoj, A.R. Jakobsen, S. Riahi, High-dose radiotherapy exposure to cardiac pacemakers may be safe in selected patients, Radiother. Oncol. 95 (2010) 133–134.
[49] T. Ferrara, B. Baiotto, G. Malinverni, et al., Irradiation of pacemakers and cardiodefibrillators in patients submitted to radiotherapy: a clinical experience, Tumori 96 (2010) 76–83.
[50] T. Dasgupta, I.J. Barani, M. Roach III, Successful radiation treatment of anaplastic thyroid carcinoma metastatic to the right cardiac atrium and ventricle in a pacemaker-dependent patient, Radiat. Oncol. 6 (2011) 16.
[51] J. Menard, F. Campana, K.M. Kirov, et al., Radiotherapy for breast cancer and pacemaker, Cancer Radiother. 15 (2011) 197–201.
[52] R. Croshaw, Y. Kim, E. Lappinen, T. Julian, M. Trombetta, Avoiding mastectomy: accelerated partial breast irradiation for breast cancer patients with pacemakers or defibrillators, Ann. Surg. Oncol. 18 (2011) 3500–3505.
[53] Y.M. Kirova, J. Menard, C. Chargari, A. Mazal, K. Kirov, Case study thoracic radiotherapy in an elderly patient with pacemaker: the issue of pacing leads, Med. Dosim. 37 (2012) 192–194.
[54] M. Kesek, T. Nyholm, T. Asklund, Radiotherapy and pacemaker: 80 Gy to target close to the device may be feasible, Europace 14 (2012) 1595.
[55] A. Makkar, J. Prisciandaro, S. Agarwal, et al., Effect of radiation therapy on permanent pacemaker and implantable cardioverter-defibrillator function, Heart Rhythm. 9 (2012) 1964–1968.
[56] J. Elders, M. Kunze-Busch, R. Jan Smeenk, J.L. Smeets, High incidence of implantable cardioverter defibrillator malfunctions during radiation therapy: neutrons as a probable cause of soft errors, Europace 15 (2013) 60–65.
[57] M.R. Keshtgar, D.J. Eaton, C. Reynolds, et al., Pacemaker and radiotherapy in breast cancer: is targeted intraoperative radiotherapy the answer in this setting? Radiat. Oncol. 7 (2012) 128.
[58] D.R. Gomez, F. Poenisch, C.C. Pinnix, et al., Malfunctions of implantable cardiac devices in patients receiving proton beam therapy: incidence and predictors, Int. J. Radiat. Oncol. Biol. Phys. 87 (2013) 570–575.
[59] I. Dell'oca, D. Tsiachris, M. Oppizzi, P. Della Bella, S. Gulletta, Radiotherapy and implanted cardioverter defibrillators: novel techniques make it feasible, J Cardiovasc Med (Hagerstown). 34 (2007) 1193–1197.
[60] T. Zaremba, A.R. Jakobsen, A.M. Thogersen, S. Riahi, B. Kjaergaard, Effects of high-dose radiotherapy on implantable cardioverter defibrillators: an in vivo porcine study, Pacing Clin. Electrophysiol. 36 (2013) 1558–1563.
[61] F. Ampil, C. Nathan, G. Ghali, D. Kim, Postoperative radiotherapy for advanced head and neck cancer in patients with cardiac pacemakers, J. Radiother. Pract. 13 (2014) 115–118.
[62] M.S. Gossman, J.D. Wilkinson, A. Mallick, Treatment approach, delivery, and follow-up evaluation for cardiac rhythm disease management patients receiving radiation therapy: retrospective physician surveys including chart reviews at numerous centers, Med. Dosim. 39 (2014) 320–324.
[63] I. Ahmed, W. Zou, S.K. Jabbour, High dose radiotherapy to automated implantable cardioverter-defibrillator: a case report and review of the literature, Case Rep Oncol Med. 2014 (2014) 989857.
[64] J.D. Grant, G.L. Jensen, C. Tang, et al., Radiotherapy-induced malfunction in contemporary cardiovascular implantable electronic devices: clinical incidence and predictors, JAMA Oncol. 1 (2015) 624–632.
[65] R. Bagur, M. Chamula, E. Brouillard, et al., Radiotherapy-induced cardiac implantable electronic device dysfunction in patients with cancer, Am. J. Cardiol. 119 (2017) 284–289.