Patients with cardiac implantable electronic devices undergoing radiotherapy in Poland

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ABSTRACT

Older age and high morbidity of the society contribute to a growing number of patients with cardiac implantable electronic devices (CIEDs) requiring effective cancer treatment, including radiotherapy (RT). The effect of RT on a CIED may vary depending on the type and physical parameters of radiation, location of the treated lesion, indications for electrotherapy, and the type of CIED. In the most dramatic scenarios, it may cause an irreversible damage to the CIED, with serious clinical consequences. The lack of precise guidelines may limit the access to RT for many patients with CIEDs who would otherwise benefit from the therapy or may lead to a therapy without taking the necessary precautions, which may worsen the prognosis. Therefore, clear and unequivocal recommendations for assessing patient eligibility for RT are aimed at ensuring that adequate precautions are taken as well as at providing patients with concomitant cardiovascular and oncologic diseases with access to safe and effective RT.

Introduction With population aging, an increase in the number of patients with implanted cardiac implantable electronic devices (CIEDs) has been observed. Every year, about 700 000 first-time pacemaker (PM) implantations and over 200 000 implantations of implantable cardioverter-defibrillators (ICDs) or cardiac resynchronization therapy (CRT) systems are performed worldwide. Every year, more than 14 million new cancer cases are diagnosed. At least half of these patients have indications for radiotherapy (RT), and this percentage has been steadily increasing with the expansion of indications for the use of certain RT techniques, for example, stereotactic radiosurgery. Effective treatment of patients with cardiovascular diseases with the use of CIEDs as well
as effective oncologic treatment with the use of RT may improve the quality of life and prolong the life of patients. However, there are no precise data on the number of patients with CIEDs undergoing RT in Poland, but considering the above facts, this number should be expected to increase.

**Aim of the paper** Modern CIEDs are technologically advanced electronic systems, which may be adversely affected by external factors, including RT. As a result of insufficient knowledge about the potential effects of radiation on CIEDs, patients may be wrongly considered ineligible for RT (often the only possible way to cure cancer), or they may be wrongly referred for removal or relocation of an existing CIED before RT, or finally, they may be subjected to RT without necessary precautions. It should be emphasized that in light of the current knowledge and with an appropriate cooperation between a cardiologist and radiation oncologist, there are practically no situations in which RT would be contraindicated in a patient with a CIED. Moreover, in the vast majority of patients, RT can be administered without the need to relocate the device.

The aim of this paper was to present the recommendations for patient management before and during RT as well as postirradiation monitoring of patients requiring radiation. The paper is based on the 2017 recommendations of the Heart Rhythm Society, and the available literature, and our own experience. We proposed eligibility protocols including risk assessment and the basis of preparation, supervision, and monitoring in patients with CIEDs treated with RT. We focused on the effect of RT on cardiac electronic devices such as PMs, ICDs, CRTs with endovascular lead implantation.

**New technologies in cardiac electrotherapy** Despite the lack of data on the irradiation of implantable loop recorders, leadless PMs, cardiac contractility modulation systems, subcutaneous ICDs, and phrenic nerve stimulators, the indications described below refer also to these types of devices. In our opinion, patients with any of the above devices should be referred for RT as well as managed during and after the therapy on an individual basis in centers with a considerable experience in the care of patients with CIEDs undergoing RT.

**Novel radiotherapy techniques** A novel RT technique combines RT and magnetic resonance imaging (MRI) during irradiation. There are no data on the impact of this treatment on CIEDs. Intuitively, it seems reasonable to apply the same eligibility criteria and procedures as with standard MRI, with consideration of the risk group assessed on the basis of the same criteria as with standard RT techniques. However, such an approach should be confirmed by clinical trials.

**The ABC of radiotherapy for a cardiologist** Depending on the indications for the use of RT and its purpose, the planned radiation dose is usually administered in fractions of 1 to 10 over consecutive days. In intraoperative RT, the dose is administered once, as in the case of some indications for stereotactic techniques. The therapy is most often based on the use of photons, less frequently electrons, while specialized hadron therapy centers also use protons, neutrons, or so-called “heavy ions” (usually carbon nuclei). Regardless of the type of radiation, the greater the energy applied, the greater the tissue penetration. A potentially harmful effect of RT on CIEDs is caused by a direct action of the therapeutic beam, electromagnetic interference caused by the working accelerator, and scattered radiation. The higher the doses and energy of radiation, the higher the risk of contamination with secondary neutrons, which are considered a significant source of adverse RT effects on CIEDs.

The dose of radiation absorbed by tissues (including CIED) is expressed in grays (Gy), while the radiation energy is expressed in megaelectron volts (MeV). The energy of photon radiation is often expressed in megavolts (MV). In fact, this unit expresses the value of the accelerating voltage. In terms of numbers, it corresponds to the maximum energy of photons expressed in MeV, although it should be noted that most of the photons emitted from the accelerator using a given accelerating voltage have lower energy (the average energy of 6 MV photons is about 2 MeV, although the maximum energy can actually reach 6 MeV). The radiation energy and the dose per CIED are relatively easy to determine by a radiation therapist before RT, although the dose per generator can only be roughly estimated before the RT is actually completed. While the first national documents stated that the total absorbed dose per device (Gy) is a principal factor in assessing the risk of RT-related CIED damage, it is now believed that radiation energy has a higher predictive value, especially for values above 10 MV.

We recommend that both parameters, that is, radiation absorbed by tissues and radiation energy, together with clinical data and data obtained during a routing device checkup, should be used to evaluate the risk of RT-related damage to the CIED in patients potentially considered for RT. Possible device dysfunctions may include hardware damage (permanent) and software damage, which may have various consequences—from serious ones, requiring external intervention (reprogramming), through moderate (not requiring reprogramming), to mild ones,
detected only at the level of the manufacturer. Potential consequences of CIED exposure to radiation during RT are listed in Table 1. Not all CIED dysfunctions lead to clinical events. Type and incidence of those dysfunctions vary depending on the type, duration, and degree of CIED dysfunction as well as the patient’s clinical profile (eg, PM dependency or the type of sudden cardiac death prevention).

Intraoperative radiotherapy and brachytherapy Intraoperative RT is a complementary treatment applied during the surgical management of solid tumors. Radiation is introduced after the removal of the tumor with a margin. The procedure is performed with the use of an intraoperative RT device and based on precise focused and direct irradiation of the evacuated tumor bed in order to destroy the remaining cancer cells.

Brachytherapy, or contact RT, involves placement of the radiation source directly next to a target neoplastic lesion. Local application of the therapy results in minimal exposure of remote areas to radiation. The procedure before, during, and after the application of these RT techniques should be the same as during standard RT.

Manufacturers’ recommendations There is no agreement in the recommendations provided by leading manufacturers of CIEDs regarding management during RT. Companies such as Boston Scientific, Medtronic, St. Jude Medical (Abbott), and ELA-Sorin (LivaNova) recommend the transfer of the CIED generator outside the irradiated area under certain conditions. The guidelines for the maximum allowable radiation dose also vary between manufacturers: Medtronic suggests that the cumulative dose of 1 to 5 Gy should be considered safe (depending on the type of device), St. Jude Medical (Abbott) and ELA-Sorin (LivaNova) do not address the problem, while Boston Scientific and Biotronik conclude that there is no safe dose. It should be noted that as new types of devices become available, manufacturers update their own guidelines on management and safety in RT.

Available guidelines and consensus statements The first recommendations for the management of patients with PMs during RT were developed in 1994 by the American Association of Physicists in Medicine. They were based on the experience with the older generation of CIEDs. As new data continued to emerge over the years, new recommendations on the management of PMs and ICDs have been published. Initially, the cumulative exposure dose exceeding 2 Gy was associated with an increased risk of RT-related CIED dysfunction. In subsequent reports, it was increased to a value higher than 5 Gy. With the development of CIEDs and technological advances in RT devices, both in vitro and in vivo studies have shown a stronger relationship of CIED damage with beam energy (MeV) and secondary neutron production than with the cumulative dose (Gy). In the most recent reports, CIED dysfunctions during RT were relatively rare: slightly more than 2% for PMs and 8.5% for ICDs, two-thirds of which were partial, reversible restorations of default settings or resets of the random-access memory. In the available literature, there is no firm evidence (except for single case reports) that would suggest a significant negative effect of RT on the electrodes in CIED systems. Therefore, we do not provide separate recommendations on management depending on the presence and type of implanted electrodes as well as the presence of redundant or inactive leads.

The analysis of the data that were the basis for these recommendations indicates that the risk of damage (or adverse events resulting from malfunction) is associated with radiation characteristics (energy and dose), patient status, and indications for device implantation (type of CIED, PM dependency). Therefore, in our opinion, these parameters are crucial for proper risk stratification before RT. By combining the risk of both the device malfunction and potential adverse clinical events, it is possible to classify patients as low, moderate, or high risk.

The present document is based on the recommendations published so far, with consideration of the most recent available literature. It is also based on our own experience, in cooperation with the Department of Radiotherapy at Maria Skłodowska-Curie Institute — Oncology Center in Gliwice, Poland, as the presented eligibility criteria and management principles were used during and after RT in our own clinical practice. These recommendations will have to be updated in the future, in line with evolving techniques and new reports.

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<tr>
<th>TABLE 1</th>
<th>Potential effects of exposure of implantable cardiac electronic devices to radiation</th>
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<tbody>
<tr>
<td>Sensory disturbances (over- and undersensitivity)</td>
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<td>Stimulation disturbances (programmed impulse amplitude, change of stimulation threshold, frequency)</td>
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<tr>
<td>Loss of stimulation</td>
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<tr>
<td>Change in stimulation mode (including asynchronous stimulation)</td>
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<tr>
<td>Reduced battery life</td>
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<td>Arrhythmia detection disorders</td>
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<td>Antiarrhythmic therapy disorders</td>
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<tr>
<td>Loss of telemetry</td>
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<td>Device reset or switch to emergency mode operation</td>
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**Patient preparation for radiotherapy** A preliminary consultation to determine eligibility for RT includes the assessment of therapy-related risk. The following information has to be provided by a radiation therapist or oncologist:

1. type of planned therapy (radical or palliative);
2. irradiated organ and distance of the beams from the CIED (if possible, avoid direct generator irradiation);
3. type of radiation with information on potential production of secondary neutrons, predicted total dose per CIED (Gy), beam energy (MV), and number of fractions;
4. scheduled date of RT.

Before RT, patients should undergo standard clinical evaluation with medical history assessment, the documentation of the planned treatment should be reviewed, and the device should undergo a preliminary checkup. All these procedures should preferably be performed by a physician with experience in the management of patients with CIEDs. The form should include information on device parameters: sensitivity of each channel, amplitude of spontaneous P and R waveforms, impedance, minimum programmable rhythm frequency, maximum conduction frequency, sensor settings, stimulation mode, battery status, as well as information on indications for device implantation and whether the patient has PM dependency, was subjected to an adequate ICD intervention in the previous 6 months, and was included in a telemonitoring program.

Patients with PM dependency constitute the potential highest-risk group associated with CIED dysfunction. Pacemaker dependency is defined as a situation involving the absence of any spontaneous ventricular activity or a heart rate of less than 30 bpm (or the lowest heart rate programmable in the device) or when spontaneous rhythm causes hemodynamic symptoms. The incidence of PM dependency ranges from 2.1% to 24%.\textsuperscript{22-24} Periodic PM dependency should be considered, as it is estimated that more than 10% of patients without PM dependency during the first device checkup may show PM dependency during subsequent checkups and vice versa.\textsuperscript{24} This may have serious consequences even in the case of a temporary loss of stimulation. Therefore, the same protection should be provided for patients with paroxysmal dependence on stimulation as for those with permanent dependence. On the other hand, a high percentage of stimulation (even 100%) is not equivalent to PM dependency. A resting electrocardiogram (ECG) should also be recorded and included in the documentation available for review during RT.

The suggested form for device control and for data necessary to assign patients to specific groups based on RT-related risk is shown in Supplementary material, Figure S1. Suggested checklists to use before, during, and after RT are presented in Table 2.

**Cardiac implantable electronic device relocation** If the radiation dose delivered to the device exceeds 10 Gy or if the generator is within the radiation beam range, some guidelines recommend CIED relocation.\textsuperscript{5,4} However, the risk of serious complications associated with CIED reimplantation or electrode revision may reach 4% and 15.3%, respectively.\textsuperscript{15,16} The clinical consequences, especially for cancer patients with immune and hematologic disorders associated with the oncologic disease and treatment, may be much more serious, particularly in those undergoing or scheduled for chemotherapy. According to the current expert consensus,\textsuperscript{3} CIED relocation is recommended—after consideration of the patient’s prognosis, the degree of CIED dependency, and predicted tolerance of the procedure—if the generator is within the radiation beam. The experts recommend CIED relocation in patients scheduled for radical RT, while in palliative patients, especially those with multiple comorbidities, individual decision making is recommended depending on the patient’s preference, clinical situation, cancer progression, prognosis, presence of frailty syndrome, and potential CIED damage. The decision on relocation can be delayed until the CIED is indeed damaged during RT (bailout procedure). Importantly, there are different descriptions of the term “relocation” in the literature. The relocation involves several technical options, including: repositioning of the generator on the same side, leaving the system inactive on the side of the planned RT and implanting a new system on the opposite side, removing the system that may potentially interfere with the RT and implanting a new system on the opposite side, or—if clinically feasible—implanting a new system after RT completion. If the patient is scheduled for relocation, technical decisions regarding the procedure should be made on a case-by-case basis.

Our experience shows that the availability of various treatment and tumor irradiation methods makes it possible in most cases to perform RT in a way that keeps the generator outside the beam range. The maximum registered radiation dose to the device located in the immediate vicinity of the target area did not exceed 9 Gy and resulted from scattered radiation. In individual cases, the assessment of the risk-to-benefit ratio for the use of a radiation beam in the immediate vicinity of a CIED is needed.

**Risk assessment and care during radiotherapy** By analyzing the parameters of planned RT as well as information obtained during the device checkup, it is possible to determine the individual risk level of RT for each patient. The classification of RT risk groups and recommendations
TABLE 2  Recommended checklists before, during, and after radiotherapy

<table>
<thead>
<tr>
<th>Preparation of a patient with a CIED for RT</th>
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<tr>
<td>Identification of the device (manufacturer, model) and verification of the manufacturer’s recommendations</td>
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<tr>
<td>Obtaining the patient’s written consent (by a radiation therapist)</td>
</tr>
<tr>
<td>Device control: standard tests, evaluation of stimulation dependency, occurrence of VT/VF episodes, battery status, printout of parameters</td>
</tr>
<tr>
<td>RT risk assessment (RT location, planned RT dose)</td>
</tr>
<tr>
<td>Informing the patient about the risks and possible consequences of RT in the aspect of CIED</td>
</tr>
<tr>
<td>Educating the patient on the behavior and possible side effects during RT (reporting problems)</td>
</tr>
<tr>
<td>Assessment of the need to relocate or remove the CIED</td>
</tr>
<tr>
<td>Ensuring that the device is outside of the RT beam range</td>
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<tr>
<td>Not exceeding the total estimated dose of RT</td>
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<th>Management during RT</th>
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<tr>
<td>Recommended radiation energy &lt;10 MV</td>
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<tr>
<td>Considering the change of parameters—asynchronous mode (AOO, VOO, DOO) in stimulation-dependent patients</td>
</tr>
<tr>
<td>Disabling ICD therapy</td>
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<tr>
<td>Evaluation of the RT dose during the first sessions</td>
</tr>
<tr>
<td>Maintaining contact with the programmer</td>
</tr>
<tr>
<td>Patient supervision, audiovisual contact, ECG, BP, SpO₂ monitoring in high-risk patients, readiness for resuscitation</td>
</tr>
<tr>
<td>Access to external defibrillator with external stimulation option</td>
</tr>
<tr>
<td>Control and appropriate modification of the program in accordance with the agreed schedule (after each RT session or once a week during the course of RT)</td>
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<th>RT follow-up</th>
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<tr>
<td>CIED control after RT completion (standard tests, battery status assessment), programming of optimal parameters (asynchronous mode deactivation, activation of ICD detection and therapy)</td>
</tr>
<tr>
<td>Considering device replacement in case of damage</td>
</tr>
<tr>
<td>CIED checkups at 1, 3, and 6 months after RT completion (including remote monitoring checkups)</td>
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<tr>
<td>Educating the patient about possible symptoms that may result from CIED malfunction (sounds, vibrations)</td>
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Abbreviations: BP, blood pressure; CIED, cardiac implantable electronic device; ECG, electrocardiogram; ICD, implantable cardioverter-defibrillator; RT, radiotherapy; SpO₂, oxygen saturation; VF, ventricular fibrillation; VT, ventricular tachycardia

for management, monitoring, and frequency of follow-up visits for each patient group are presented in FIGURE 1.

In doubtful cases, it is recommended to assign a patient to a higher-risk group. In patients with multiple comorbidities, it is reasonable to apply an individualized approach.

During irradiation, it is necessary to maintain continuous audiovisual contact with the patient and to monitor ECG, pulse oximetry, and capillary pulse wave recordings. During RT, in moderate- and high-risk patients, it is necessary to provide access to an external defibrillator, and in the case of patients dependent on stimulation, also to external stimulation options.

During RT, it is recommended to temporarily switch off ventricular tachycardia/ventricular fibrillation detection and therapy in patients with ICDs or CRT defibrillators (CRT-Ds). This should be done using a magnet placed directly over the CIED generator. Cardiologist supervision of each RT fraction is preferable in these patients. However, due to the limited possibilities of providing cardiovigilance, we consider it safe to have the ICD and the therapy deactivated (by placing a magnet over the generator as described above) by trained radiation technicians. In this case, the ICD/CRT-D check-up should be conducted on a weekly basis during the RT. In patients with a cumulative dose per device of more than 5 Gy or a radiation beam energy greater than 10 MV, it is recommended that each RT fraction be supervised by a cardiologist (a higher risk of CIED dysfunction).

Radiotherapy follow-up  Every patient undergoing RT should be scheduled for a device check-up visit within 1 month after the end of therapy, and then after 3 and 6 months, to detect potential late CIED dysfunctions. If the follow-up checkup
vice checkups should preferably be performed RT, complications can be divided into device re-

EXPERT OPINION AND POSITION PAPER Patients with CIEDs undergoing RT

FIGURE 1 A recommended approach to supervision, monitoring, and follow-up visits of patients with cardiac implantable electronic devices undergoing radiotherapy depending on their assignment to a specific risk group

Abbreviations: BLS, basic life support; CRT-P, cardiac resynchronization therapy pacemaker; PM, pacemaker; others, see TABLE 2

is not possible in a center where the patient received RT, the patient should be referred to a cardiological center that provides CIED checkups.

Transport of patients with cardiac implantable electronic device during and after radiotherapy Device checkups should preferably be performed at the center providing RT. However, if this is not possible, the checkup during RT should be provided by a cardiology center with appropriate facilities. If there is no suspicion of CIED dysfunction, the patient may be transported for consultation without additional precautions: ambulatory patients may use their own transport, while hospitalized patients may be transported without physician’s assistance. If CIED dysfunction is suspected (fainting, ECG abnormalities, arrhythmia, ICD discharge), a resuscitation protocol should be immediately implemented, if indicated, and only then specialized patient transport (a medical transport team with a physician) to the appropriate center may be considered.

Management of radiotherapy-related complications In patients with CIEDs undergoing RT, complications can be divided into device-related and non-device related.

In the case of serious ventricular arrhythmias, sudden cardiac arrest, or pulmonary edema (events not related to the presence of a CIED), the management should follow the current guidelines for resuscitation.27 In the case of CIED-related complications such as loss of effective stimulation or inadequate discharge, in addition to implementing a cardiopulmonary resuscitation algorithm, the management should include actions to restore effective CIED operation or to stop inadequate discharges. Asynchronous stimulation in PMs and the temporary switch-off of high energy detection and therapy in patients with ICDs/CRT-Ds can be achieved by placing a magnet over the CIED generator. For ICDs/CRT-Ds provided by Boston Scientific and St. Jude Medical, the response to the magnet can be programmed, and, in addition to the possibility of standard therapy inactivation, it may include ignoring the magnet. Therefore, in the case of these specific ICDs and CRT-Ds, it is necessary to verify the reaction to the magnet application during every device checkup. Except for ICD/CRT-D by Sorin (ELA Medical), the application of the magnet affects only antiarrhythmic therapies, but not the stimulation mode. In the case of the devices by Sorin, asynchronous stimulation may be activated.28 Malfunction of CIEDs during the course of RT mostly often manifests as “soft” errors...
associated with the software or the zeroing of the CIED and the activation of the emergency mode. These errors can be removed with a programmer. Permanent damage, which cannot be removed by device reprogramming, may require replacement of the damaged generator with a new one. In the case of any disturbances in the operation of the device during RT, it is recommended to stop the RT and have the CIED immediately checked by a cardiologist specializing in cardiac device monitoring and programming, as well as to consult the technical support of the manufacturer to decide on the next steps. The optimal solution is the remote monitoring of patients, which allows an early detection of potential CIED dysfunctions after RT. Patients should be educated about the symptoms related to CIED malfunction as well as the alarming signals sent by the implanted device (sounds, vibrations).

**Summary** The increasing number of patients requiring RT due to cancer necessitates the development of recommendations that would systematize knowledge on this topic as well as facilitate safe management of these patients. In light of the current knowledge, it is unacceptable that patients with CIEDs have no or limited access to RT. Consensus-based and unified management can help create a national registry of patients with CIEDs undergoing RT as well as a registry of RT-related device dysfunctions. Reporting of adverse events and their careful analysis can become a valuable source of knowledge and conclusions that may translate into clinical practice. As new data emerge, along with novel CIED technologies and RT methods, regular updates to recommendations will be necessary.

**SUPPLEMENTARY MATERIAL**

Supplementary material and the Polish version of the paper are available at www.mp.pl/kardioziapolska.

**ARTICLE INFORMATION**

**CONFLICT OF INTEREST** None declared.

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