TOPICS IN REVIEW

# What do national radiotherapy guidelines for patients with cardiac devices teach us?

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The incidence of cardiac implantable electronic device (CIED) malfunctions caused by radiotherapy (RT) is approximately 5%. Although individual national guidelines and expert consensus documents exist, the increased use of RT to treat various cancers points out the need for a standardized document to guide risk assessment and management of CIEDs during RT. We describe potential adverse RT-related events on CIEDs as well as the proposed mechanism of dysfunction. We review the main current guidelines and recommendations, emphasizing similarities and differences.

**KEYWORDS** Radiotherapy; CIED malfunction; National guidelines; Recommendations; Device monitoring

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## Cardiac implantable electronic device malfunctions associated with radiotherapy

Radiotherapy (RT) is frequently used for the treatment of cancer and can be administered before or after surgery or as an alternative to surgery, or for palliative purposes. Radiation induces cell death directly via DNA strand damage and indirectly through the development of reactive oxygen species. RT is generally delivered in multiple treatments called fractions, spaced according to radiation repair differences between cancer and normal tissues. Normal tissues heal faster than cancer, and thus the use of fractionation can decrease side effects from RT.[1]

RT can be classified as either brachytherapy (internal radiation) or external beam radiation. The latter typically requires the use of a linear accelerator to direct either electrons or photons to the neoplasm. While electrons have low penetration and are used for superficial tumors, photons are preferred for deeper tissues. The development of proton therapy has provided another method to reduce the radiation dose to certain critical structures in select patients. Through simulation with radiotherapy, computed tomography, proton emission tomography, or magnetic resonance imaging, the radiation oncologist establishes the volume of tissue to be treated, the dose to be delivered (measured in Gy), and the number of fractions prior to the delivery of RT.

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Radiation has the potential to damage not only surrounding healthy tissue, but also cardiac implantable electronic device (CIEDs), including permanent pacemakers (PMs) and implantable cardioverter-defibrillators (ICDs).[2] While the radiation dose absorbed by a CIED has often been considered a major factor in device malfunction, it has become increasingly clear that beam energy plays a more substantial role. Beam energy >10 MV leads to neutron contamination, which is especially damaging to devices.[3] To provide a better understanding of the 10-MV threshold, most of the deeply located tumors such as gastrointestinal and prostate tumors receive more than 10 MV. There are 3 main underlying mechanisms for RT-induced CIED dysfunction.[4] The most frequent is the formation of electron-hole pairs, which is a proton (positive charge) that is not paired with an electron (negative charge) typically from high-energy beams producing either neutrons or protons. These excess electron-hole pairs positively charge the oxide component of the CIED.[5] Both the silicon semiconductor and the silicon oxide insulation are susceptible to this ionizing damage. The second mechanism is the creation of aberrant electrical circuits within the CIED.[4] Finally, radiation beams induce CIED dysfunction by influencing a change in the applied voltage of the CIED.[4] Moreover, ICDs are more sensitive to radiation damage than PMs, as they have a random-access memory component with higher amounts of boron and lithium.[6] Additionally, older, bipolar transistors are more resistant than their newer complementary metal oxide semiconductor counterparts.[3]

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## KEY FINDINGS

- As numerous national guidelines exist for preventing radiotherapy-related cardiac implantable electronic device dysfunction, a simplified, ready-to-use version is necessary.
- There are 3 major factors determining the risk of cardiac implantable electronic device–related radiotherapy complications: (1) pace dependency, (2) presence of ventricular tachycardia/ventricular fibrillation, and (3) radiation type.
- Based on the risk stratification, patients will need a checkup only after the first radiotherapy round, after half of them or after each one with a 1-, 3-, and 6-month follow-up.

Device malfunction related to x-ray RT can be classified as either hard or soft errors.[7] Soft errors refer to damage to device software, whereas hard errors are more significant and cause device hardware malfunction. While device malfunction from x-ray RT is rare, soft errors occur more frequently than hard errors. The various soft errors include reverting to backup factory settings, temporarily increased pacing or sensing rates, and/or temporary oversensing. By contrast, hard errors include complete device failure and early battery depletion, which require device replacement.[8,10,17]

Currently, the guidelines are concerned with the generator's malfunction. The leads play a minor role. A prior study showed that there was a nonsignificant change in the lead's parameters when exposed to radiation therapy.[11] As pacemakers advance toward a leadless model, a study comparing effects of RT on leadless PM versus classic PM might unveil rare lead-related complications.

## Current management recommendations for CIEDs exposed to RT

Guidelines and recommendations for CIED management during x-ray RT have evolved over time. In 1994, the American Association of Physicists in Medicine published the first management guide, followed by an update in 2019.[12,13] The next consensus was developed by the Dutch Society of Radiotherapy and Oncology in 2012.[6] The German DEGRO/DGK consensus integrated recommendations from the Dutch document along with new findings into a national guideline in 2015.[3] Following this publication, Heart Rhythm Society (HRS) wrote its first consensus for physicians in the United States in 2017.[14] Most recently, the European Society of Cardiology (ESC) cardio-oncology guidelines provided additional recommendations for RT in the setting of a CIED. The European Heart Rhythm Association provided in 2022 an internationally accepted guideline as well.[7]

## Comparison between current guidelines

### Absorbed dose

From 1994 to 2023, there was an increase in what was considered a safe absorbed dose of radiation to the CIED from 2 to 5 Gy, based primarily on data from in vitro studies.[8] Data from a recent meta-analysis of the in vitro research of particle beam therapy identified 3 key studies as guiding this shift.[15] It is now believed that distance, rather than dose, has a greater impact on CIED function.[7]

### Beam energy

There is variability regarding what is considered a safe beam energy. Most of the consensus documents use a threshold of 10 MV.[2,4,6,8] In contrast, the German document from 2015 takes a more conservative approach, providing a range of 6 to 10 MV.[3]

### Novel approaches to radiation delivery

The use of flattening filter-free (FFF) beams may be more efficient than traditional radiation delivery methods, as they reduce the treatment time and have increased power.[9] The downside is that it increases the risk of CIED damage at lower energy thresholds. One experiment demonstrated that 75% of the devices exposed to 6-MV FFF and 100% of those exposed to 10-MV FFF had pacing inhibition.[9] The pacing inhibition occurred simultaneously with irradiation and ceased once the irradiation stopped.

The German consensus proves that sometimes developing novel approaches is a better solution to using already established ones.[3] One such example is introducing 3-dimensional conformal radiation fields and stereotactic treatments for patients who need thoracic RT and are at high risk for CIED dysfunction.[3] To prevent the risks, the German consensus adds to the treatment strategy plan the option of measuring the radiation applied above the CIED via thermoluminescent dosimetry or optically stimulated dosimetry during the first fraction.[3] Of note, brachytherapy does not seem to have any impact on CIEDs and is considered a safe treatment option for patients with implantable devices.[3]

### Specific considerations

Device relocation is generally not necessary in patients receiving RT. The ESC guidelines discourage relocation in patients at high risk for complications receiving palliative RT (Table 1).[2] Relocation should be pursued only if the CIED impedes efficient delivery of radiation to the tumor. Leadless devices might make thoracic RT delivery more difficult, depending on the tumor location, potentially increasing the need for device relocation in this specific patient population.

There are also various recommendations regarding CIED reprogramming before radiation. The concept of temporarily deactivating the sensor of a rate-adaptive PPM during the radiation session is for the first time recommended in the ESC guidelines. Although many of the consensus statements

**Table 1** Device and radiotherapy checklist

| | | | |
|---|---|---|---|
| **Device checklist preradiotherapy** | | | |
| Implant date: | | | |
| Implant indication: | | Pacemaker dependency: | Yes___ No___ |
| Manufacturer and model: | | | |
| Device settings: | Pacemaker/CRT-P ___<br>Pacing mode:<br>Min pacing rate:<br>Max tracking rate:<br>Max sensing rate: | ICD/CRT-D ___ | |
| Recent pertinent recorded events: | | Ventricular arrhythmias ___<br>ATP ___<br>Shocks ___ | |
| Is the device stable: | Yes___ No___ | | |
| Pending device-related concerns prior to starting radiotherapy: | | | |
| **Radiotherapy planning checklist** | | | |
| Will device location interfere with adequate tumor treatment? | | | Yes___ No___ |
| What type of radiation is planned? | | | |
| | Electron ___ | Photon ___ | Proton ___ |
| | Neutron-producing: | Yes___ No___ | |
| What is the max expected cumulative incident dose? | | | ____ Gy |
| **Follow-up plan** | | | |
| Frequency of device checks during radiotherapy: ___ | | | |
| Frequency of device checks after radiotherapy: ___ | | | |

ATP = antitachycardia pacing; CRT-D = cardiac resynchronization therapy defibrillator; CRT-P = cardiac resynchronization therapy pacemaker; ICD = implantable cardioverter defibrillator.

suggest the inactivation of antitachycardia therapies for ICD patients,[3-6,8,12,16-18] the ESC guidelines indicate that it is infrequently done in the clinical practice because arrhythmia induction and/or oversensing rarely occur.[13] As such, device reprogramming prior to radiation therapy may not be an essential recommendation.

It is also important to note that there is a paucity of data regarding RT and its effects on leadless pacemakers and subcutaneous ICD systems. The Japanese guidelines highlight the need for studies focusing on this new type of devices.[2] As such, the same recommendations are applied to these novel devices as to traditional transvenous systems.

## Device monitoring after RT

The European Heart Rhythm Association consensus document recommends remote monitoring for any device expected to receive $\geq$2 Gy of absorbed dose.[2] Nevertheless, there remains an inconsistency regarding the frequency of device monitoring before, during, and after radiation. The Japanese, European, HRS, and Australian consensus recommend a check at 1 to 6 months after RT.[2,5,8,16,19] However, the Italian and German consensus prefers a check at 1, 3, and 6 months to ensure the CIED's functioning.[3,4,19] It remains to be seen whether the frequency of the checks can be adjusted to the risk the patient has to develop CIED malfunctions, if a clear risk stratification were to become available. In light of the aforementioned recommendations, a research question arises: 'Would it be preferable to adjust the frequency of checks based on the risk class that the patient has?'.

## Harmonized recommendations for practitioners

Given the multitude of recommendations for the safe delivery of x-ray RT to patients with CIED, our goal was to create a simplistic and harmonized guide for practitioners, regardless of specialty or practice location.

Prior to RT, an assessment of the device and the radiation type should be made, quantifying the potential risk of radiation to the device (Table 1). It is important to know detailed information about the CIED: implantation date, device manufacturer, indication, pacing mode, minimum pacing rate, maximum tracking rate, maximum sensor rate, sensing, impedance and threshold measurements, pacing burden, and prior history of ventricular tachyarrhythmias. It is also essential to assess the type of radiation (ie, electrons, photons, or protons), the beam energy, and the total dose of radiation, with an estimation of the device's absorbed dose.

All treatment centers should have an emergency crash cart, the ability for audiovisual monitoring, and personnel familiar with CIEDs available, should device malfunction occur. For certain higher-risk patients, continuous electrocardiogram and oxygen monitoring can be considered; however, in most circumstances this is not necessary.

**Table 2** Device risk assessment recommendations

| Anticipated device absorbed dose | | | |
|---|---|---|---|
| | <2 Gy | 2–10 Gy | >10 Gy |
| Pace dependency | | | |
| No | Low risk | Medium risk | Elevated risk |
| Yes | Medium risk | Elevated risk | Elevated risk |
| ICDs | | | |
| No history of VT/VF | Low risk | Medium risk | Elevated risk |
| History of VT/VF | Medium risk | Elevated risk | Elevated risk |
| Risk of secondary neutron production | | | |
| Radiation type | Low risk | — | Elevated risk |
| Electrons | <20 MeV | — | >20 MeV |
| Photons | <10 MV | — | >10 MV |
| Protons | — | — | Elevated risk |

ICD = implantable cardioverter defibrillator; VF = ventricular fibrillation; VT = ventricular tachycardia.

Most of the guidelines[2,3,5,6,16-19] use a 3-tier risk assessment (low, medium, and elevated risk) based primarily on absorbed dose, pacer dependency, and history of ventricular arrhythmias as well as based on radiation type and risk of neutron production (Table 2).

During and after RT, the patient should have multiple device checks (Figure 1). Low-risk patients should have their CIED interrogated before the first and after the last RT fraction. Medium-risk patients would undergo CIED interrogations in the beginning, midway through the radiotherapeutic protocol, and at the end. High-risk patients require weekly interrogation or after each session. All checks can be done remotely.[7] When the sensing and pacing parameters or the thresholds are changed, reprogramming may be required. In the case of altered battery capacity or safe-mode resets, replacement of the device may also be needed. Checks are run at 1, 3, and 6 months following the completion of the radiotherapeutic regimen.

## Conclusion

Guidelines develop over time as new technologies appear on the market or as new research on the topic becomes available. However, many practitioners might not have the time or the mental resources to go through detailed guidelines. Therefore, documents simplifying to the essential best practices such as this one are invaluable for clinicians. Last, contrasting various national guidelines when there is no international one is useful, to uncover future directions to be explored by cardiology societies and by research facilities.

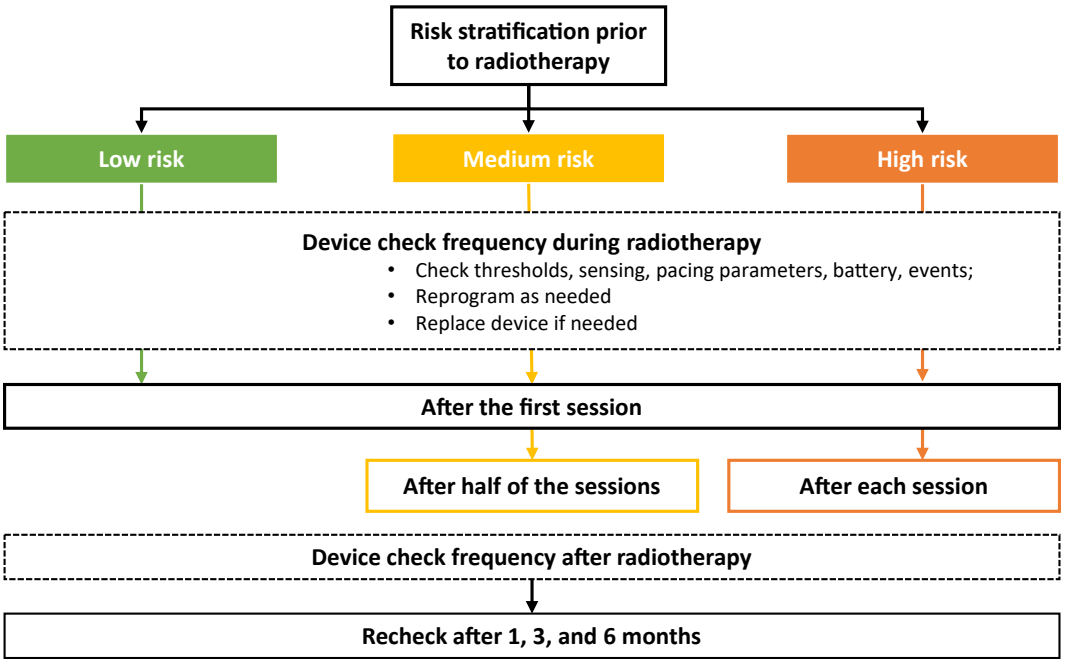


**Figure 1** Device monitoring recommendations during and after radiotherapy.

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