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JASTRO/JCS Guidelines for radiotherapy in patients with cardiac implantable electronic devices

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ABSTRACT

This publication is an English version of the Japanese Society for Radiation Oncology (JASTRO) and The Japanese Circulation Society official guidelines for patients with cardiac implantable electronic devices (CIEDs). Several radiotherapy-associated malfunctions have been reported for CIEDs such as pacemakers and implantable cardioverter-defibrillators. Accordingly, guidelines for radiotherapy in patients with CIEDs have been issued by other countries and societies. In August 2010, JASTRO published the 'Radiotherapy Guidelines for Patients with Pacemakers and Implantable Defibrillators' (hereafter referred to as the former guidelines). Given new findings in this decade, a multidisciplinary working group of radiation oncologists, medical physicists, radiation therapists and cardiologists jointly reviewed and revised the former guidelines.

Keywords: guidelines; cardiac implantable electronic devices; radiotherapy; malfunctions

INTRODUCTION

Diseases, indications and epidemiology [1]

A pacemaker (PM) is indicated for bradyarrhythmia such as heart block, sick sinus syndrome, atrial fibrillation and hypertrophic cardiomyopathy. The symptoms range from asymptomatic to repeating syncope. In 2017, about 60 000 cases received implants annually, including replacement, and the number of cases is increasing. An implantable cardioverter-defibrillator (ICD) is the most effective method for preventing sudden cardiac death due to ventricular fibrillation or ventricular tachycardia, and is indicated for patients at high risk. The annual number of cases of device exchange in 2017 was ∼6700, and is increasing. In addition, cardiac resynchronization therapy (CRT) for biventricular pacing was established as a treatment for intraventricular conduction disorder, and ICD with biventricular pacing (CRT-D) was also developed to prevent sudden cardiac death due to ventricular fibrillation. These kinds of implantable devices for treating circulation diseases are comprehensively called cardiac implantable electronic devices (CIEDs).

Components of CIEDs [2, 3]

A CIED basically comprises two parts: the main body and the lead. The main body contains a control circuit of semiconductor elements and a battery covered with a titanium case. The lead transmits the electrical

Table 1. Comparison of risk classification

	Low risk	Medium risk	High risk
These guidelines: • When using an FFF beam, consider raising the risk by one step according to the patient's condition. • For brachytherapy, manage as a photon beam and risk classification is based on other requirements.	Meet all the following conditions: Photon <10 MV or electron <20 MeV PM Not PM-dependent No irradiation of the chest • Devise dose <2 Gy • No history of ventricular tachycardia	Other than low and high risk	A patient with any of the following is classified at high risk. Photon ≥10 MV Electron ≥20 MeV Proton beam Carbon-ion beam PM-dependent CIED dose >10 Gy History of ventricular fibrillation History of ICD intervention
AIAC/AIRO/AIFM [3]	PM Photons or electrons ≤6 MV, dose to CIED ≤2 Gy, and not PM-dependent ICD Photons or electrons ≤6 MV, not PM-dependent, no frequent ICD interventions, and dose to CIED ≤2 Gy	Other than low and high risk	Dose to CIED >10 Gy Electrons or photons ≤6 MV, but PM-dependent, and dose to CIED 2–10 Gy Protons or photons > 6 MV, PM-dependent, and dose to CIED >10 Gy Electrons or photons ≤6 MV, but PM-dependent, and dose to CIED >2 Gy Protons or photons >6 MV and PM-dependent or frequent ICD interventions.
Salerno *et al.* [7]	Pacing-independent patient and dose to CIED <2 Gy	Pacing-independent patient and dose to CIED 2–10 Gy Pacing-dependent patient and dose to CIED < 2 Gy	Pacing-independent patient and dose to CIED >10 Gy Pacing-dependent patient and dose to CIED >2 Gy
DEGRO/DGK [4]	Non-pacemaker-dependent ICD without VT/VFib CIED dose <2 Gy Pacemaker-dependent ICD with VT/VFib before/after implantation	CIED dose 2–10 Gy CIED dose < 2 Gy	CIED dose >10 Gy CIED dose >2 Gy
NVRO [2]	Pacing-independent patient and CIED dose <2 Gy	Other than low and high risk	CIED dose >10 Gy
Guidelines without risk classification			
HRS [8]	Production of secondary neutrons is the strongest predictor of CIED malfunction in contemporary devices. Non–neutron-producing treatment is preferred over neutron-producing treatment in patients with a CIED to minimize the risk of device reset. Evidence is lacking to define an appropriate frequency of CIED evaluation for a case with a CIED dose 5 Gy.		

AIAC = The Italian Associations of Arrhythmologists, AIRO = The Italian Associations of Radiation Oncologists, AIFM = The Italian Associations of Medical Physicists, DEGRO = the German Society for Radiation Oncology, DGK = the German Society for Cardiology, NVRO = The Dutch Society of Radiotherapy and Oncology; HRS = the Heart Rhythm Society, VFib = ventricular fibrillation, VT = ventricular tachycardia.

Table 2. Comparison of preparation steps for radiotherapy by risk classification[a]

	Low risk	Medium risk	High risk
These guidelines	• Obtain informed consent. • Consult with cardiologists. • Check CIED identification book. • Classify the risk. • Discuss with a cardiologist with regard to response in a case of abnormal operation during radiotherapy. • Radiotherapy staff should fully understand abnormalities of the operation. • Simulation CT performed with the same procedure as diagnostic CT. • No direct beam to CIED • Recommend < 10 MV photon beam and < 20 MeV electron beams. • Evaluate total dose to CIED. • Discuss with a cardiologist whether asynchronous pacing should be used if pacing suppression occurs during irradiation.	In addition to low risk actions: • If there is an ICD function, discuss with a cardiologist whether to stop ICD function during irradiation. • Discuss with a cardiologist whether to perform function checks every week.	In addition to medium-risk actions: • Consider relocating CIED for appropriate cancer treatment. Be aware that there is a guideline that suggests CIED relocation is not recommended for a CIED dose < 5 Gy. • Discuss with a cardiologist whether to check function after every radiotherapy session. • For a PM-dependent patient, discuss with a cardiologist whether to prepare temporary out-of-body pacing during irradiation.
AIAC/AIRO/AIFM [3]	Consider situation Use of magnet Device reprogramming Device relocation Presence of electrophysiologist/nurse/technician Presence of anesthesiologist		
Salerno *et al.* [7]	Information regarding CIED Determine pacing-dependency of patient If ICD, determine if anti-tachycardia therapy can be switched off by magnet Estimate dose to CIED		
DEGRO/DGK [4]	1. Identification of CIED-bearing patient, labeling in patient's chart, specification of CIED (manufacturer, model). 2. 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 treating cardiologist. 3. Documentation of RT-associated risks in consent form, including risk of radiation-induced CIED failure und potential device replacement surgery. 4. If CIED is located in beam: consult with treating cardiologist; discussion of relocation is advised. 5. Presentation to cardiologist: indication for CIED, examination and documentation of all programmed parameters, pacemaker-dependency (VVI, 30/min), documented episodes of VT/VFib in RAM, percentage of mandatory cardiac stimulation, battery capacity. 6. RT planning: acquisition of CIED in planning CT if feasible, limitation of energy to 6 MV (10 MV) when photons are used, computation/recording of cumulative radiation dose to CIED, no direct placement of CIED in beam. 7. Classification into risk category (low, intermediate, high).		

(Continued)

Table 2. Continue

	Low risk	Medium risk	High risk
	Emergency protocol • Cooperation between radiation oncology and cardiology • Personnel qualified for specific procedures for CIED patients	Examination of CIED before and after every RT session PM in asynchronous modes (VOO, AOO, DOO) • Continuous ECG and SpO2 monitoring • External defibrillator and external pacemaker available, ECG, NIBP, SpO2, programming device • Personnel trained to recognize and treat asystole or ventricular fibrillation according to BLS guidelines	Surgical relocation or replanning of RT with the goal of reducing CIED dose If reduction of CIED dose is impossible then consider RT on individual basis • Cardiologist or anesthesiologist present • CIED examination immediately after RT session Transportation of ICD patient with deactivated ATA therapy under surveillance to the cardiology outpatient clinic should remain an exception
NVRO [2]	• Inform treating cardiologist and inform patient • Determine pacing-dependency of the patient • If ICD, determine if anti-tachycardia therapy can be switched off by magnet • If CIED check-up > 3 months ago, plan check-up prior to start of radiotherapy • Photon beam energy < 10 MV • Estimate dose to CIED (seed drawing for indication) • Minimize dose to CIED with treatment plan optimization • If CIED dose > 10 MV (high risk), reconsider radiotherapy or CIED relocation.		
Guidelines without risk classification			
HRS [8]	• Prior to initiation of radiotherapy, a complete CIED evaluation should be performed and the treatment team should be informed of: (a) whether the device is a PM or ICD, (b) whether the patient is pacing-dependent, (c) the minimum programmed pacing rate, and (d) the maximum programmed tracking and sensor rates. • Non–neutron-producing treatment is preferred over neutron-producing treatment in patients with a CIED to minimize the risk of device reset. • CIED relocation is recommended if the current location will interfere with adequate tumor treatment; however, this is not recommended for a case with a CIED dose < 5 Gy.		

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Table 3. Comparison of measures before, during and immediately after irradiation by risk classification[a]

	Low risk	Medium risk	High risk
These guidelines	• Establish an emergency support system that can immediately manage events, including unexpected changes in CIED settings. • At the time of using MV X-rays for verification photographs and linac graphy, be careful not to expose the CIED to the irradiation field. • IGRT by MV X-ray CBCT is not recommended if the CIED body is in the image range. • For IGRT with fluoroscopy or kV X-ray CBCT using kV X-ray, the same management should be used as that for diagnosis of patients with CIEDs in the facility. • When pacing suppression occurs during irradiation, discuss with a cardiologist in advance whether to use asynchronous pacing. • Observe the patient's condition with an in-room video camera and microphone during each entire radiotherapy session. • Examine subjective abnormalities and pulse after each session. • When CIED settings are changed before irradiation, return to the required settings immediately after irradiation.	In addition to low-risk actions: • Monitor the circulation by an electrocardiogram or pulse oximeter for pulse abnormalities during the first radiotherapy session, and if necessary, continue monitoring for subsequent sessions. • When a CIED has a function as a cardioverter-defibrillator, discuss with a cardiologist in advance whether to terminate this function during irradiation. (Then, prepare for an external cardioverter-defibrillator including an AED.)	In addition to medium-risk actions: • In high-risk patients, monitor the circulation by an electrocardiogram or pulse oximeter for pulse abnormalities during each session. • For a PM-dependent patient, discuss with a cardiologist in advance whether to prepare for temporary external pacing during irradiation.
AIAC/AIRO/AIFM [3] Salerno *et al.* [7]	Audiovisual monitoring • Audiovisual monitoring of patient • For an ICD: suspend tachycardia therapy or use a magnet	ECG/pulse oximeter + audiovisual monitoring. In addition to low risk actions: • Crashcart present during RT • Possibility of external pacing • Trained staff with cardiology expertise can be present within 10 min (if not, patients should be referred to another institute)	ECG/pulse oximeter + audiovisual monitoring. In addition to medium-risk actions: • Consider RT or CIED relocation • In an exceptional case a decision to start RT can be made • Safety measures that are at least those used for medium-risk patients • ECD-monitoring during every fraction • CIED checked within 24 h by pacemaker technician

(Continued)

Table 3. Continue

	Low risk	Medium risk	High risk
DEGRO/DGK [4]	1. Evaluation of radiation dose to CIED during first fraction and comparison with calculated CIED dose. 2. Pacemaker-dependent patients: consider asynchronous stimulation (VOO, DOO, AOO); either through reprogramming or magnet placement (only possible with a pacemaker, two adhesive stripes necessary!). 3. ICDs: Deactivation of ATA therapy throughout each RT session; either through reprogramming or magnet placement (pacemaker stimulation is not affected, two adhesive stripes necessary!). 4. Continuous audiovisual contact. Continuous ECG and SpO2 monitoring in patients with suspended ATA therapy and high-risk patients. Personnel should be able to recognize ventricular fibrillation or asystole and to act accordingly (to initiate BLS until arrival of emergency team). 5. Availability of cardiologist and programming device. 6. Emergency protocol: immediate notification/activation of a reanimation team, high-risk patients need continuous presence of cardiologist, anesthesiologist, emergency physician. 7. CIED examination after every RT session, including reprogramming and reactivation of initial settings or anti-tachycardia therapy. • Emergency protocol • Cooperation between radiation oncology and cardiology • Personnel qualified for specific • procedures for CIED patients	• Examination of CIED before and after every RT session. • PM in asynchronous modes (VOO, AOO, DOO) • Continuous ECG and SpO2 monitoring • External defibrillator and external pacemaker available, ECG, NIBP, SpO2, programming device • Personnel trained to recognize and treat asystole or ventricular fibrillation according to BLS guidelines	• Surgical relocation or replanning of RT with the goal of reducing CIED dose • If reduction of CIED dose is impossible then consider RT on individual basis • Cardiologist or anesthesiologist present • CIED examination immediately after RT session • Transportation of an ICD patient with deactivated ATA therapy under surveillance to cardiology outpatient clinic should remain an exception
NVRO [2]	Audiovisual monitoring of patient For an ICD: program tachycardia therapy off or use a magnet Letter to cardiologist ICDs: weekly check-ups	In addition to low-risk actions: Prepare crash cart Weekly check-up of CIED Possibility of external pacing Trained staff with cardiology expertise can be present within 10 min (if not, patients should be referred to another institute)	In addition to medium-risk actions: In exceptional cases a decision to start RT can be made. Safety measures that are at least those used for medium-risk patients ECG-monitoring during every fraction CIED checked within 24 h by pacemaker technician
Guidelines without risk classification			
HRS [8]	• Continuous visual and voice contact is recommended during each treatment fraction.		

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Table 4. Comparison of timing of functional checks[a]

	Low risk	Medium risk	High risk
These guidelines May use a higher risk classification.	• After the first radiotherapy session. • Discuss with a cardiologist whether to check function after 1–6 months.	• In addition to the low-risk actions: • Check function after about half of the planned radiotherapy is complete. In treatment preparation, discuss with a cardiologist whether to check function every week.	• In addition to the medium-risk actions: Check function every week. In treatment preparation, discuss with a cardiologist whether to check function every time radiotherapy is performed.
AIAC/AIRO/AIFM [3]	• In office/remote evaluation after 1 session • At half course • At the end of RT course • After 1 month • After 6 months	• In office/remote evaluation after 1 session • At half course • At the end of RT course • After 1 month • After 6 months	• In office/remote evaluation after 1 session • Weekly • At the end of RT course • After 1 month • After 6 months
Salerno *et al.* [7]	• ICDs: weekly check-up • After 1 month • After 3 months • After 6 months	• Weekly check-up of CIED • After 1 month • After 3 months • After 6 months	• Every RT session • After 1 month • After 3 months • After 6 months
DEGRO/DGK [4]	1. Final examination (threshold levels, sensing and stimulation parameters, lead impedance, battery capacity), reprogramming of CIED. 2. Asynchronous stimulation for no longer than necessary (competitive stimulation against intrinsic heart rhythm may cause malignant ventricular arrhythmias; R-on-T phenomenon). 3. Analysis of CIED irregularities in connection with RT and forwarding of data to manufacturer; note that clinically insignificant changes in parameter settings may precede CIED defects. 4. Exchange of CIEDs with significant defects even if the malfunction is temporary and full device recovery is observed. 5. Repeat examinations 1, 3 and 6 months after RT; telemetric surveillance if available. 6. Education of patient with regard to clinical symptoms of CIED failure (irregular or slow cardiac rhythm, dizziness, syncope), emergency sounds emitted by CIED.		
NVRO [2]	• Extra CIED check after last RT fraction by pacemaker technologist (at 1, 3 and 6 months)	Examination of CIED before and after every RT session.	CIED examination immediately after RT session.
Guidelines without risk classification			
HRS [8]	• A complete CIED evaluation should be performed at the conclusion of the course of radiotherapy. • Perform weekly complete CIED evaluations for patients undergoing neutron-producing treatment. • It might be reasonable to perform a complete CIED evaluation weekly for patients who are pacing-dependent and are undergoing non-neutron-producing treatment.		
Zaremba *et al.* [17]	• Electrons or kV-photon: device evaluations unnecessary • PM (including CRT-P) and photons < 10 MV: device evaluations before RT and after completed RT • PM (including CRT-P) and photons < 10 MV or ICD (including CRT-D) and photons < 10 MV: device evaluations before RT, weekly during the RT course, and after completed RT. • ICD (including CRT-D) and photons < 10 MV: device evaluation before RT and after every RT fraction.		

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Table 5. Comparison of recommendations of major manufacturers and sales providers issued in August 2018. Please check with the respective manufacturer for the latest information.

		Boston Scientific	St. Jude Medical	Medtronic	Biotronik	Japan Lifeline
Before RT session	Consultation	Prior to a course of radiotherapy, radiation oncologists should consult with the cardiologist or electrophysiologist to develop strategies specific for each patient.			Establish a consultation system between the radiation oncologist and cardiologist.	
Before treatment	Radiation treatment planning	Recommended maximum total dose of 2 Gy to the implanted device. Consider using all available shielding options.	Do not use ionizing radiation in the vicinity of an implanted device.	PM <5 Gy, ICD <1–5 Gy Depends on the model.	<10 MV CIED <2 Gy No direct beam to CIED	No direct beam to PM PM < 5 Gy.
	Device relocation	If the beam cannot be moved from the implanted device	If radiotherapy is required in the vicinity of an implanted device. The following recommendations will help in patient management:			Device relocation is recommended if the irradiated field is close to the implant area.
Before RT session	Changing setting	ICDs and CRT-Ds: If inhibition of pacing occurs, a programmer can be used to initiate temporary asynchronous pacing. Deactivate tachytherapy. Pacemakers and CRT-Ds: A magnet can be placed over the device to pace asynchronously at the magnet rate. The device can be programmed to an asynchronous pacing mode.	ICD: Deactivate tachyarrhythmia detection and response functions. Rate-adaptive devices: The sensor can be programmed to PASSIVE or OFF before administering radiotherapy. If inhibition or other forms of oversensing occur during the initial procedures, the clinician may consider programming the device to an asynchronous pacing mode or using a magnet to inhibit sensing during subsequent treatment.	Switch the mode appropriately. ICD: Deactivate tachyarrhythmia (VT/VFib) detection and response functions.	Stop ICD function for ICD/CRT-D during radiotherapy session.	

(Continued)

Table 5. Continue

		Boston Scientific	St. Jude Medical	Medtronic	Biotronik	Japan Lifeline
During RT session	Monitoring	Determined by the physician team, including the cardiologist or electrophysiologist.	ECG monitoring. During the initial therapy sessions, the clinician can determine if there is an interaction between the device and the radiation equipment. The clinician can decide if subsequent ECG monitoring is necessary during each therapy session. It is recommended to monitor and record the cumulative radiation dose to which a device has been exposed.		Monitor pulse continuously by a pulse oximeter or electrocardiogram. Prepare for an external cardioverter- defibrillator Assign medical staff and medical engineer who are familiar with the programming of CIEDs.	ECG monitoring. Prepare for external pacing.
After irradiation		If any programming changes were made, the device should be reprogrammed back to the desired settings after the procedure. Evaluation of device function following radiation treatment is recommended. The extent, timing and frequency of this evaluation should be determined by the cardiologist.	Pacemaker-dependent patient should undergo a detailed evaluation of the pacing system once or twice during the course of treatment.		Check CIED.	
After RT session		Physicians should continue to monitor device function closely and use caution when programming a feature following radiotherapy because the effects of radiation exposure on the implanted device may remain undetected until sometime after exposure.	It may be necessary to evaluate device. Examination of pacing sensing function, and analysis of device diagnostics. For ICD patients induction testing should also be considered to evaluate high-voltage functions of the device.		Since malfunction may appear later, evaluate device function again after a radiotherapy session (after the next day) or follow-up with home monitoring.	

signal of the heart to the main body and sends electrical stimulation from the main body to the heart.

CIED malfunction caused by ionizing radiation exposure

Malfunctions

There are two kinds of malfunctions: errors in software and in hardware. Software errors include a reset that is changed to a backup setting, oversensing that occurs temporarily only during irradiation, and inappropriate ICD operation. Hardware errors cause permanent damage and require replacement.

Cause of CIED malfunction

Direct irradiation of the semiconductor with low-energy X-rays may cause abnormal operation such as oversensing due to a photoelectric effect. With high-energy X-rays ($\geq$10 MV), secondary neutrons generated can cause a nuclear reaction in the semiconductor material, mainly with boron, even outside the irradiation field, and then heavy ions that are emitted from a nuclear reaction by boron-neutron capture can ionize inside the material. This may cause abnormal operation by a single event inducing a software error. Electromagnetic noise such as electromagnetic interference may also cause this problem.

The main cause of CIED malfunction in relation to high-energy X-ray radiotherapy is charged particles produced as a result of a neutron capture reaction between secondary neutrons and nuclei within the semiconductor circuit. These reactions may occur when high-energy X-rays of $\geq$10 MV or particles beams (proton and carbon ion) are used. Particular care is needed in such cases because the abnormal operation may occur stochastically, even at low doses. In principle, X-rays of $\leq$ 6 MV and gamma rays from a radioactive seed for brachytherapy are not a concern for photonuclear reactions producing secondary neutrons. Nevertheless, malfunctions due to unexpected current by electromagnetic induction or a photoelectric effect may occur.

Reported cases of serious complication caused by CIED malfunction

Malfunction of CIEDs can cause arrhythmias that manifest as palpitations, dizziness and loss of consciousness [4]. Rarely these events can be life-threatening, as in the following two cases.

The patient in the first case had polymorphic ventricular tachycardia triggered by inappropriate rapid ventricular pacing. Recovery eventually occurred after a course of cardiopulmonary resuscitation, including intubation and intravenous epinephrine [5]. In this case, the ICD was implanted in the left infraclavicular region, and was outside the direct irradiation beam. During the third session of radiotherapy the cumulative prescription dose was <5.4 Gy out of a total dose of 59.4 Gy/33 fractions. This case could not be classified into one of the risk categories described below because the radiation energy was not mentioned in the report.

The patient in the second case had fast inappropriate atrial pacing ('runaway pacing') due to an error in PM software [6]. The patient fell into cardiac shock and had to be transferred to an intensive care unit. PM-induced tachycardia could not be stopped without disconnecting the lead because the device did not accept configuration changes from outside the body. In this case, the estimated irradiation dose was 0.11 Gy, but the radiation energy was not mentioned. The authors concluded that the malfunction may have been induced by electromagnetic interference during radiotherapy. This case also could not be classified into a risk classification because no description of the beam energy was given in the report.

Both patients recovered after the CIED malfunction-induced cardiac event.

Tolerance dose for CIEDs

The tolerance dose for a CIED to prevent malfunction has not been clearly determined. Until August 2018, each manufacturer specified device dose limits of <1–5 Gy (Table 5), However, the dose limit varies depending on the manufacturer, model and presence or absence of ICD functions. Many manufacturers do not assume direct irradiation to the main body. In practical use, medical staff need to check the latest information from each manufacturer.

REVISION METHOD

JASTRO and the Japanese Circulation Society (JCS) formed a subcommittee to revise the former guidelines using literature that matched certain criteria. The subcommittee was organized with recruitment and recommendations by the two societies, which are both engaged in radiotherapy for patients with CIEDs. The revision started in June 2018. In the guidelines, there are no clinical questions and no determination of evidence level in individual documents because each event is relatively rare.

Two radiation oncologists and a medical physicist on the subcommittee were in charge of the document search in the systematic review. Searches of PubMed using '*radiotherapy* AND *pacemaker*' and '*radiotherapy* AND *ICD*' for 10 years until June 2018 identified 102 and 114 papers, respectively. Based on the title and abstract, the primary documents were retrieved, and a secondary selection was carried out by discussion. Other documents that were considered to be eligible studies were also added to the references with the consent of the subcommittee.

An original draft was jointly evaluated by the guidelines committees of both societies. From May to June 2019, public comments were invited through the JASTRO and JCS websites. The final draft was prepared based on the opinions of the joint evaluation and public comments, and was finally approved and issued by both societies.

These guidelines are limited to management of patients with CIEDs who receive radiotherapy. Treatment with implanted electrical devices other than a CIED, such as deep brain stimulation therapy for Parkinson's disease and vagal nerve stimulation therapy for intractable epilepsy, are excluded in the guideline framework because there are an insufficient number of reports.

Also, these guidelines are intended for medical professionals engaged in radiotherapy and/or management of CIEDs in Japan, including doctors, nurses, radiation therapists and medical physicists.

MANAGEMENT OF CIED, PATIENT AND RADIOTHERAPY

General remarks

These guidelines use three levels of risk classification: low, medium and high, which are the most common levels used in guidelines of other academic societies [2–4, 7]. Depending on the circumstances surrounding the patient such as medical resources and emergency medical care system, patients can be applied and managed in higher risk classification. If a potentially life-threatening event cannot be managed by a particular facility, the case should be referred to an appropriate institution.

Risk classification

Low risk

A case that meets all the following conditions is classified as low risk.

- X-Ray energy <10 MV or electron energy <20 MeV
- Not PM-dependent
- No irradiation to the chest
- The main body of CIED dose estimated to be <2 Gy
- No history of ventricular tachycardia

Medium risk

A case that is not in the low or high risk classification.

High risk

A case that meets any of the following conditions is classified as high risk.

- X-Ray energy ≥10 MV
- Electron beam energy ≥20 MeV
- Proton beam
- Carbon-ion beam
- PM-dependent
- The main body of CIED dose estimated to be >10 Gy
- A history of ventricular fibrillation
- A history of ICD intervention

When using flattening filter-free (FFF) beams, consider raising the risk classification by one level depending on the patient's condition. With use of a radioactive seed, the risk classification is based on X-rays <10 MV. Neutron capture therapy is contraindicated for patients with a CIED. Table 1 summarizes comparison of risk classification for each guidelines.

Rationale of classification

X-Rays ≥10 MV are classified as high risk because they generate secondary neutrons which can result in clinical abnormalities [8–10]. Electron beams ≥20 MeV are also considered to be high risk due to similar generation of secondary neutrons equivalent to X-rays ≥10 MV. Proton beams also generate secondary neutrons, and CIED malfunction during proton beam therapy has been reported [11]; therefore, proton beams are also high risk. Fewer secondary neutrons are generated by carbon-ion beams compared to protons, but carbon ions are still considered to be high risk [12].

X-Rays <10 MV or electron beams <20 MeV are low risk because this radiation does not generate secondary neutrons. Clinical malfunction in these conditions is extremely rare and very few cases have been reported; however, malfunction is still possible. Therefore, the risk is classified as low only when other criteria are satisfied. No malfunctions are likely in cases with no chest irradiation and no PM dependence, and so these are included as criteria for a low-risk assignment [13].

FFF beams may induce malfunction depending on the dose rate *in vitro* [14]. High dose-rate X-rays may induce overcurrent on the circuit, which creates a high potential risk to CIEDs even if the radiation does not generate secondary neutrons. There is no report of abnormal operation in clinical practice due to FFF beams, but it is possible that a high dose-rate could induce enough photoelectronic current to cause a malfunction. Therefore, an FFF beam is considered to be high risk and needs further investigation.

Radioactive seeds such as ^{192}Ir and ^{125}I for brachytherapy do not generate secondary neutrons and no malfunction in their use *in vivo* has been reported. Thus, assuming that brachytherapy corresponds to use of X-rays <10 MV, the risk classification depends on other criteria [8, 15].

Other documents are based on the former guidelines, the guidelines of overseas academic societies, and materials prepared with the agreement of the committee members.

Preparation before radiotherapy

1. Obtain informed consent, including providing information to the patient on possible CIED malfunction due to radiotherapy. The patient should be informed about the consultation with a cardiologist.
2. Consult with a cardiologist to examine arrhythmia (including history of ventricular fibrillation) and CIED dependence (including history of ICD intervention) before treatment.
3. Check the CIED identification book for the manufacturer's contact information, model and settings, and copy this information into the medical record.
4. Classify the risk by modality of radiotherapy, energy, treatment site, type of CIED, pathogenesis of cardiovascular system and dependence on CIED.
5. Discuss with a cardiologist the management of the patient in a case of abnormal operation during radiotherapy.
6. Collect information from the manufacturer on backup settings at the time of a malfunction, such as a reset, etc. Abnormal operation can be detected when the pulse rate in the pulse monitor changes to the backup setting value.
7. Radiotherapy staff (radiation oncologists, medical radiation therapists, medical physicists, nurses, etc.) should fully understand the dependence on CIED, settings, and response in case of CIED malfunction requiring immediate medical attention.
8. Prepare a support system for an emergency.
9. Perform simulation CT using the same procedure as that used for diagnostic CT for CIED patients in the facility.
10. In radiation treatment planning, pay special attention not to irradiate the main body of the CIED directly. It is not enough to shield with multileaf collimators and monoblocks; do not expose the CIED body to the irradiation field surrounded by the linear accelerator aperture or jaw. The total amount of dose of the main body of the CIED should be as small as possible.
11. Recommend use of <10 MV X-rays and <20 MeV electron beams.
12. Evaluate the total dose to the CIED and describe this in the medical record prior to irradiation. However, be aware that even a small dose does not ensure safety.
13. Discuss with a cardiologist whether asynchronous pacing should be used if pacing suppression occurs during irradiation.
14. In a PM-dependent patient, discuss with a cardiologist whether to prepare temporary external pacing during irradiation.

15. If there is an ICD function, discuss with a cardiologist whether to stop this function during irradiation.
16. For medium-risk patients, discuss with a cardiologist whether to perform function checks every week.
17. For high-risk patients, discuss with a cardiologist whether to check function after every radiotherapy session.
18. For high-risk patients, consideration of relocating the main body of CIED may be needed for appropriate cancer treatment. However, Poole reported complications requiring treatment due to replacement occurred at a rate of 4–15% [16], and the 2017 Heart Rhythm Society guidelines suggest that relocation is not recommended when the estimated total dose to the device is < 5 Gy, [8].

Preparation for radiotherapy during or immediately before and after treatment

1. For all patients, establish an emergency support system that can immediately be used to manage events, including unexpected changes in the settings of the CIED.
2. At the time of using MV X-rays for verification images and linac graphy, be careful not to expose the main body of CIED to the irradiation field surrounded by the aperture (jaw). Generally, image-guided radiotherapy (IGRT) by MV X-ray cone beam CT (CBCT) is not recommended when the main body of the CIED is in the image range. For IGRT with fluoroscopy or CBCT using kV X-rays, management should be similar to that for imaging diagnosis for patients with a CIED in the facility. There is insufficient data to establish the impact of IGRT imaging validation on a CIED, and the decision to use this approach should balance the risk and benefit for each case.
3. Consult with a cardiologist on the potential use of asynchronous pacing if pacing suppression occurs during irradiation.
4. For a PM-dependent patient, consult with a cardiologist on whether to prepare for temporary external pacing during irradiation.
5. If the CIED has a cardioverter-defibrillator function, consult with a cardiologist on whether to terminate this function during irradiation, and prepare for an external cardioverter-defibrillator including use of an automated external defibrillator (AED).
6. Observe the patient's condition with a camera throughout the radiotherapy session, and examine subjective abnormalities and pulse after each irradiation.
7. For medium-risk patients, monitor the circulation using an electrocardiogram or pulse oximeter for pulse abnormalities during the first radiotherapy session and, if necessary, continue monitoring in subsequent sessions.
8. For high-risk patients, monitor the circulation using an electrocardiogram or pulse oximeter for pulse abnormalities in every radiotherapy session.
9. If the setting of the CIED is changed before irradiation, return to the required setting immediately after irradiation.
10. For all patients, perform a functional check of the CIED after the first treatment session and describe this in the medical record. If no malfunction is detected in the first session, it should still be recognized that an unpredictable malfunction may occur in a subsequent session.
11. For medium-risk patients, check function after approximately half of the planned radiotherapy has been completed. The need for a weekly check in these patients should be discussed with a cardiologist at the time of preparation.
12. In high-risk patients, check function every week. The need for a daily check in these patients should be discussed with a cardiologist at the time of preparation.
13. For all patients, consult with a cardiologist, including the need for follow-up after 1–6 months, check the function of the CIED, and add this information to the medical record.

Preparation steps for radiotherapy of each guidelines are listed in Table 2.

Management measures of each guidelines before, during and immediately after irradiation are summarized in Table 3.

Recommended times for functional checks of each guidelines are listed in Table 4.

The specific managements of major manufactures and sales providers are provided in Table 5.

A comparison of recommended measures before, during and immediately after irradiation of the other society is shown in Table 3.

Implantable cardiac monitor and leadless pacemaker

On 29 March 2019, during a third-party evaluation of these guidelines, the Japanese Society of Cardiology/Japan Arrhythmic Cardiology Association jointly revised the guidelines for non-pharmacotherapy for cardiac arrhythmias. Implantable heart monitors and leadless pacemakers were newly added as CIEDs in their guidelines. In response to public comment that our guidelines should also mention these implantable devices, we agreed to add the following information.

Implantable cardiac monitor

An implantable cardiac monitor is a subcutaneously inserted electrocardiograph that can capture electrocardiogram findings at the onset of syncope and atrial fibrillation that can cause latent cerebral infarction, making it extremely useful for identifying an underlying arrhythmia. There are few reports on radiotherapy for a patient with an implantable cardiac monitor, but abnormalities of the device caused by radiation may make it difficult to detect underlying disease. Therefore, the preparation and emergency support system described above should be discussed with a cardiologist for use in cases with an implantable cardiac monitor.

Leadless pacemaker

A leadless pacemaker basically consists of a capsule-shaped body and a hook-shaped tine attached to the tip of the body. The tine is inserted and fixed into the myocardium. This device was developed to avoid the complications associated with leads and subcutaneous pockets that are required for a conventional PM. There are few reports on radiotherapy for patients with leadless pacemakers, but the same considerations as those for a PM are assumed to apply because of the function of the device. Thus, the latest information from the manufacturer should be checked for a leadless pacemaker.

CONFLICT OF INTEREST

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