THE UNIVERSITY OF PARDUBICE

FACULTY OF HEALTH STUDIES

BACHELOR'S THESIS

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The University of Pardubice

Faculty of health studies

Radiotherapy of patients with pacemakers and cardioverter-defibrillators

Bachelor's Thesis

2022 Ariela Bertini Cumba Mavungo

Univerzita Pardubice
Fakulta zdravotnických studií
Akademický rok: 2020/2021

ZADÁNÍ BAKALÁŘSKÉ PRÁCE

(projektu, uměleckého díla, uměleckého výkonu)

Jméno a příjmení:	**Ariela Bertini Cumba Mavungo**
Osobní číslo:	**Z19346**
Studijní program:	**B5345 Specializace ve zdravotnictví**
Studijní obor:	**Radiologický asistent**
Téma práce:	**Radioterapie pacientů s kardiostimulátorem a kardioverter-defibrilátorem**
Téma práce anglicky:	**Radiotherapy of patients with pacemakers and cardioverter-defibrillators**
Zadávající katedra:	**Katedra klinických oborů**

Zásady pro vypracování

1. Studium literatury, sběr informací a popis současného stavu řešené problematiky.
2. Stanovení cílů a metodiky práce.
3. Příprava a realizace výzkumného šetření dle stanové metodiky.
4. Analýza a interpretace získaných dat.
5. Zhodnocení výsledků práce

Rozsah pracovní zprávy:	**35 stran**
Rozsah grafických prací:	**dle doporučení vedoucího**
Forma zpracování bakalářské práce:	**tištěná/elektronická**
Jazyk zpracování:	**Angličtina**

Seznam doporučené literatury:

Ellenbogen, K.A., Wilkoff, B.L., Kay, G.N. and Lau, C.P. 2011. Clinical Cardiac Pacing, Defibrillation and Resynchronization Therapy. Elsevier Health Sciences. ISBN 978-1-4377-1616-0.

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ŠLAMPA, Pavel a kol., 2022. Radiační onkologie. Praha: Maxdorf, Jessenius. 772p. ISBN 978-80-7345-674.

Vedoucí bakalářské práce:	**Mgr. Jan Pospíchal, Ph.D.** Katedra klinických oborů
Datum zadání bakalářské práce:	**1. prosince 2020**
Termín odevzdání bakalářské práce:	**28. dubna 2022**

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AUTHORS DECLARATION

I declare:

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In Pardubice on 28.04.2022

Ariela Bertini Cumba Mavungo

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ACKNOWLEDGEMENTS

Firstly, I would like to thank my supervisor Mgr. Jan Pospíchal Ph.D. for his time and cooperation throughout the whole process. Secondly, I would like to thank my family, who made this golden opportunity possible, and all the patience and advice. To my friends Selasi and Maria, without whom this would not have been possible, thank you for making my life a little lighter and BSc. & Bc. Wusu Sorie Nanday Kamara for guidance, support, and all the cups of tea. Lastly, but far more important, to the Almighty God for the knowledge, courage, persistence, discipline, and life.

ANOTACE

Tato bakalářská práce zkoumá, jak radiační terapie muže ovlivnit funkce implantovaný srdeční elektronický přístroji (CIEDs- cardiovascular implantable electronic devices), konkrétně kardiostimulátorů a kardioverter-defibrilátorů, s cílem poskytnout informace o tom, jak často dochází k poruchám, a možné pokyny k léčbě pacientů a zvýšení efektivity péče. První část je zaměřena na elektrický převodní systém srdce a patologii rytmu, využití CIEDs, konstrukci kardiostimulátorů a kardioverter-defibrilátorů, jak funguje, řízení pacienta a radioterapie. Druhá část poskytne přehled o výskytu poruch funkci a důsledků ozáření u pacientů se srdečními elektronickými přístroji.

KLÍČOVÁ SLOVA

Arytmie, implantovaný srdeční elektronický přístroji, cor, porucha přístroje, kardioverter-defibrilátor, kardiostimulátor, radioterapie.

TITLE

Radiotherapy of patients with pacemakers and cardioverter-defibrillators

ANNOTATION

This bachelor's thesis examines how radiotherapy may affect the functioning of cardiovascular implantable electronic devices, specifically pacemakers and cardioverter-defibrillators, aiming to provide accurate information on how often error occurs and possible reccomendations to facilitate the management of patients and increase care effectiveness. The first part focuses on the heart's electrical conduction system and the rhythm pathology, cardiovascular implantable electronic devices, the construction of pacemakers and implantable cardioverter-defibrillators, its functioning, patient management, and radiation therapy treatments and its modalities. The second part will provide an overview of the incidence of device malfunction, focusing on the consequences of radiation in patients with cardiac devices malfunctions.

KEYWORDS

Arrhythmia, cardiovascular implantable electronic devices, cor, device malfunction, implantable cardioverter-defibrillator, pacemaker, radiotherapy.

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LIST OF ABBREVIATIONS AND SYMBOLS

AAPM	American Association of Physicists in Medicine
ABC	Active breathing-coordinator
AF	Atrial fibrillation
AP	Action potential
AV	Atrioventricular
AVN	Atrioventricular node
BPEG	North American Society for Pacing and Electrophysiology
CCS	Cardiac conduction system
CIED	Cardiovascular implantable electronic devices
CMOS	Complementary Metal-Oxide technology Semiconductors
CRT	Cardiac resynchronization therapy
EMI	Electromagnetic interference
ICD	Implantable cardioverter- defibrillator
IMPT	Intensity-modulated proton therapy
IMRT	Intensity-modulated radiation therapy
JBI	Joanna Briggs Institute
mV	Millivolt
NASPE	North American society for pacing and electrophysiology
NBD	Generic Defibrillator Code
PBT	Proton beam therapy

PM	Pacemaker
PTV	Planning target volume
RT	Radiotherapy
SAN	Sinoatrial node
SBRT	Stereotactic body radiotherapy
SND	Sinus node dysfunction
TMP	Transmembrane potential
VMAT	Volumetric modulated arc therapy

INTRODUCTION

The annual rate of radiation treatments in patients with pacemakers (PM) or Implantable cardioverter-defibrillators (ICD) has risen dramatically in the last decade. With more than 700 000 new PMs and more than 200 000 new ICDs implanted worldwide each year indicating an increase in the rate of both PM/ICD implants in Europe and on a global scale (Zaremba et al., 2016).

Because of the direct or diffuse effects of ionizing radiation and electromagnetic interferences caused by employing linear accelerators on cardiac devices, the proper functioning of PMs and ICDs may be harmed by radiation therapy. Tool failure occurs in around 2.5 percent of PM patients and 6.8 percent of ICD patients after radiation therapy (Salerno et al., 2016).

This bachelor's thesis will consist of two parts. The first part critically examines the structure and physiology of the heart, concretely its conduction system, radiotherapy as a science, the functioning of the pacemaker and cardioverter-defibrillator, and effective management strategies.

The second part of this thesis will focus on the research aspects based on a literature review on radiotherapy’s effects and possible risks in patients with cardiac implantable electronic devices, malfunctioning incidence, including radiation interference values for such devices, and the type of malfunctions.

1 THESIS OBJECTIVES AND METHODOLOGY

1.1 Thesis objectives

The main goal of this bachelor thesis is to provide a comprehensive review of the interaction of radiation therapy and cardiovascular implantable electronic devices. Specifically, focusing on the malfunction it causes in pacemakers and cardioverter-defibrillators.

Furthermore, the practical part aims to provide new insight into the available data regarding the incidence of such malfunctions, including the type of malfunctions, while presenting selected studies.

1.2 Methods of achieving objectives

The methodological approach taken in this thesis is based solely on literature review, using background PCC (patient, context, concept) review question to narrow the search while presenting relevant studies and articles with the help of collective information from search databases such as PubMed, and Science Direct, manufacturers technical reports, and institutional experiences in the past years.

THEORETICAL PART

2 ELECTROPHYSIOLOGY OF THE HEART

To better understand the techniques involved and the indications of radiotherapeutic procedures and cardiovascular implantable devices usage, it is essential to have a thorough understanding of the anatomical, physiological, and electrical aspects of the cardiac cells and tissues.

2.1 The heart (cor)

The heart is a hollow, fibromuscular organ in the shape of an irregular cone and weighs around 350g. Situated between the right and left pleural sacs in the middle mediastinum (Mahadevan, 2018). This muscle, like any other, has the ability to contract and relax, the contraction of the heart is referred to as *systole*, and the relaxation is called *diastole*. The heart consists of four chambers; two upper chambers called atria functioning mainly as collecting chambers, and the two lower chambers, the ventricles (Weinhaus, 2005). Inside we can find structures that work as mechanical systems and help in the circulation of the blood, known as heart valves. There are four heart valves, the tricuspid, pulmonary, mitral, and aortic valve, one for each chamber. They work like doors, opening to allow the blood flow and closing to prevent the backward flow.

The walls consist of three layers: *endocardium*, the inner layer, *myocardium* known as the middle layer, and a superficial visceral *pericardium* or *epicardium* forming the protective layer. The epicardium is composed primarily of loose connective tissue, including elastic fibers and adipose tissue, and its function is to protect the inner heart layers. We can also find the coronary blood vessels in this layer, supplying the heart's wall with blood. The inner layer of the epicardium is in direct contact with the myocardium (Bailey, 2021). The myocardium, which is the muscle layer of the heart, comprises heart cells known as *cardiomyocytes*. This layer is found in the walls of all four heart chambers, though it is thicker in the ventricles than in the atria. This disparity is due to the difference in the generation of the force of contraction needed for propelling blood between the atria and the ventricles, with ventricles requiring much more power (Tran et al., 2020). The cardiac muscles use electrochemical gradients and potentials to create a contractile force for each pulse which is significant for this thesis and will be better explained in the subsequent chapters. The endocardium is a sheet of epithelium called *endothelium* that rests on a thin layer of the connective tissue basement membrane. This sheet lines the heart chambers and composes the valves of the heart.

2.1.1 Cardiovascular system

All structures mentioned are fundamental for the cardiovascular or blood circulatory system. The circulation starts when deoxygenated blood from the body enters the heart through the right atrium, and it flows to the vena cava. The blood then proceeds to the right ventricle passing through the tricuspid valve. From the right ventricle, it then goes to the pulmonary valves flowing to the truncus pulmonalis and then to the right and left pulmonary arteries. The blood then is lead to the lungs forming the circulation known as *pulmonary circulation* (Chaundhry et al., 2021).

Thenceforth, starts the systemic circulation. The oxygenated blood from the lungs flows through the four pulmonary veins to the left atrium and, passing through the mitral valve, is led to the left ventricle. The left ventricle pumps oxygen-rich blood through the aortic valve preventing the backflow of blood right into the aorta and then is distributed to the whole body (Chaundhry et al., 2021).

The heart has its own electrical conduction system and other essential structures, apart from chambers, valves, walls, and blood vessels.

2.2 The cardiac conduction system

The heart generates and propagates the electrical impulses required to initiate coordinated contractions to efficiently pump blood throughout the body. This is accomplished by a group of nodes and specialized conduction cells, the myocytes, forming the cardiac conduction system (CCS).

As shown in figure 1, the CCS comprises the sinoatrial node, atrioventricular node, bundle branches or Tawara brunches, atrioventricular bundle or bundle of His and Purkinje fibers. It can be broadly divided into impulse-generating nodes and impulse-propagating systems (Park et al., 2011). The cells that produce impulses are capable of spontaneous depolarization; they serve as a natural pacemaker carrying the impulses to the cells of the heart muscle that ensure the contraction of the cardiac chambers.

The sinoatrial node (SAN) is located near the opening of the superior vena cava and the right atrium; it has the highest rate of depolarization in the whole system. It is responsible for initiating the electrical impulse that flows over the right and left atrium, causing them to contract and move the blood into the ventricles. When that same impulse reaches the atrioventricular node (AVN), a slight delay occurs because the fibers of the AVN are smaller, giving the atria

time to contract and empty blood into the ventricles before the ventricular contraction occurs (Jarvis et al., 2018). The AVN is located between the septal leaflet of the tricuspid valve, the coronary sinus, and the membranous portion of the interatrial septum; this area is known as the triangle of Koch. After the impulse leaves the AVN, the signal travels down to the bundle of His; the impulse is then divided into the bundle branches. These branches divide, forming conducting fibers that continue spreading the action potential (AP), reaching the ventricular cardiomyocytes and causing their contraction. When this happens, the right ventricle pumps the blood to the lungs, and the left ventricle pumps it to the rest of the body. Propagation of impulses in the heart involves action potential generation by cardiac cells and its propagation in the multicellular tissue. Action potential conduction results from complex interactions between cellular electrical activity, electrical cell-to-cell communication, and the cardiac tissue structure (Kleber et al., 2004).

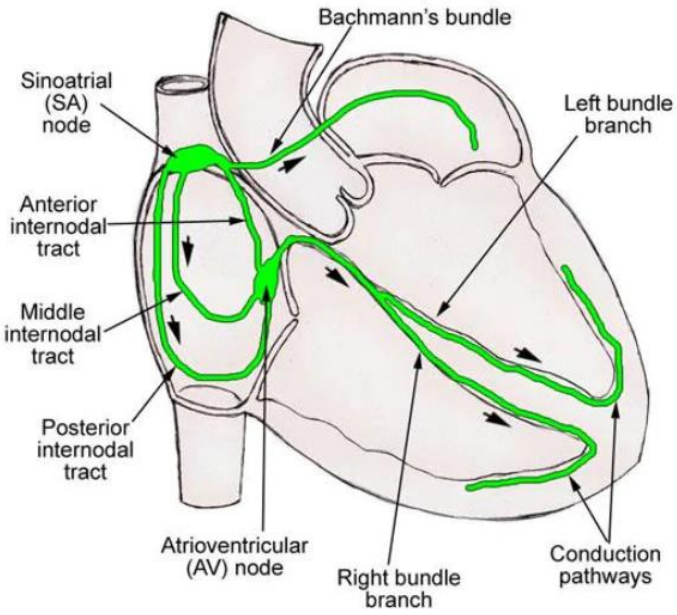

Figure 1- Heart electrical conduction system and impulse propagation (Assadi, 2016)

2.2.1 Action potential

The cardiac cells can only propagate action potentials because of an electrochemical potential gradient across cellular membranes. Ions, mainly sodium (Na+), potassium (K+), and calcium (Ca2+), are present in different concentrations inside the cells vs. their surrounding environments (Wei et al., 2021). This variation in concentration results in electrical potential difference, or voltage, between the inside and the outside of the cell, known as transmembrane potential (TMP). When positive ions enter the cell, the TMP becomes more positive, and when positive ions leave the cell, the TMP becomes negative (Ikonnikov, 2014).

The action potential in normal cardiomyocytes is divided into five phases, as shown in figure 2 below, beginning with 0 and ending with phase 4. The first one is *depolarization* of the membrane and the high flow of sodium and decrease in potassium flow, shifting the membrane potential into a positive voltage range; phase 1 is partial membrane *repolarization* due to the fast decline of sodium ions and quick closing of the channels, this phase sets the potential for the next phase. Phase 2, also known as the *Plateau phase*, is the longest and is characterized by the movement of calcium ions out of the cell, maintaining the depolarization, and right after happens phase 3 as both channels of sodium and calcium close, returning the membrane potential to its standard level. Phase 4 is the *resting potential* with a value of -90 millivolt (mV) (Wei et al., 2021).

For this thesis is essential to know that the extracellular space is positively charged due to the sodium ions. For that reason, generating cardiac stimulation is necessary to induce depolarization and create action potential by using a negative impulse(Wei et al., 2021).

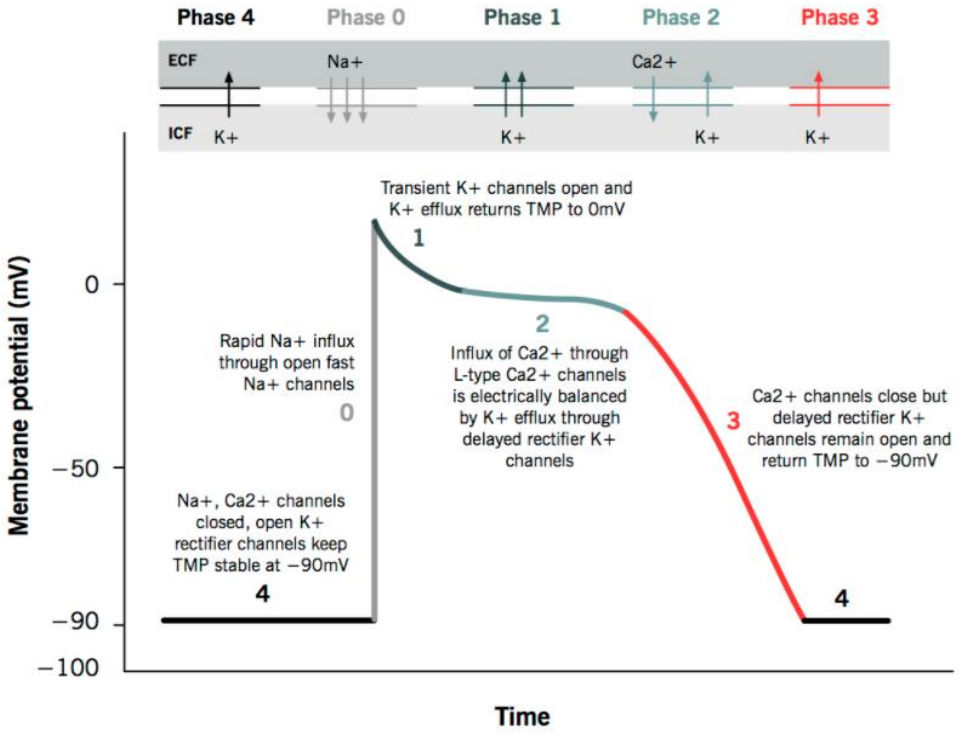

Figure 2- Action potential of cardiac muscles (Ikonnikov, 2014)

2.3 Heart rhythm

The human heart beats 2.5 billion times during an average lifespan, which is accomplished by cells of the CCS (Park et al., 2011). A regular heartbeat is known as *sinus rhythm*; Normally, as seen in figure 1, electrical impulses are initiated in the SA node and then carried through the AV node, the bundle of His, bundle branches, and Purkinje fibers, as it was mentioned. An irregularity in these impulse passages can cause an abnormal heart rate and rhythm. The abnormalities are known as arrhythmias (Mitchell, 2021).

2.3.1 Arrhythmias

The pathogenesis of cardiac arrhythmias has three primary mechanisms: enhanced or suppressed automaticity, triggered activity, or re-entry (Fu, 2015). Automaticity is the ability of cardiac cells to generate spontaneous action potentials as a result of diastolic depolarization. The enhancement or suppression of automaticity can be caused by heart medications, ischemia, and others. The triggered activity causes multiple spontaneous depolarizations resulting in ventricular arrhythmias. In re-entry, cardiac tissue is repetitively excited by a propagating wave circulating an obstacle or circulating freely in the tissue as a spiral (Fenton et al., 2008).

The arrhythmias that lead to the use of a pacemaker and implantable cardioverter-defibrillator will be better explained in the subsequent chapter.

3 CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICES

The advances in cardiac surgery around the mid-20th century led to the development of an artificial technique for stimulating the heart. Initially developed as large external devices, technological advancements resulted in the miniaturization of electronic circuitry and eventually the development of totally implantable devices (Mulpuru et al., 2017).

Cardiovascular implantable electronic devices are battery-operated medical devices that help patients with conduction abnormalities or heart failure, regulate and monitor arrhythmias. Cardiovascular implantable electronic devices can be divided into two main types, pacemakers (PM) and implantable cardioverter-defibrillators (ICD), and these may be co-implanted, creating the ICD-pacemaker combination (Mulpuru et al., 2017).

3.1 Pacemaker

A pacemaker (PM) or artificial pacemaker is a small device weighing about 20-50g, usually implanted in the chest just under the collarbone, as shown in figure 3, but can also be inserted in the abdomen. When the heart's natural pacemaker malfunctions, sent signals may become erratic. These signals may be either too slow or fast, commonly known as bradycardia and tachycardia, respectively.

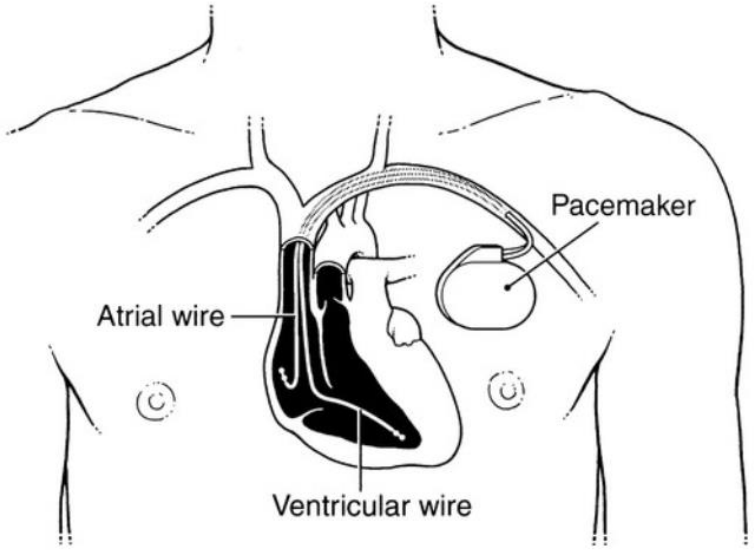

Figure 3- Dual-chamber pacemaker (Wood, 2002)

Pacemakers are typically used for the treatment of dangerously slow arrhythmias, bradycardias. Some of the most common indications for the use of such devices include sinus node dysfunction (SND) and high-grade atrioventricular (AV) block (Dalia et al., 2018).

Sinus node dysfunction includes sinus pause, sinus arrest, and sinoatrial exit blocks. In contrast, a high-grade AV block happens when the heart's electrical signals can't effectively go through the AV node to the ventricles, whether because the impulses are delayed or the signals from the atria to the ventricles are entirely blocked. Different types of pacemakers are used depending on the clinical indication. There are three types:

- *Single chamber system*- only one lead is implanted. Depending on the chamber to be paced, it can be inserted in the atrium or ventricle. It can be used in patients with chronic atrial fibrillation (AF) or SND but with no AV block history because the lead does not provide AV synchrony.
- *Dual-chamber system*- have two leads implanted, one in the atrium and another in the ventricle. It provides AV synchrony and pacing in patients with AV block in the absence of AF or patients with SND presenting AV block.
- *The triple chamber system*- also called Cardiac Resynchronization Therapy (CRT) comprises three leads implanted in the right atrium and ventricle. The third one is inserted in the left ventricle. It paces both ventricles together, resynchronizing the beat.

After the implant, some patients might not be able to ever have a normal heartbeat without the device, a condition known as pacemaker dependency. It can be described as the presence of bradycardia-related symptoms or indications that induce an acute urgent clinical condition when pacing suddenly stops. Many individuals who receive an implantable pacemaker for symptomatic bradyarrhythmias have only occasional ones and an acceptable unpaced heart rate the majority of the time. These individuals are not pacemaker-dependent and will most likely only be paced for a minimal amount of time. On the other hand, pacemaker-dependent patients are paced almost all of the time (Korantzopoulos et al., 2009).

3.1.1 Components of the pacemaker

Pacemakers consist of a pulse generator that contains the battery, electrodes, and leads that travel from the generator to contact the myocardium delivering a depolarizing pulse and sensing intrinsic cardiac activity (Mulpuru et al., 2017). Certain PMs do not possess all these constituents, such as leads. Leadless pacemakers are currently available only for patients with

specific medical conditions and bradycardia who need single-chamber pacing. One of its advantages is not requiring wires connected to the generator and since no surgical pocket is created after the implant, there is no lump under the skin on the chest (ClevelandClinic, 2022).

The main body of the pacing system is the pulse generator containing the biocompatible titanium case, circuitry, and lithium battery. The battery can last 5 to 10 years; its function is to deliver pacing pulses while sensing and storing electrocardiograms. The leads have insulated conductors that deliver the electrical impulses to the heart while sensing its electrical activity and sending the information back to the pulse generator with the help of the electrodes located at the end of each lead.

3.1.2 Modes of cardiac pacing

The modes of pacemakers are based on the generic code known as NBG, a combination of the North American Society for Pacing and Electrophysiology (NASPE) and British Pacing and Electrophysiology Group (BPEG), generally consisting of 5 letters.

Table 1- NBG code. The usual pacing modes (Rozner, 1999)

I	II	III	IV	V
Pacing chambers	**Sensing chambers**	**Responses to sensing**	**Programmability**	**Anti-tachycardia functions**
O- None	**O- None**	**O- None**	**O- None**	**O- None**
A-Atrium	**A-Atrium**	**I-Inhibited**	**P-Programmable**	**P-Pacing**
V-Ventricle	**V- Ventricle**	**T- Triggered**	**M- Multi programmable**	**S- Shock**
D-Dual (A+V)	**D-Dual (A+V)**	**D-Dual (I+T)**	**C- Communicating**	**D-Dual (P+S)**
			R-Rate modulation	

The modes are explained by dividing them into single-chamber or dual-chamber categories.

3.1.2.1 Single Chamber Modes

- VOO- in this mode, the pacemaker is programmed at a rate regardless of the heart's intrinsic electrical activity.
- VVI- the pacemaker senses the electrical activity and withholds pacing when not required.
- AOO-the pacemaker is programmed at a rate and holds it regardless of the heart's intrinsic electrical activity.
- AAI- here, the pacemaker can adapt to the natural atrial rate, pace when needed, and inhibit when not required.

3.1.2.2 Dual Chamber Modes

Dual Chamber Modes are divided into Tracking Modes and Non-Tracking modes.

Tracking Modes:

- DDD- this mode can adapt to intrinsic heart rhythm and imitate normal conduction as much as possible.
- VDD- here, the atrium cannot be paced, but an intrinsic atrial activity can trigger an AV delay helping to maintain AV synchrony.

Non-tracking modes:

- DDI- This mode's primary use is in patients with atrial tachyarrhythmias. It results in AV dissociation if the atrial rate goes high than the set rate.
- DOO- results in AV sequential pacing at the lower rate limit regardless of the heart's intrinsic activity. It is usually used in situations, such as when a magnet is placed over a pacemaker or sometimes while a patient is having surgery.
- R- rate response is used in patients with chronotropic incompetence, which means that the heart is not able to appropriately increase its rate with increased activity or metabolic demand, which leads to exercise intolerance (Lak et al., 2021).

3.2 Implantable cardioverter-defibrillator

The implantable cardioverter-defibrillator (ICD) was developed to detect dangerous arrhythmias such as ventricular fibrillation (VF) and ventricular tachycardia (VT), which may cause cardiac arrest and cessation of blood flow. It also has the function of preventing or terminating them by delivering therapy in the form of anti-tachycardia pacing (ATP), low-energy cardioversion, and high-energy defibrillating shock to the heart (Kirk, 2006). The newer ICDs generation usually has a dual role that includes the ability to serve as a pacemaker treating bradycardia.

An ICD, like the pacemaker, consists of a generator pulse, electrodes, and leads. It is commonly implanted in a subcutaneous location in the left pectoral region. Typically, depending on the patient's handedness, the condition of the upper venous system, the presence of other devices, or physician preference. Another variation is to place the device in an abdominal location. This is mainly done in small children to avoid discomfort or interference with the motion of the arm (Laizzo, 2010).

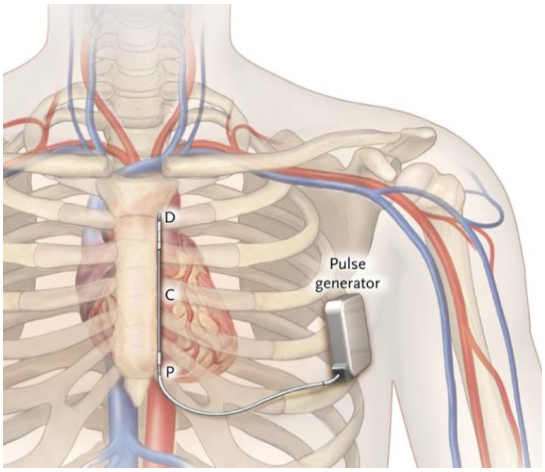

Figure 4- Subcutaneous implantable cardioverter-defibrillator (Bardy et al., 2010)

Modern CIEDs use Complementary Metal-Oxide technology Semiconductors (CMOS) in integrated complex circuits. They contained more than 50 million CMOS circuits compared to 1,000 in the most advanced bipolar transistors decades ago. The advantage is high noise resistance, low power consumption, and reliability. Increased elements density, miniaturization, and interconnection lead to very low energy consumption but are also more sensitive to ionizing radiation than the initially used integrated circuit (Nečasová et al., 2021).

Complications can be due to the presence of the defibrillator system as a foreign body, apparent or real system malfunction, and acute complications related to the procedure itself: hemothorax, pneumothorax, subclavian artery puncture, and myocardial perforation (Rapsang et al., 2014).

3.2.1 Generic defibrillator code

Implantable cardioverter-defibrillators, just like pacemakers, also has a code given by NASPE/ BPEG (2002) known as Generic Defibrillator Code (NBD). The fourth position of the code is the three/five-letter code for the pacemaker capability of the device (Rapsang et al., 2014).

Table 2- Generic defibrillator code (Rapsang et al., 2014)

I	II	III	IV
Shock chambers	**Antitachycardia pacing chambers**	**Tachycardia detection**	**Antibradycardia pacing chambers**
O-None	**O-None**	**E-Electrogram**	**O-None**
A-Atrium	**A-Atrium**	**H-Hemodynamic monitors**	**A-Atrium**
V-Ventricle	**V-Ventricle**		**V-Ventricle**
D-Dual (A+V)	**D-Dual (A+V)**		**D-Dual (A+V)**

I. Position- serves to distinguish among devices capable of delivering atrial, ventricular, and both chambers shocks.
II. Position- it identifies the location of anti-tachycardia pacing without defining the pacing protocol.
III. Position- it determines devices that detect tachycardia by using an electrogram signal or more hemodynamics.
IV. Position- it identifies the anti-bradycardia location without determining the mode of pacing. (Bernstein et al., 1993).

3.3 Electromagnetic interference on CIEDs

The electromagnetic field is used to describe combined electric and magnetic fields. They are characterized by wavelength, frequency, and field strength. A magnetic field is generated when electric current flows in a conductor with magnetic field lines perpendicular to the current flow.

Technological advances have led to new sources and types of interferences that have exponentially increased over the last two decades, parallel to the increased number of implanted pacemakers and ICDs.

It is confirmed that the function of cardiac devices can be disrupted by electromagnetic waves, an effect referred to as electromagnetic interference (EMI). The interference can occur as a result of conducted radiated electromagnetic energy. Today's CIEDs are generally well shielded against this interference, with filters and bipolar leads aiming to mitigate EMI; however, devices such as magnetic resonance imaging and ionizing radiation devices should still be given special attention in a medical setting for patient safety. The effects of electromagnetic waves depend on the type of CIED, construction of leads and electrodes, CIED program, fields strength, and conditions of medical imaging (Nečasová, et al., 2021).

A strong electromagnetic field can affect CIEDs in different ways.

a. Electrode heating - conductive implants and leads, mainly when placed in a loop configuration, can significantly increase the risk of burns due to inductive heating of the lead conductor from radiofrequency fields damaging the tissues adjacent to the electrode.
b. Unintentional stimulation - time-varying gradient magnetic fields may be associated with transient and permanent effects on CIEDs. The main concern is the potential for current induction within conductive wires in the field that may result in transient inhibition of pacemaker output and direct stimulation of the myocardium and permanent effects attributable to heating of the conductor and tissue burns (Beinart et al., 2013).
c. Mechanical motion - spatial gradients in static magnetic fields result in translational and rotational forces on ferromagnetic objects. If the translational force exceeds counterforces from sutures, scarring, and tissue ingrowth, permanent and dangerous effects may occur from dislodgement and movement of CIED (Beinart et al., 2013; Nečasová et al., 2021).

Despite the given possible effects, the impact of EMI is not clearly distinguished from other malfunctions mechanisms. The CIED sensitivity to EMI is relatively minimal or only a temporary effect exclusive to the electromagnetic field exposure. Modern radiotherapy (RT) techniques such as active breathing-coordinator (ABC) RT technology seem to have no interference on CIEDs (Nečasová et al., 2021).

4 RADIOTHERAPY

Radiotherapy, also known as radiation therapy, radiation oncology, or therapeutic radiography, is one of the three main treatment methods for malignant illness, with surgery and chemotherapy being the other two.

Radiotherapy aims to treat cancer and spare the normal tissue as much as possible. There have been advances that allow the delivery of higher doses of radiation to the tumor while sparing a significant amount of healthy tissue, thus achieving more cures and fewer acute and long-term side effects.

Even at relatively low doses, high-energy ionizing radiation used in radiation therapy can cause considerable damage to pacemaker semiconductors. Some studies affirm that pacemaker malfunction usually requires dosages higher than 50 Gy. However, pacemaker failure can occur with as low as 10 Gy (Rapsang et al., 2014).

Long after the radiation therapy has ended, the pulse generator may recover, but it is usually insufficient, and the pacemaker cannot be used effectively after that. As a result, following regulations for achieving the lowest possible radiation dosage for the CIED is crucial.

4.1 Modalities of the radiation therapy

Ionizing radiation can be delivered externally where a machine is used to aim beams of radiation at the cancer cells or by brachytherapy when the sources of ionizing radiation are placed directly inside or near the tumor. In both cases, fractionated radiotherapy is used. The total dosage is divided into several fractions providing time to restore healthy tissues such as organs located in the irradiation area. A particular case is stereotactic irradiation, in which the number of fractions is extremely low, or the full recommended dosage can be delivered in a single fraction (Nečasová et al., 2021).

Today's standard treatment for external radiation therapy includes Intensity-modulated radiation therapy (IMRT), or Volumetric modulated arc therapy (VMAT).

IMRT allows the oncologist to create irregular-shaped radiation doses that conform to the tumor while simultaneously avoiding critical organs. IMRT is possible through inverse planning software and computer-controlled intensity-modulation of multiple radiation beams during treatment (Baskar et al., 2012). VMAT is a technique in which radiation doses are achieved continuously as the machine rotates, improving target volume coverage and sparing normal tissues.

Other necessary modalities of radiation therapy include Intensity-modulated proton therapy (IMPT), also known as pencil beam proton therapy is a sophisticated model of proton therapy that is analogous to IMRT and an active area of investigation in cancer care (Moreno et al., 2019). Generally, we can say that the higher the supplied energy in all modalities deeper the tissue penetration.

The most often employed modality is high-energy photon beam treatment in clinical practice, and it is accomplished using linear accelerators. The accelerator head has a collimation system that ensures field shaping and modulation intensity using a multi-lamellar collimator. Radiation beams enter the body at different angles and collide at the isocenter. The planning system is a fundamental part of any radiation facility and simulates behavior bundles and their interactions with treated tissues.

4.2 Effects of ionizing radiation on CIEDs

It is difficult to predict how therapeutic radiation affects implanted devices. However, the impact can be determined by several factors.

According to BostonScientific 2012 and Nečasová 2021, such factors include the type of implanted device, whether it is a PM or ICD when undergoing RT might have different side effects. Results have shown that radiation in patients with pacemakers can cause chemical changes in the structure of the pacemaker and electrical energy disturbances during the treatment. Implantable cardioverter-defibrillators are more sensitive to ionizing radiation than pacemakers. They are believed to pose a higher risk for dysfunctions due to their internal circuitry's increased amount of boron. In addition, an elevated RT dose rate can lead to oversensing and inappropriate ICD shocks (Fradley et al., 2021). The device's proximity to the radiation beam is also an important factor to take into account, and it is recommended that the CIED should not be in the planning target volume (PTV) in order to minimize the dose to the device, which should not exceed 5 Gy (Lester et al., 2015). That occurs primarily when the planned target for radiotherapy includes the thorax, neck, or proximal upper extremity. In general, the dose to the device should be <2 Gy if the radiation field is ≥ 5 cm away from the device. The radiotherapy beam energy should not exceed 10 MV even at a low absorbed dose due to potential neutron contamination (Fradley et al., 2021). Regarding CIEDs tolerance dose the results are quite inconsistent. Based on different manufacturers' guidelines, the recommendations range from 1Gy-30Gy (Baerh et al., 2021). The device shield as well as

patient anatomy and physiology, should also be taken into account when analyzing the effects of radiation on these devices.

Because of these variations, it is difficult to determine a safe radiation dosage or dose rate to ensure that the device remains effective after being exposed to ionizing radiation. (BostonScientific, 2012).

Unexpected electric current accumulation in the irradiated semiconductor is among the base causes of radiation-induced CIED malfunction. Integrated circuits are composed of many transistors grouped in a silicone base covered with silicon oxide insolating layers (SiO2). Ionizing radiation absorbs the electric charge inside these layers, which may cause a change in the transistor's properties. As a result of the absorbed dose, an increase in charge accumulation can cause a variety of abnormalities and transients phenomena, including a considerable reduction in the battery's life (Nečasová et al., 2021).

A large accumulated dose can cause irreversible damage being is the most prevalent cause of CIED problems associated with therapeutic radiation exposure. Depending on the accumulated dose, the circuit system in CIED might fail, resulting in a decrease in output amplitude, increase in current leakage, sensor failure, or total malfunction, including inaccurate cardiac detection activities. During irradiation, the dose rate may also cause momentary interference. High radiation levels on electrical circuits can trigger interferences in voltage and physiological sensors in specific circuits, particularly those connected to heart rhythm monitoring (Nečasová et al., 2021).

4.3 Risk assessment and care when undergoing radiotherapy

It is possible to estimate the individual risk level of RT for each patient by assessing its parameters and information collected during the device's checkup.

The preparation for patients with PM or ICD before radiotherapy consists of device identification and validation of the manufacturer's recommendations, receiving the patient's written authorization about the procedure, device control such as routine tests, informing the patient about all the risks and possible effects of RT, considerating the relocation or removal of the device and ensuring the entire estimated RT dosage is not exceeded (Tajstra et al., 2019). Continual audiovisual contact with the patient is required during irradiation, monitoring ECG, pulse oximetry, and capillary pulse wave recordings. Throughout RT, in cases of patients who depend on stimulation, external stimulation alternatives are needed. In patients with ICDs, it is advised to temporarily disable ventricular tachycardia / ventricular fibrillation detection and

treatment during RT. After RT, the patient should be scheduled for a device check-up visit within one month after the end of therapy and after three and six months to detect potential late CIED dysfunctions (Tajstra et al., 2019).

Aside from these recommendations, there have been efforts to improve the prediction of the clinical effects and device malfunction during RT by categorizing the risk to the patient as low, medium, or high. In low-risk patients, audio-visual examination of the patient during and after the entire RT course is advised. Patients at medium and high risk should be examined weekly and daily, respectively. In addition, cardiac rhythm monitoring throughout each RT fraction has been proposed, particularly in high-risk individuals (Zaremba et al., 2016).

5 REVIEW METHODOLOGY

For the review part of this thesis, comprehensive research was developed to identify relevant literature describing the impact of radiation on cardiovascular implantable electronic devices. Selected articles, clinical trials, and guideline documents were reviewed for inclusion.

The main search terms included radiotherapy, cardiovascular implantable electronic devices, pacemaker, implantable cardioverter-defibrillator, and malfunction incidence. A well-defined methodological approach by the Joanna Briggs Institute (JBI) updated in 2020 was used, which has roots in the PICO (population, intervention, comparator and outcome) framework as well as Preferred Reporting Items for Systematic Reviews and Meta-Analyses Scoping Review extension (PRISMA-ScR) commonly used to focus clinical questions and develop systematic literature search strategies.

Furthermore, an adequate question was compiled based on the PCC formula, (P)-Population or participants, (C)-Concept, (C)-Context. The framework consists of five main consecutive stages: identifying the research question, identifying relevant studies, study selection, charting the data, and reporting results. The review was conducted using online databases such as Pubmed, Scopus, ScienceDirect and Medvik.

The targeted group for this study was patients over 18 years old undergoing radiotherapy with an implantable pacemaker or cardioverter-defibrillator, whether with a cancer indication or other pathologies.

Table 3- Inclusion and exclusion criteria according to the PCC framework

Population	Patients over 18 years with a functional PM and/or ICD. There are no limitations regarding the type of cancer, sex, or indications for device implant.
Concept	Effects of radiation therapy Device malfunction due to external beam RT exposure Hazards during or after undergoing radiotherapeutic procedures with direct or indirect device exposure
Context	Considered clinical trials and studies were up to 10 years back Occurred dysfunctions during or after undergoing radiotherapy Used studies and information were in English or Czech language.

The initial search was based on the chosen keywords entered in databases where the system generated several articles and studies. The research was time-limited and most found articles were studies published mainly in English. Only one study was found on the Czech Medvik database, but it did not meet my criteria.

Review question (PCC)

What is the incidence of malfunctions when undergoing RT in patients with a pacemaker and/or implantable cardioverter-defibrillator?

Table 4- PCC keywords

Population	Patients, cardiac electronic devices, pacemaker, cardioverter-defibrillator
Concept	Radiotherapy, radiation therapy, ionizing radiation
Context	Malfunction incidence, induced malfunction, device dysfunction

Individual terms were inserted into some of the best health research databases such as PubMed, ScienceDirect, Scopus, EBSCO, CINAHL, and Cochrane library. Tables 5 and 6 show the results of searches of the first two databases, respectively, after inserting specific keywords and combinations using the Boolean AND and OR operators.

Table 5- Research strategy on PubMed

Numbers	Keywords	Number of results on PubMed database	Filter Humans,18+and in the last ten years
1.	Patients	7,860,997	
2.	Cardiac electronic devices	29,331	
3.	Pacemaker	53,746	
4.	Cardioverter-defibrillator	12,667	
5.	**2 OR 3 OR 4**	**88,452**	**20,785**
6.	Radiotherapy	401,876	
7.	Radiation therapy	499,248	
8.	Ionizing radiation	175,197	
9.	**6 OR 7 OR 8**	**650,489**	**77,559**
10.	Malfunction incidence	2076	
11.	Induced malfunction	2414	
12.	Device dysfunction	183,834	
13.	**10 OR 11 OR 12**	**187,964**	**43,147**
14.	**1 AND 5 AND 9 AND 13**	**89**	**23**

Table 6- Research strategy on ScienceDirect

Numbers	Keywords	Number of results on ScienceDirect database	Filter In the last ten years
1.	Patients	5,000,000+	
2.	Cardiac electronic devices	34,903	
3.	Pacemaker	116,954	
4.	Cardioverter-defibrillator	27,792	
5.	**2 OR 3 OR 4**	**158,600**	**73,731**
6.	Radiotherapy	358,553	
7.	Radiation therapy	459,022	
8.	Ionizing radiation	325,647	
9.	**6 OR 7 OR 8**	906,875	
10.	Malfunction incidence	27,083	
11.	Induced malfunction	57,751	
12.	Device dysfunction	154,076	
13.	**10 OR 11 OR 12**	**216,823**	**35,186**
14.	**1 AND 5 AND 9 AND 13**	**19**	**14**

After following search rules and tips for these databases and using delimiters such as parenthesis and hyphens, my results were narrowed to 37 potential studies and detected duplicates were immediately eliminated. About ten articles and studies were removed based solely on their titles and abstracts. Resulting in 27 articles that were analysed and selected based on my criteria. In order to keep a record of my results, I used the citation manager Mendeley, and after reading the most relevant studies, my results were narrowed to 13 best matches. The diagram of the included studies, also known as flow chart graph, shows the entire process (see Figure 5).

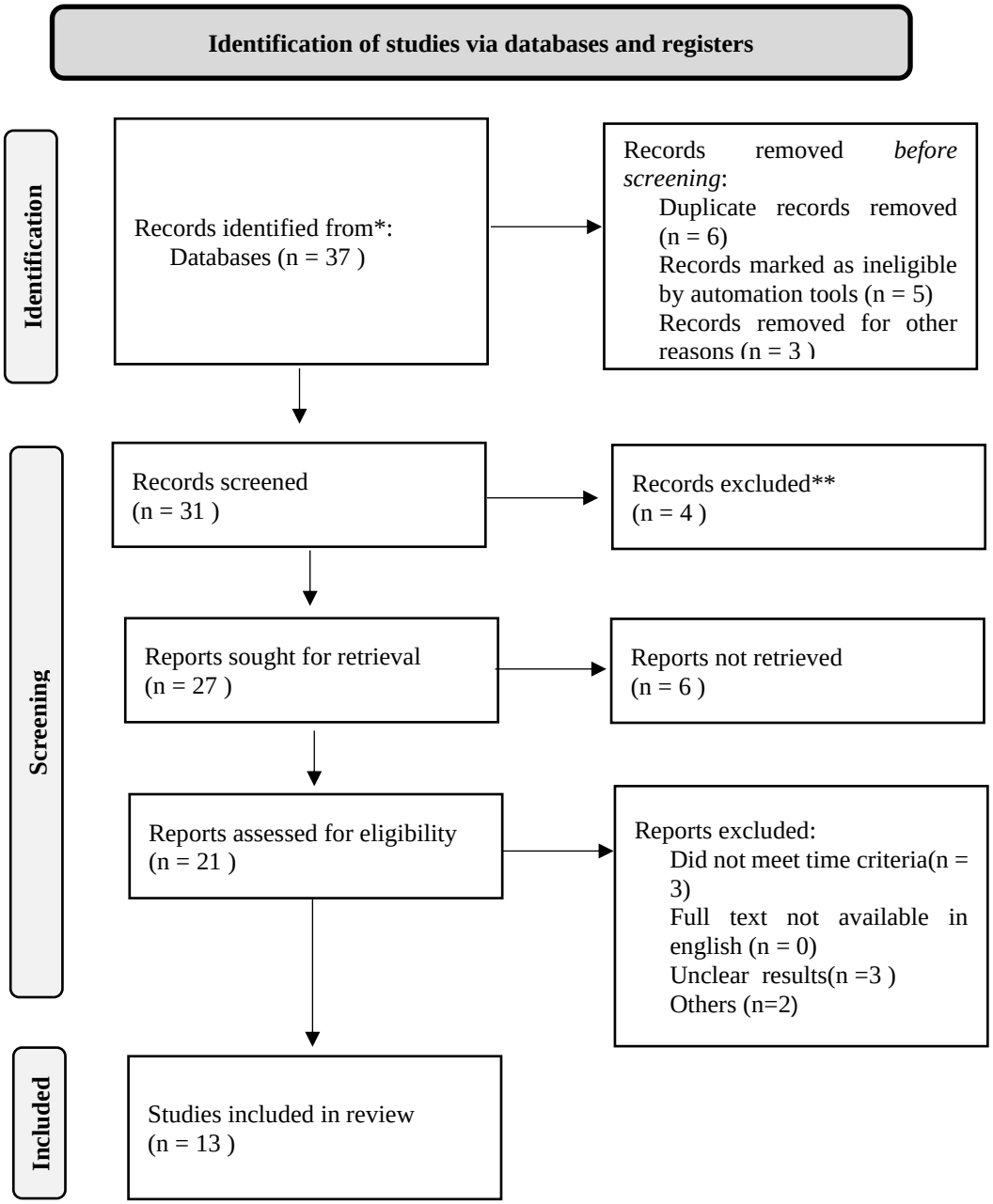

Figure 5- Flow chart graf

As a result, my literature review includes a total of thirteen studies. The articles were placed in chronological order, from the oldest to the most recent.

Table 7- List of selected studies

Number	Title	Author (year)
1.	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)	Hurkmans et al. (2012)
2.	Malfunctions of implantable cardiac devices in patients receiving proton beam therapy: incidence and predictors	Gomez et al. (2013)
3.	Radiotherapy-Induced Malfunction in Contemporary Cardiovascular Implantable Electronic Devices	Grant et al. (2015)
4.	Radiotherapy in patients with pacemakers and implantable cardioverter defibrillators: a literature review	Zaremba et al. (2016)
5.	Malfunction of cardiac devices after radiotherapy without direct exposure to ionizing radiation: mechanisms and experimental data	Zecchin et al. (2016)
6.	Effect of Therapeutic Ionizing Radiation on Implantable Electronic Devices: Systematic Review and Practical Guidance	Tajstra et al. (2016)
7.	Radiotherapy in patients with cardiac implantable electronic devices: clinical and dosimetric aspects	Riva et al. (2018)
8.	Radiotherapy for patients with cardiovascular implantable electronic devices: an 11-year experience	Yeung et al. (2019)
9.	Radiation Therapy–Induced Dysfunction in Cardiovascular Implantable Electronic Devices	Brouillard et al. (2019)
10.	Radiotherapy in Patients With a Cardiac Implantable Electronic Device	Sharifzadehgan et al. (2020)
11.	Radiotherapy is safe in patients with implantable cardiac devices. Analysis	López-Honrubia (2020)

	of a systematic interrogation follow-up	
12.	Radiotherapy-induced malfunctions of cardiac implantable electronic devices in cancer patients	Malavasi et al. (2020)
13.	Assessment of Radiation-Induced Malfunction in Cardiac Implantable Electronic Devices	Zagzoog et al. (2021)

5.1 Evaluation of the selected studies

1. **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)**

The first and oldest article presented is from 2012 and is composed by collective authors. This study aimed to be the base of a factual consensus guideline for the care of patients with pacemakers or implanted cardioverter-defibrillators. It was projected to find clinical acceptability outside Netherlands, considering new radiation procedures and modern CIED technology at the time.

Methods: A diverse team was formed to provide an evidence-based guideline for treating patients with CIEDs receiving radiation. External photon and electron beams up to 21 MeV were examined as major modalities considered for the study. A table overview of 18 of some of the most relevant literature on the subject at the time was presented, dated from 1991 by collective authors Rodriguez et al. to 2010 by Ferrara et al.. The studies varied from reviews, case reports, in vitro research and in vivo retrospectives. There was still a data shortage, and many articles were based on individual patient case reports rather than large cohorts of patients or vast numbers of CIEDs irradiated in vitro.

Results: The article did not provide a distinct total amount of PMs or ICDs in the studies presented and did not mention the exact number of participants. The intervention doses considered were as low as 0. 11 Gy in Zweng et al. (2009) case report to as high as 300Gy in vitro Wilm et al. (1994). Type of reported defects included runaway PM, which induces ventricular tachycardia, a reset of the device to factory settings, electrical reset, runaway ICD causing the device to deliver a high energy and inappropriate shocks in normal sinus rhythm decrease of battery load and even total device failure.

Table 8- Frequency of malfunction

Doses in Gy	Number of defects (PM/ICD)
0,11	1 out of 1
0,15	1 out of 1
0.2	4 out of 96
0.5	4 out of 11
<1	1 out of 1
1,7	2 out of 18
2	21 out of 96
2.5	5 out of 18
3	1 out of 33
7	11 out of 18
10	2 out of 20
14	21 out of 23
20	1 out of 19
120	14 out of 19
120	11 out of 11

Conclusion: On the malfunctions table, the frequency was not distinguished between PMs and ICDs.The risk of device failure grows with cumulative radiation exposure, and no specific threshold for damage had been established.

Table 9- Hurkmans et al., 2012

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	Yes	All patients were undergoing RT
2. Are all patients implanted with the same CIED?	No	Patients had PMs or ICDs and were divided accordingly
3. Was there an estimative treatment dose?	Unclear	
4. Were patients submitted to the same dose?	No	Doses varied up to 300Gy in vitro
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Unclear	It was based on previous literature, and it did not specify the length of monitoring
7. Were the CIEDs revised prior to exposition?	Unclear	
8. Were participants analyzed based on device dependence?	Yes	The low-risk group received a dose below 2 Gy and were not dependent Medium risk received doses from 2 to 10 High risk received doses over 10 Gy

2. Malfunctions of implantable cardiac devices in patients receiving proton beam therapy: incidence and predictors

The second study I examined gives clearer information directly on the incidence of malfunction and is specific for patients undergoing proton beam therapy(PBT). The selected participants received therapy from 2009 to 2012 at a single institution.

Methods: The study was carried out from March 2009 to July 2012. The patients underwent 42 courses of PBT for thoracic, prostate, liver and base of skull tumors. The total number of patients was 42, all with cardiac implantable electronic devices (28 pacemakers and 14 cardioverter-defibrillators) The median administered dose was 74 Gy, and the median distance from the treatment field to the CIED was 10 cm. For each treatment, it was calculated the maximum proton and neutron doses. If the exposure to the CIED was predicted to exceed the manufacturer's recommendations, high-risk patients were not treated with PBT and were instead referred for IMRT. All CIEDs were tested before radiation administration and monitored during therapy. Not only was data retrieved on the presence of a CIED, but also on whether the patient was classified pacemaker-dependent or pacemaker-independent, as well as data generated by the CIED.

Results: In all patients, the median calculated peak proton and neutron doses to the CIED were 0.8 Gy and 346 Sv, respectively. Six CIED failures occurred in five patients (two pacemakers and three defibrillators). Five of these dysfunctions were CIED resets, while the sixth was determined to be unrelated to RT. Among devices that reset, the median distance from the proton beam to the CIED was 7.0 cm, and the median maximum neutron exposure was 655 mSv. All resets happened in individuals getting thoracic PBT and were repaired without causing any clinical problems.

Conclusion: It was found that CIED resets occurred in around 20% of individuals undergoing PBT to the thorax. It is recommended to avoid PBT in pacing-dependent patients, and patients with any kind of CIED who gets thoracic PBT should be constantly monitored.

Table 10- Gomez et al., 2013

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	Yes	All patients underwent RT
2. Are all patients implanted with the same CIED?	No	Patients had PMs or ICDs and were divided accordingly
3. Was there an estimative treatment dose?	Yes	The prescribed dose was 74 Gy
4. Were patients submitted to the same dose?	No	Relative biological effectiveness range from 46.8 to 87.5 Gy
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Yes	It was over 3 years research
7. Were the CIEDs revised prior to exposition?	Yes	
8. Was patient exposure based on patient-device dependence?	Yes	

3. Radiotherapy-Induced Malfunction in Contemporary Cardiovascular Implantable Electronic Devices

This study focused on identifying malfunction incidence and describing clinical consequences in several patients undergoing photon and electron-based radiotherapy. Post-treatment patients were interrogated in order to evaluate long-term function. Patients without CIED interrogations during or following RT were excluded.

Methods: A retrospective examination of all patients with a functional CIED who underwent RT between August 2005 and January 2014, including CIED interrogation data following the treatment. A total number of 286 patients was reported. There were 249 photon- and electron-based RT courses identified in 215 patients with 123 pacemakers and 92 implantable cardioverter-defibrillators. A considerable neutron production was generated in 71 courses. Among them, 203 patients received external-beam photon-only therapy, 22 received a mix of photons and electrons, and 10 received GammaKnife treatment. Therapeutic energies ranged from 6 to 16 MeV for the 14 electron-only treatments, with the majority employing 6- or 9 MeV energies.

Results: CIED malfunction as a result of RT occurred in 18 courses, with 15 CIEDs having single-event dysfunction and three exhibiting transient signal interference. Most single event dysfunctions occurred during neutron-producing RT. No single-event dysfunctions were discovered among 178 courses of non–neutron-producing RT. The dose exposure on CIED did not correspond to device malfunction. Patients who had treatment to the abdomen and pelvis were more likely to experience a single-event malfunction. Six patients who had their CIED parameters reset showed clinical symptoms: three had hypotension and/or bradycardia, two had abnormal chest ticking, usually common with pacemaker syndrome, and one had a congestive cardiac failure. The three instances of signal interference had no clinical consequences.

Conclusion: All incidents of single-event malfunction in a cohort of modern CIEDs happened in the setting of substantial neutron generation, with a rate of 21% for neutron-producing RT and 0% for non–neutron-producing RT. Non–neutron-producing RT is recommended if clinically feasible. Given the absence of relation between CIED failure and incident dose seen up to 5.4 Gy. Taking into account associated expense and potential risks, it may be safe to decrease the number of performed relocation procedures.

Table 11- Grant et al., 2015

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	Yes	All patients were undergoing RT
2. Are all patients implanted with the same CIED?	No	Patients had PMs or ICDs and were divided accordingly
3. Was there an estimative treatment dose?	Yes	Consistent dose distribution was up to 5.4 Gy
4. Were patients submitted to the same dose?	No	
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Yes	From 2005 to 2014 with post-treatment patient interrogation
7. Were the CIEDs revised prior to exposition?	Yes	
8. Were participants analyzed based on device dependence?	Unclear	In 1 pacing-dependent patient treated with 6-MV photons, the ventricular pacing threshold increased following RT and a revision was ensured for safety reasons.

4. Radiotherapy in patients with pacemakers and implantable cardioverter defibrillators: a literature review

A collective study compiled by Zaremba et al. with the goal of presenting the current research on the predictors and causes of device faults during RT at the time, as well as a brief explanation of the concepts of RT.

Methods: This research provides a brief overview of RT principles and presents the most recent studies on the predictors and mechanisms of device malfunctions during therapy. It also includes practical recommendations from current publications and industry sources. Malfunctions reported in the literature were often temporary software disruptions that rarely resulted in irreversible device damage. Some studies presented differences in the reported frequency of device faults. Hurkmans et al., for example, exposed 19 PMs to a dosage of up to 120–130 Gy using 6 MV photons. The initial malfunction points ranged from 10 to 120 Gy, and five devices were irradiated with the entire dosage without any damaging effects. Mouton et al.46 conducted the biggest in vitro investigation at the time, examining the effects of direct irradiation with 18 MV photons on 96 PMs, reaching doses of up to 200 Gy per device, administered at varied doses rates. Failures were reported in all devices, with initial failure doses ranging from 0.5 to 120 Gy. It should be noted that sensing interference was seen in all of the ICDs, which could lead to shock treatment in the event of a clinical situation. At the same time, Kapa et al. observed no device failures after exposing 20 ICDs to 4 Gy of dispersed radiation from a 6 MV photon beam.

Results: the recommendations from PM/ICD manufacturers seem to lack consistency regarding the suggestions on follow-up and safe radiation doses. Failures were reported in all devices, with initial failure doses ranging from 0.5 to 120 Gy. It should be noted that sensing interference was seen in all of the ICDs, which could lead to shock treatment in the event of a clinical situation. At the same time, Kapa et al. observed no device failures after exposing 20 ICDs to 4 Gy of dispersed radiation from a 6 MV photon beam.

Conclusion: Devices may be damaged even when exposed to low-level radiation exposure during high-energy photon RT. PM/ICD malfunctions, on the other hand, appear to be of little concern during RT with kV photons or electrons. Radiotherapy may be administered safely to carefully chosen patients without removing the PM/ICD from the RT field.

Table 12- Zaremba et al., 2016

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	Yes	All patients were undergoing RT
2. Are all patients implanted with the same CIED?	No	Patients had PMs or ICDs and were divided accordingly
3. Was there an estimative treatment dose?	Yes	Depended on the study reviewed
4. Were patients submitted to the same dose?	No	
5. Are the results evaluated using objective criteria?	?	
6. Was the monitoring of participants carried out for sufficient time?	Unclear	It was based on previous literature
7. Were the CIEDs revised prior to exposition?	Unclear	
8. Were participants analyzed based on device dependence?	Yes	Depended on the study reviewed

5. Malfunction of cardiac devices after radiotherapy without direct exposure to ionizing radiation: mechanisms and experimental data

This in vitro study aimed to analyze the effects of scattered radiation on different types and models of CIED and possible sources of malfunctions. Throughout the study, not only the occurred malfunctions and doses were approached but also the device manufacturer and year of production.

Methods: Before June 2014, a phantom presented as Jimmy weighing 37 kg and with a composition similar to human tissue and thus equivalent in terms of neutron absorption was used, and after that, another phantom presented as Ryan weighing 71 kg was assembled by employing the size of an average man as Jimmy was no longer available. All devices were placed on the phantom at a location corresponding to the pectoral area, behind a 3 cm polyethylene layer representing the adipose tissue and skin for neutrons. Fifty-nine explanted CIED was implanted on these tissue-equivalent phantoms, and a high-energy photon of 15 MV, irradiation course with a total dosage of 70 Gy was conducted for prostate treatment. Before and after radiation, all devices were examined. The radiation dose, electromagnetic field, and neutron fluence were all measured at the CIED site.

Results: A total of 59 CIED from different manufacturers, 34 PMs (ten from Boston Scientific/Guidant/Intermedics, nine from Medtronic/Vitatron, ten from Biotronik, three from Sorin, and two from St Jude Medical), and 25 ICDs (11 Boston Scientific/Guidant, 7from Medtronic, and seven from St Jude Medical) were analyzed. Before the radiation, no defects were discovered. A software failure was observed following radiation in 13 ICDs (52%) and 6 PMs (18%). No substantial electromagnetic fields or photon radiations were detected in the thoracic area.

Conclusion: Due to dispersed neutron radiation produced by the linear accelerator, high-energy radiation can induce various problems on CIED, notably ICD, even without direct exposure to ionizing radiation.

Table 13- Zecchin et al., 2016

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	No	Phantoms were used
2. Are all patients implanted with the same CIED?	No	Patients had PMs or ICDs and were divided accordingly
3. Was there an estimative treatment dose?	Unclear	
4. Were patients submitted to the same dose?	?	To simulate an RT course the dose was of 70Gy
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Unclear	
7. Were the CIEDs revised prior to exposition?	Yes	
8. Were participants analyzed based on device dependence?	?	?

6. Effect of Therapeutic Ionizing Radiation on Implantable Electronic Devices: Systematic Review and Practical Guidance

This article provides an overview of the possible causes and consequences of direct and scattered radiation on CIEDs while giving practical guidance.

Methods: Few in vitro and in vivo studies have been performed, with the majority of them focusing on the influence of radiation on the PM; research on the effects of radiation treatment on the ICD is far less prevalent. The greatest in vitro research to investigate the effect of radiation was undertaken in 2002, with 96 explanted PMs treated to varying doses of radiation, ranging from the value equivalent to dispersed radiation to the direct irradiation of 200 Gy. Device failures were classified into eight categories. There were fundamental changes in the amplitude of the electrical impulse in 66 percent of the devices at the minimum dose of 2 Gy, permanent absence of stimulation in 50 percent (observed at a dose of only 0.5 Gy), and disruptions in electrical pulses lasting more than 10 seconds in 41% which was already observed at a dose of 0.15 Gy.

Results: Two serious failures were recorded at doses comparable to dispersed radiation. When exposed to radiation 5Gy, it was determined that 16.7% of the gadgets experienced a catastrophic mishap. The number of PMs impacted by a significant accident with a dosage of 2 Gy was 11.5%. one of the studies included 69 patients, 50 with PM and 19 with ICD, where the patients were separated into two groups: those who received low energy of 6 MV radiation and those who received high energy radiation 16 MV. PMs received an average dosage of 0.84 Gy, whereas ICDs received an average dose of 0.92 Gy. There was a partial reset of the memory devices with data loss after 1.23 Gy and as low as 0.04 Gy of irradiation in two individuals with ICDs. Six months after treatment, there was no early battery depletion or failure.

Conclusion: It is crucial to define clear guidelines for radiotherapy procedures in patients with implanted CIEDs and enable multidisciplinary cooperation between oncologists, radiotherapists, and cardiologists based on the Heart Team model.

Table 14- Tajstra, 2016

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	_Unclear	
2. Are all patients implanted with the same CIED?	No	Patients had PMs or ICDs and were divided accordingly
3. Was there an estimative treatment dose?	Yes	PMs had an average dose of 0,84 Gy and ICDs of 1,23 Gy
4. Were patients submitted to the same dose?	No	
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Unclear	It was based on previous literature, and it did not specify the length of monitoring
7. Were the CIEDs revised prior to exposition?	Yes	
8. Were participants analyzed based on device dependence?	Yes	

7. Radiotherapy in patients with cardiac implantable electronic devices: clinical and dosimetric aspects

This study considered patients with different types of CIEDs: permanent pacemakers 73, cardiac resynchronization therapy 9, implantable cardioverter–defibrillators 11. Techniques used to treat patients with CIEDs included 3D conformal radiation therapy (3D-CRT), intensity-modulated radiation therapy (IMRT), and stereotactic body RT (SBRT).

Methods: This retrospective study was part of a larger study on the clinical and dosimetric aspects of image-guided radiotherapy for prostate, gynecological, gastrointestinal, head and neck, and breast cancers, as well as stereotactic treatments, which was reported to the Institute's Ethical Committee. From June 2010 to December 2016, the Institute treated 63 patients with a CIED undergoing RT. In a total of 17,693 sessions, 93 treatment courses were provided in the presence of a cardiac device. Data was evaluated from patients who met the following inclusion criteria: histological diagnosis of a malignant tumor; the presence of CIED; external-beam RT as a local therapy from June 2010 to December 2016; signed informed consent for RT; written informed consent for the use of anonymized data for research and education purposes.

Results: The study's main finding is that just 2.1 percent of patients suffered RT-related CIED malfunction, and none had a life-threatening adverse event. Although this incidence is lower than in other research, the continuing growth in the number of persons with CIED who require RT is sufficient to provide a therapeutic challenge in their care. The number of RT treatments performed at the Institute in the presence of CIEDs increased from 0.3 percent in 2011 to 0.5 percent in 2014 and 1.2 percent in 2016.

In the investigation, only the high-risk neutron-producing category had RT-related failures. Furthermore, dysfunctions occurred in 18% of all ICDs that received the recommended dosage of 2 Gy.

Conclusion: In the research, nearly 2% of patients with CIEDs sustained device damage, all of whom were from the high-risk patient cohort, 15% incidence in neutron-producing RT and 4.1% incidence in the chest–neck RT.

Table 15- Riva et al., 2018

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	Yes	
2. Are all patients implanted with the same CIED?	Yes	Patients had both PMs and ICDs
3. Was there an estimative treatment dose?	Yes	
4. Were patients submitted to the same dose?	No	
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Yes	
7. Were the CIEDs revised prior to exposition?	Yes	
8. Were participants analyzed based on device dependence?	Unclear	

8. Radiotherapy for patients with cardiovascular implantable electronic devices: an 11-year experience

This study's objective was to evaluate the management of and malfunctions in patients with CIEDs undergoing RT. Analysis of paper charts and computerized charts from the ARIA radiation therapy treatment record at KHSC revealed data on the details of the RT, oncological diagnoses, and the CIED forms. Clinical charts and patient notes from the computerized Patient Care System or paper charts were evaluated to identify medical history.

Methods: From March 2007 to April 2018, patients with CIEDs who had RT at Kingston Health Sciences Center were studied retrospectively. For the key outcome of the device malfunction, data on demographics, RT, devices, and management were compared.

Results: Four (2.1 percent) of the 189 patients with CIEDs who had 297 courses of RT encountered device problems. In dosage 0.05Gy, higher beam energy was connected with a malfunction. Patients who had malfunctions received a lower dosage of radiation per fraction and were much younger than patients who did not have malfunctions.

Conclusion: Although RT-induced device faults are uncommon, considering the possible risks, a greater knowledge of the potential predictors of malfunction and the creation of evidence-based guidelines would aid in optimizing patient safety.

Table 16- Yeung et al., 2019

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	Yes	All patients were undergoing RT
2. Are all patients implanted with the same CIED?	No	Patients had PMs or ICDs and were divided accordingly
3. Was there an estimative treatment dose?	Yes	The approximate dose to the device was inconsistently calculated reported as a maximum or an average
4. Were patients submitted to the same dose?	No	Doses varied up to 300Gy in vitro
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Yes	An 11 year monitoring
7. Were the CIEDs revised prior to exposition?	Yes	
8. Were participants analyzed based on device dependence?	Yes	The treatment team was informed of the type of device, the extent of pacemaker dependency the minimum programmed pacing rate, and the maximum programmed tracking and sensor rates

9. Radiation Therapy–Induced Dysfunction in Cardiovascular Implantable Electronic Devices

This study aimed to evaluate the incidence and predictors of newer CIED malfunctions in RT patients. Reviewed data included 230 patients with CIEDs who received radiation therapy at the CHU de Québec - Université Laval Radiation Oncology Center between February 2007 and November 2013.

Methods: Patients with CIEDs were evaluated before, during, and after radiation therapy. High- and low-energy photon or electron beam radiation from linear accelerators, orthovoltage machines, and high-dose rate brachytherapy delivery were applied. Incidents included entire or partial deprogramming of the CIED settings, the development of new symptoms, or the occurrence of a new arrhythmia.

Results: This research was based on one of the biggest cohorts available at the time. A total of 18 incidents (7.8 %) were observed in 16 patients. In 16 of the 18 events, photo neutrons producing high-energy RT neutron producing RT had been used to deliver radiation therapy. During non-neutron producing RT, only two incidents happened. The prescribed dose and the dose assessed at the pacemaker's location were both associated with the risk of malfunction incidence. Clinical signs were observed in just one of the 16 participants (6.3%)

Conclusion: CIED malfunctions are relatively uncommon and do not seem life-threatening. We recommend limiting the dose at the CIED and avoid neutron-producing RT to reduce the risk of CIED malfunction.

Table 17- Brouillard et al., 2019

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	Yes	All patients were undergoing RT
2. Are all patients implanted with the same CIED?	Unclear	
3. Was there an estimative treatment dose?	Yes	
4. Were patients submitted to the same dose?	No	
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Yes	Monitoring from 2007 to 2013
7. Were the CIEDs revised prior to exposition?	Unclear	
8. Were participants analyzed based on device dependence?	Unclear	

10. Radiotherapy in Patients With a Cardiac Implantable Electronic Device

Between March 2006 and June 2017, a monocentric observational research was conducted at the European Georges Pompidou Hospital. Patients who received RT while having a PM or an ICD were identified. At baseline and throughout frequent follow-up, detailed information on the RT plan and CIED features were acquired.

Data regarding the RT plan, data on the tumor location, number of fractions, type of external beam radiation, and energy range were gathered.

Methods: Between March 2006 and June 2017, 90 (1%) of the 12,736 patients who underwent RT had a CIED: 82 pacemakers and 8 implantable cardioverter-defibrillators. Before starting RT, all patients were carefully evaluated, including CIED questioning and patients were then categorized as low-, intermediate-, or high-risk. The median total dosage administered to the tumor was 49.5 Gy. Neutron-generating beams were administered to 49 (55 percent) of the patients, whereas non-neutron producing beams were delivered to 40. (45 percent). In the latter group, one received simply electrons, two received a mix of photons and electrons, and two were treated with Cyberknife. Systematic cardiac monitoring was performed for all patients during RT delivery, and electrocardiograms before and after radiation exposure in 12 intermediate- and high-risk patients.

Results: CIED malfunctioning was reported in 5 patients (6%), primarily due to backup mode resetting (80%), with 4 patients initially classed as intermediate risk and 1 as low risk. Four of the five individuals with CEID dysfunction had been exposed to neutron-producing beams. The findings highlight the need for more comprehensive monitoring of patients having RT, as well as the need to evaluate neutron generating beams for risk categorization, as suggested in recent guidelines.

Conclusion: The results highlighted the absence of systematic monitoring and follow-up of CIED patients having RT, despite CIED malfunction being an uncommon and generally benign occurrence. Local policy optimization, particularly concerning energy beam type, might significantly ease monitoring without jeopardizing patient safety.

Table 18- Sharifzadehgan et al., 2020

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	Yes	All patients were undergoing RT
2. Are all patients implanted with the same CIED?	No	Patients had PMs or ICDs and were divided accordingly
3. Was there an estimative treatment dose?	Yes	
4. Were patients submitted to the same dose?	No	The total dose varied from 36Gy to 74Gy
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Yes	
7. Were the CIEDs revised prior to exposition?	Yes	
8. Were participants analyzed based on device dependence?	Yes	

11. Radiotherapy is safe in patients with implantable cardiac devices. Analysis of a systematic interrogation follow-up

This study used a database of systematically checked CIEDs to evaluate the frequency of CIED malfunction during a course of radiotherapy and to identify whether it has a predictable pattern. The study included all patients who had a CIED and were irradiated at the Hospital General Universitario de Albacete between January 2006 and June 2017. During this time, all irradiated patients were thoroughly screened for CIED dysfunction.

Methods: At the time of the analysis, patients were categorized as the NVRO-12 according to the patient dependence to the CIED and the expected dose absorbed by the CIED. Patients in the high-risk group wearing a CIED were expected to be irradiated with more than 10 Gy. Patients in the intermediate-risk category are non-pacemaker dependent patients with a predicted cumulative total radiation ranging from 2 to 10 Gy. Patients in the low-risk category, also considered not pacemaker dependent, were expected to receive <2 Gy to the CIED. Except for one patient, all radiation courses involved active ICD devices throughout each radiotherapy fraction. The devices were tested regularly, except when the danger of generator malfunction was deemed minimal due to the generator's distance from the radiation beam. There was no monitoring during the irradiation.

Results: Between January 2006 and June 2017, 56 CIED-wearing patients, 43 males and 13 women, were irradiated. The average age was 78.2 years. The most prevalent cardiac illnesses were valvular heart disease (23.2%), dilated cardiomyopathy (10.7%), and hypertrophic cardiomyopathy (5.3%). Of the total patient amount, 87.5% had a pacemaker, 39% were PM dependent, and the others had an ICD. Only ten patients had a detectable dose of irradiation. The 69.1% CIEDs were examined daily, with the remaining checked weekly. During the radiation treatment, 82% of the patients reported no cardiological events. The CIED of five patients observed a rise in the threshold, while another instance reported a dramatic decrease in the duration of the battery

Conclusion: All patients must be followed up on by cardiologists. Even though patients in risk groups 2 and 3 experienced higher adverse events in this trial, no safe dosage threshold was observed. Patients who use CIEDs would most likely benefit from device checks on a daily basis.

Table 19- López-Honrubia et al., 2020

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	Yes	All patients were undergoing RT
2. Are all patients implanted with the same CIED?	No	Patients had PMs or ICDs and were divided accordingly
3. Was there an estimative treatment dose?	Unclear	>10Gy
4. Were patients submitted to the same dose?	No	It was based on device dependence
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Yes	
7. Were the CIEDs revised prior to exposition?	Unclear	
8. Were participants analyzed based on device dependence?	Yes	

12. Radiotherapy-induced malfunctions of cardiac implantable electronic devices in cancer patients

This is a single-centered, observational, retrospective research. Our goals were to describe CIED malfunctions and their clinical consequences and investigate possible predictors of CIED malfunctions. The study included all patients with pre-existing CIED who had RT at the University Hospital of Modena between January 2004 and July 2018.

Methods: The strategy used was a retrospective evaluation of all pacemaker and implanted cardioverter-defibrillator medical records in patients who received RT in the previous 14 years. A total of 127 individuals who underwent 150 separate RT treatments were evaluated (99 with a PM and 27 with an ICD). It is important to note that 21/127 (16.6 percent) of the patients were PM-dependent. Neutron-producing RT was employed in 37/139 (26.6%) of the courses, while non-neutron-producing RT was used in 102/139 (73.4%) of the courses. Only 2/132 (1.5 percent) of the cumulative dose given to the CIED exceeded 5 Gy.

Results: Two malfunctions occurred in the 37 patients who received neutron-producing RT (5.4%), and one malfunction occurred in the 102 patients who received non-neutron-producing RT (1%). In 2/127 (1.6 percent) patients, device relocation from the RT field was performed. If conducted in an adequately controlled setting, RT in patients with CIED is essentially safe, with few CIED malfunctions and no severe clinical consequences. Neutron-producing energy appears to increase the risk of malfunction.

Conclusion: The incidence of RT-related malfunctions in the study population was 2%, a figure that is consistent with the majority of the larger studies and confirms the data supporting the safety of RT in patients with CIED. The problems included two PM and one ICD and could be reversed with device resetting. In our 14-year-long study, no clinical repercussions were found.

Table 20- Malavasi et al., 2020

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	Yes	
2. Are all patients implanted with the same CIED?	No	Patients had PMs or ICDs and were divided accordingly
3. Was there an estimative treatment dose?	Yes	> 2Gy
4. Were patients submitted to the same dose?	No	
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Yes	
7. Were the CIEDs revised prior to exposition?	Yes	
8. Were participants analyzed based on device dependence?	Yes	

13. Assessment of Radiation-Induced Malfunction in Cardiac Implantable Electronic Devices

Several modalities of radiation therapy (RT) are utilized in the treatment of cancer. A linear accelerator is most commonly used to generate and deliver photons or electrons. This retrospective study aimed to identify types of malfunction and risk factors that could influence these malfunctions while determining their incidence. The included patients received RT between 2007 and 2018 at four different centers in Canada.

Methods: The patients that were considered for this study were undergoing external beam radiation therapy in megavoltage electron therapy, megavoltage photon therapy, kilovoltage photon therapy, as well as both external beam radiation therapy and brachytherapy. Data was obtained on device type, RT modality, total radiation dose, anatomic location of cancer, and other important aspects. Defects in CIEDs were classified as minor or significant. Serious malfunctions included premature battery loss and an electrical reset that led to total dysfunction and consequently to battery replacement. Malfunctions reported apart from these were considered minor.

Results: There were 811 patients with accessible data among the 1041 patients with CIEDs who received RT. The median age of patients with CIEDs who did not report any malfunction was 78.4 and 79.3 for those who did. Most patients with CIED malfunction (5.2 %) were male; women experienced only two CIED failures out of 236. Device errors occurred in 24 PMs out of a total of 624 PMs, accounting for 3.8 %, and in 8 ICDs out of a total of 185 ICDs, accounting for 4.3 %. The most prevalent device malfunction was reduced ventricular/atrial sensing posing 41 % of malfunctions. The findings also support previous research and expert consensus statements that show neutron-producing radiation and the associated beam energy are the most important predictors of CIED malfunction. Due to the proximity of the CIED to targeted cancer and potential therapy interference, 11 PMs representing 1.8 %, needed relocation. There was no need to relocate any of the ICDs.

Conclusion: Device errors are found in 2% to 7% of individuals undergoing RT. Malfunctions are more common in patients receiving high beam energy over 10 MV. However, several factors such as RT treatment technique, total device radiation dose, and anatomic location of the treated site have all been postulated as risk factors for device failure severity and frequency.

Table 21- Zagzoog et al., 2021

Criteria	Answers (yes, no, unclear, not eligible)	Comments
1. Is the patient sample representative of the population?	Yes	
2. Are all patients implanted with the same CIED?	No	Patients had PMs or ICDs and were divided accordingly
3. Was there an estimative treatment dose?	Yes	570 patients received low beam energy < 10MV while 189 received doses > 10MV
4. Were patients submitted to the same dose?	No	
5. Are the results evaluated using objective criteria?	Yes	
6. Was the monitoring of participants carried out for sufficient time?	Yes	
7. Were the CIEDs revised prior to exposition?	Yes	Clinical and device-related data were collected for all patients with CIEDs retrospectively who underwent RT for cancer between 2007 and 2018
8. Were participants analyzed based on device dependence?	Unclear	

6 DISCUSSION

The initial objective of this research was to evaluate the incidence of cardiac electronic devices malfunctions when undergoing radiotherapy with the help of search engines and a compilation of a literature review. The results of the presented studies have shown that the incidence of device malfunction can be affected by the radiation dose the device received. In the first study by Hurkmans 2012, for being a literature review itself, the results presented were more complex in interpretation. It did not clearly give percentages of the total study's results compared to more recent findings. I created a table based on the results that presented the direct relation of the radiation dose the devices were exposed to, corroborating with previous observations that the amount of radiation the device receives intrinsically influences device malfunctions even from doses as low as 0,11Gy. The second study by Gomez 2013 reported that in a total of 42 patients, CIED resets occurred in around 20% of patients undergoing proton beam therapy to the thorax and recommends avoiding it in pacing-dependent patients. In the third study that I examined by Grant 2015, in a total number of 286 patients that underwent 249 courses of photon- and electron-based RT CIED malfunction was reported in 18 courses, with 15 CIEDs having single-event dysfunction and 3 exhibiting transient signal interference in 178 courses of non–neutron-producing RT, no single-event dysfunctions was discovered. However, the findings in this study did not support the previous results on the interconnection between the incidence of failure and the dose the CIED was exposed to, reporting no consequences in doses up to 5,4Gy. The rest of the courses were not specified, but the final result included a rate of 21% for neutron-producing RT and 0% for non–neutron-producing.

The findings from the fourth study by Zaremba 2016, as well as the sixth by Tajstra 2019 and the eleventh by López-Honrubia 2020, reported malfunctions of CIEDs even when exposed to low-level radiation exposures supporting the first presented study. On the other hand, most of these failures occurred during high-energy photon RT; malfunctions seemed of little risk in radiotherapy with kV photons or electrons. The exposition to radiation of 5Gy, determined malfunctions on 16.7% of the gadgets, and the number of PMs impacted by an error when exposed to doses of 2 Gy was 11.5%. Radiation treatment of 82% of the patients was reported with no dysfunction, and 18% presented a rise in the threshold and a dramatic decrease in the duration of the battery; these were reported respectively.

Concerning the fifth study by Zecchin 2016 that used phantoms with similar human-tissue composition, a software error was observed in 52% of ICDs and 18% of PMs, posing a higher risk of malfunction compared to human in vivo studies.

In the seventh presented study by Riva 2018, nearly 2% of patients with CIEDs sustained device damage. All were high-risk patients, raising the previously mentioned possibility that the patient's dependency directly influences the malfunctions on the device and whether the patient's patient belongs to low, medium or high-risk category. There was a reported incidence of malfunctions of about 15% in neutron-producing RT and 4.1% chest–neck RT. The eighth study by Yeung 2019 presented 2.1% of device malfunction in 189 patients with CIEDs. They had a total of 297 courses of RT, while the ninth study by Brouillard 2019, based on the largest cohorts at the time, reported a total of 18 incidents (7.8 %) observed in 16 patients. The tenth study by Sharifzadehgan 2020 reported CIED malfunctioning in 5 patients (6%), the primary reason being backup mode resetting in 80%.

Conversely, all results must be interpreted with caution due to the lack of unanimity of the examined factors. The study by Malavasi 2020 presented in its results two malfunctions in 37 patients who received neutron-producing RT, representing 5.4%, and one malfunction out of 102 patients who received non-neutron-producing RT, representing 1% supporting previous findings on the correlation of incidence and neutron-producing therapy compared to non-producing. Lastly, the most recent and largest presented study investigating such malfunctions by Zagzoog 2021 compared to the others presented important overlooked factors such as sex and age, proposing not only that men are more prone to present malfunctions than women but also that older patients present a higher incidence of CIEDs malfunction than younger ones with the median age being around 79 years, reporting a total of 2.5% of malfunctions after receiving low-beam energy of less than 10MV and 9.5% malfunctions in high-beam energy over 10MV. Zagzoog 2021 also reported that the strongest malfunction predictor, supported by Grant 2015, Riva 2018 and other recent studies, is neutron-producing radiation.

7 CONCLUSION

This thesis aims were to present a review on the consequences of radiation therapy on pacemakers and cardioverter-defibrillators and provide updated recommendations and guidelines for the understanding of the device-radiation interaction as well as better patient care. The research part was developed with the help of literary sources focusing on determining the incidence of CIEDs malfunctions induced by radiotherapy.

The information used to develop this thesis was obtained mainly from professional articles and medical journals. The sources used were both in English and Czech.

Data has shown that radiation in patients with pacemakers can cause chemical changes in the PMs structure and electrical energy disturbances during the treatment. Although several elements were identified as risk factors, such as RT treatment modality, total device radiation dose, and anatomic location of the treated site, there is still a lack of information on the correlation of these factors among themselves and the malfunction incidence. For this reason, it is difficult to determine a safe radiation dose to avoid device dysfunctions.

A European survey found that only 39% of radiation oncology departments have policies regarding CIEDs, and 18% manipulate CIEDs without collaboration with cardiac electrophysiologists despite the drastic increase in the proportion of patients with CIEDs undergoing radiotherapy (Zagzoog et al., 2021).

The results highlighted the absence of systematic monitoring and follow-up of CIED patients after or while undergoing radiotherapy. The proposed recommendations included an appropriate evaluation of the devices even months after exposure. Although CIED malfunctions are rare and generally of benign occurrence, a greater knowledge of the potential predictors of malfunction and the creation of evidence-based results would help to optimize patient safety. It is also important to define clear guidelines for radiotherapy procedures in such patients and incentivize multidisciplinary cooperation.

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