Thesis - An investigation into the effects of radiotherapy on implanted cardiac devices

Ph.D – Doctor of Philosophy (Engineering)

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Abstract

Introduction

The number of cancer patients with CIEDs presenting for radiotherapy treatment is increasing. Technological advances in CIEDs have now made them more sensitive to ionising radiation and electromagnetic interference (EMI) than older bipolar semi-conductor devices. External beam radiotherapy has the potential to cause CIED malfunction, this might be temporary but nevertheless, could result in catastrophic failure of the cardiac conduction system of the heart. It is not possible to predict the exact behaviour of a CIED when it is within, or close to, the radiotherapy treatment field. Published literature is inconsistent in its findings regarding the safe levels of ionising radiation dose delivered to CIEDs. The aims of this research are to determine the effects of ionising radiation and electromagnetic interferences upon CIEDs and leads.

Method

This research will adopt an experimental approach to data collection, under laboratory conditions, when CIEDs and CIEDs leads are exposed to ionising radiation and EMI.

Results

The scientific arm of this research focused on the effect of ionising radiation and EMI on CIEDs and CIED leads. The results showed that CIEDs exhibited a range of temporary and permanent malfunctions when exposed to cumulative ionising

radiation doses ranging from 0.5Gy to 3Gy. Results also, recommend that CIED leads should not be in the treatment field however, if this is unavoidable the radiation dose should be kept as low as possible. All CIEDs exhibited an effect when exposed to EMI and it is recommended that all patients with CIEDs receiving radiotherapy treatment should be monitored when in the radiotherapy treatment room.

Conclusion

This research identifies how CIEDs are adversely affected by ionising radiation and / or EMI, how these effects can be minimised, provide safe radiotherapy tolerance doses to CIEDs and issue recommendations for the publication of national guidelines for the safe management of patients with CIEDs undergoing radiotherapy treatment.

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Glossary of terms and acronyms

AAPM	American Association of Physicists in Medicine
AF	Atrial fibrillation
AV block	Atrioventricular block
AV node	Atrioventricular node
BHF	British Heart Foundation
CASP	Critical appraisal skills program
CHD	Coronary heart disease
CIED	Cardiac implanted electronic device
CMOS	Complementary metal oxide semiconductors
COIN	Clinical Oncology Information Network
CRT	Cardiac resynchronisation therapy
CT	Computerised tomography
DC	Direct current
DNA	Deoxyribonucleic acid
DNA	Deoxyribonucleic acid
EBRT	External beam radiotherapy
ECG	Electrocardiogram

EMC	Electromagnetic compatibility
EMI	Electromagnetic interference
ESTRO	European Society for Radiotherapy and Oncology
ETFE	Ethylene tetrafluoroethylene
Gy.	Gray
HCM	Hypertrophic cardiomyopathy
HR	Heart rate
IC	Integrated circuit
ICD	Implanted cardioverter defibrillator
IGRT	Image guided radiotherapy
IMRT	Intensity modulated radiotherapy
IPEM	Institute of Physicists in Medicine
ISO	International standards
LA	Left atrium
LINAC	Linear accelerator – radiotherapy treatment machine
LV	Left ventricle
MeSH	Medical subject headings
MeV	Mega electronvolt
MP35N	Nickel-cobalt base alloy

MRI	Magnetic resonance imaging
MV	Megavolt
NASPE/BPEG Generic	North American Society of Pacing and Electrophysiology (NASPE) and the British Pacing and Electrophysiology Group (BPEG).
NCS	Neurocardiogenic syncope
NICE	National Institute for Health and Care Excellence
OAR	Organ at risk
PM	Pacemaker
PTFE	Polytetrafluoroethylene
QA	Quality assurance
R&D	Research and development
RA	Right atrium
RAM	Random access memory
RCR	Royal College of Radiologists
RCW	Radiotherapy Centre in Wales
ROM	Read only memory
RT	Radiotherapy
RV	Right ventricle
SA node	Sinoatrial node

SF_6	Sulphur hexafluoride
SoR	Society and College of Radiographer
TIA	Transient ischemic attack
TLD	Thermoluminescent Dosimeter
VF	Ventricular fibrillation
VNA	Vector network analyser
VT	Ventricular tachycardia

Thesis - An investigation into the effects of radiotherapy on implanted cardiac devices

Chapter One

Background and setting the scene

1.1 Introduction

This research identifies how cardiac implantable electronic devices (CIEDs) are adversely affected by ionising radiation and / or electromagnetic interference (EMI), how these effects can be minimised, provide safe radiotherapy tolerance doses to CIEDs and issue national guidelines for the safe management of patients with CIEDs undergoing radiotherapy treatment.

This first chapter provides the background for the research and outlines the context of the problem and why this research needs to be carried out. The limitations of the current research and literature are discussed and the contributions are detailed in order to explore the principles and theories, which will underpin the research. This chapter includes the study aims and objectives and the approach to achieving them. It concludes with an overview of the contents of each chapter.

1.2 Background

Cardiovascular disease is a group of disorders of the heart and blood vessels and is the number one cause of death globally. An estimated 17.5 million people died from cardiovascular diseases in 2012, representing 31% of all global deaths (World Health Organisation, 2018). It is also the main cause of death and disability in the UK, but the disease can often largely be prevented with a healthy lifestyle. CIED implantation is indicated for the treatment of a number of cardiovascular diseases. The aim is to maintain the patient's heart rate based on circulatory needs and 'pacing' in a manner that mimics the natural physiology of the cardiac conduction system.

Cancer is the name given to a collection of related diseases that involve abnormal cell growth and results from a series of molecular events that alter the normal properties and functions of cells (Stuart, 2014). There are more than two hundred different types of cancer and this disease can be treated by surgery, chemotherapy, radiotherapy, hormonal therapy and targeted therapy. Cancer is the second leading cause of death globally, with approximately fourteen million new cases in 2012 and the number of new cases is expected to rise by about 70% over the next two decades (Torre et al, 2015). It was responsible for 8.8 million deaths in 2015 or nearly one in six of all global deaths (World Health Organisation, 2018).

Globally, life expectancy has increased by more than 37% in the past century (United Nations, 2017) whilst in the English and Welsh population it has increased by more than 65% in the same period (Office of National Statistics, 2018). One consequence of this is a higher prevalence of cardiovascular morbidity, leading to an increase in the number of patients with CIEDs (Fernandez-Ballesteros et al, 2013 and Last, 1998). In addition, the age-standardised incidence of cancer has increased by more than 25% over the past thirty years (Office of National Statistics, 2016). It has been estimated that 50-60% of all patients with cancer will undergo radiotherapy during the course of their illness (National Radiotherapy Advisory Group, 2007). Therefore, with an ageing population, and an increase in the incidence of both cardiovascular morbidity and cancer, the number of patients with CIEDs presenting for radiotherapy treatment will likely increase (Fernandez-Ballesteros et al, 2013). These patients are therefore experiencing issues in dealing with not one, but two life threatening diseases, whilst also possibly being affected by a third factor, of an iatrogenic basis, whereby the treatment (radiotherapy) for one of those diseases (cancer) may in itself threaten the patient's life by impacting upon the CIED that is treating/controlling their other health (cardiac) condition.

1.3 Context of the research problem

Although most medical treatments pose little danger to the functioning of CIEDs, radiotherapy has the potential to alter CIED function. CIEDs may be affected in two ways: direct damage via ionising radiation and / or by electromagnetic interference (EMI), both of which may cause temporary or permanent CIED malfunction (Last, 1998). Over the past three decades, the demand for smaller, reliable and more energy efficient devices has led to the replacement of bipolar transistors with complementary metal oxide semiconductor (CMOS) components (Hurkmans et al, 2012). As the CIEDs evolved they became more complex in design, have thinner housing, less shielding and limited battery capacity plus a greater sensitivity to ionising radiation than the bipolar semiconductor devices previously used. Thus there is a potential for increased damage and device failure (Little, 1994 and Mouton et al, 2002).

CIED leads are insulated flexible wires that conduct electrical signals from the CIED generator to the heart muscle and relay information concerning the heart's intrinsic electrical activity back to the CIED pulse generator. Although ionising radiation may affect the function of the CIED, CIED leads are considered to be resistant to these effects (Lau, 2008). None of the CIED manufacturers have issued any ionising radiation tolerance doses for CIED leads. CIEDs are afforded some protection against exposure to ionising radiation and EMI, however, the CIED leads still remain vulnerable to noise pickup and the effects of EMI (Tiikkaja et al., 2012).

In discussing CIEDs, leads and their functions, this research looks to provide an understanding of how radiotherapy has the potential to alter CIED function by ionising radiation and / or EMI. It will describe the nature of cancer, the management of cancer patients with CIEDs receiving radiotherapy treatment and any adverse clinical effects that these patients exhibit as a result of exposure of the CIED to

ionising radiation and EMI. The research will also look at the issue of national evidence-based guidelines for the safe management of cancer patients with a CIED receiving radiotherapy treatment in the UK.

1.4 Limitations in research

Research has shown that the CMOS circuits in CIEDs can be more sensitive to ionising radiation than the bipolar semiconductor devices used previously (Little, 1996). However, this increased sensitivity can lead to damage to both the hardware and software components of the CIED (Last, 1998). Mouton et al (2002) state that such damage could be transient, for example, dropped beats, transient inhibition, altered sensitivity, increased or decreased pulse width and frequency or triggering of CIEDs. However, the consequences could be serious and permanent. For instance, severe circulatory damage could potentially lead to a major catastrophic failure of the cardiac conduction system and ultimately death of the patient (Little, 1994).

It is not possible to predict the exact behaviour of any given CIED when it is in, or in close proximity to the radiotherapy treatment field (Solan et al, 2004). In addition, there is limited published research on the effect of ionising radiation and EMI on CIEDs and the published literature is often inconsistent in its findings and recommendations. This research will investigate if there is any evidence to show that radiotherapy and / or EMI can cause device malfunctions or failure with potentially life-threatening consequences.

The American Association of Physicists in Medicine (AAPM) report by Marbach et al (1994) recommends that the maximum dose to a pacemaker should be limited to less than 2Gy. The largest and most comprehensive study to date by Mouton et al, in 2002 supported the AAPM recommendations. In their in vitro study, ninety-six

patients having thoracic radiotherapy treatment whose pacemakers were adjacent to the radiotherapy treatment field exhibited a range of short and long-term CIED malfunction side effects. Results showed that one pacemaker exhibited clinically significant disturbances at a cumulative dose of only 0.15Gy, two pacemakers exhibited defects at a dose of 1Gy and nine pacemakers failed at a cumulative dose of 2Gy.

Hurkmans et al (2005) directly irradiated nineteen new pacemakers; the commonest damage reported was loss of output. In contrast to the Moulton study, only one pacemaker malfunctioned below 50Gy, suggesting modern pacemakers may be relatively radioresisitant. Hurkmans et al (2005) concluded that the 1994 AAPM recommendations were still valid. However, a limitation of this study, was that the pacemakers were not returned to the CIED manufacturers for a more detailed analysis after exposure to ionising radiation. Therefore, their conclusions were based on CIED in-house testing data only.

To date, Frizzell (2009) has published the most up to date review of CIEDs and radiotherapy. He made a distinction between pacemakers and ICDs. He further recommended that that the maximum cumulative ionising radiation dose to the ICD should be limited to less than 0.5Gy as a consequence of their increased sensitivity. The evidence and distinction provided by Frizzell, was a major development in the management of patients with CIEDs receiving radiotherapy treatment. He concluded that the 1994 AAPM recommendations are no longer a complete guide and policies need to be updated to reflect advances in CIED technology. Research has shown that there are no national guidelines and that most radiotherapy departments in the UK have neither a formal risk management strategy in place nor a CIED policy (Solan et al, 2004). The AAPM report and Frizzell's recommendations are the basis of most of the current CIED departmental radiotherapy policies in the UK. However,

the AAPM report (Marbach et al, 1994) is more than two decades old and Frizzell's (2009) paper was published in 2009 and these do not reflect recent advances in CIED or radiotherapy technology. When this study started there were no UK or national guidelines on the use of radiotherapy in patients with CIEDs and most radiotherapy departments had no formal risk management strategy or appropriate policy in place. Therefore, there was a need for the research in order to provide accurate, up to date and evidence-based guidelines on CIEDs and safe radiotherapy tolerance doses. This research must be carried out in collaboration with CIED manufacturers and a cardiology department. CIED manufacturers will provide CIEDs, leads, testing equipment, detailed analysis of any abnormalities detected and their expertise in evaluating any changes or damage to the CIEDs and leads. The expertise of a cardiology department will provide a clear understanding of the cardiac implications to the CIED, leads and the patient. This holistic approach will provide a comprehensive understanding of the management required for patients with CIEDs receiving radiotherapy treatment.

1.5 Original contributions to the area of research

The starting point of this research was to ascertain an understanding of the CIED policies in use in UK radiotherapy departments, what these policies were based on and how they were implemented or even if such policies existed. In order to achieve this, the researcher carried out the first national audit of radiotherapy department CIED policies.

- Previous studies investigated the effect of ionising radiation and EMI on CIEDs. As part of this research project, this is the first study to investigate the effects of only EMI on CIEDs

- Current literature and advice from CIED manufacturers, consider CIED leads to be resistant to the effect of ionising radiation, therefore this is the first research project to investigate the destructive effect ionising radiation has on CIED leads.

- As a result of the development and improvement in CIED technology, rate response activated CIEDs are increasingly being implanted in patients for the management of their cardiac conditions. However, there is no research into the effect of ionising radiation and / or EMI on these devices. This is the first research conducted to investigate such effects.

- Results from the research project provided evidence to support recommendations for the safe management of patients with CIEDs receiving radiotherapy treatment. Based on the researcher's knowledge and expertise in this field, they were invited to chaired a multi-disciplinary working party comprising clinical oncology, cardiology, therapeutic radiography and medical physics to develop guidelines for the management of these patients. These guidelines are the first comprehensive recommendations provided to UK radiotherapy departments and resulted in a major change in current clinical practice. These guidelines have been supported by all disciplines involved and their professional bodies (The Royal College of Radiologists, the Society and College of Radiographers and the Institute of Physics and Engineering in Medicine).

1.6 Study aims and objectives

Aims:

- To determine the effect of ionising radiation and EMI on CIEDs and leads
- To provide data to support the implementation of UK guidelines for the safe management of cancer patients with CIEDs receiving radiotherapy treatment

Objectives:

- To establish current UK practice regarding the management of patients with CIEDs receiving radiotherapy treatment
- To determine the effects of ionising radiation and EMI on patients with CIEDs receiving radiotherapy treatment at a radiotherapy centre in Wales (RCW)
- To evaluate the relationship between cumulative ionising radiation dose and EMI and damage sustained to CIEDs
- To evaluate the relationship between cumulative ionising radiation dose and EMI on the physical condition of the leads
- To determine whether there is a safe minimum radiation tolerance dose to CIEDs and leads
- To determine the effect of ionising radiation and EMI of rate response activated CIEDs

This research adopted an experimental approach to data collection. Due to the nature and involvement of ionising radiation in the research, at this stage it would be inappropriate to expose patients to the ionising radiation doses and EMI levels required to investigate the destructive effects upon the CIEDs and leads by ionising radiation and EMI. The research was therefore conducted under laboratory conditions.

1.7 Outline of the chapters

Chapter Two – Cardiovascular diseases, the cardiovascular system and CIEDs.

This chapter aims to put into context why an increasing number of patients with CIEDs are presenting to UK radiotherapy departments for radiotherapy treatment. It describes the nature of cardiovascular disease, the range of cardiovascular diseases and the symptoms related to these conditions. It then outlines the components and functions of the cardiovascular system and discusses the role of the heart, blood vessels and blood within this system. This chapter details the sequence of mechanical and electrical events that make up the cardiac cycle and how this is represented in a normal electrocardiogram (ECG) trace. It also explores the clinical indications for CIED implantations and how these conditions are represented on abnormal ECG traces. In describing the CIED hardware, there is a basis to compare any damage to such hardware as a result of ionising radiation and / or EMI; this being one of the main aims of the research. This chapter concludes that with an increasing number of patients with CIEDs presenting for radiotherapy treatment, further research is needed to identify and quantify the effects of ionising radiation and EMI on CIEDs and the specific hardware components.

Chapter Three – Cancer and the effect of ionising radiation and EMI on CIEDs

This chapter aims to put into context the effect of ionising radiation and EMI on CIEDs and the associated leads. It discusses the role and function that radiotherapy plays in the management of patients with cancer and detailing the radiotherapy planning and treatment delivery process. It provides an analysis of how ionising radiation and EMI causes CIED malfunctions and discusses the affect and impact on both the CIED and the patient. It will also explore the safety recommendations and guidelines that have been previously issued for treating patients with cancer and concludes that the policies that are in place are based on evidence, which is twenty-

three years old and does not reflect advances in CIEDs or radiotherapy technology and treatments.

Chapter Four – Research methods

This chapter formulates the research questions and objectives that led to the development of the research design and the research studies. The purpose of this chapter is to outline and explain the reasoning and approach by which the research was undertaken. The chapter will describe the choice of research approach and research method to establish current UK practice regarding the management of patients with CIEDs undergoing radiotherapy treatment. It will then detail the choice of research approach and present the research design for the three scientific studies investigating the effect of ionising radiation and EMI on CIEDs and CIED leads. The chapter will discuss the choice of research approach when conducting a systematic review to determine current 'gold standard' practice for the safe management of patients with a CIED receiving radiotherapy treatment.

Chapter Five - Test compliance, knowledge, understanding and perception

This chapter will consider current UK practice regarding the management of patients with CIEDs undergoing radiotherapy and compare this practice to current 'gold standard' evidence-based guidelines. The chapter details the findings of the national audit and reinforces the principle that patients with CIEDs are being put at significant risk of harm when exposed to ionising radiation and EMI when receiving radiotherapy treatment. In this chapter, the results from two clinical audits carried out RCW are documented. It details the observed clinical reactions in patients and discusses the need for research into the effect of ionising radiation and EMI on these contemporary CIEDs as part of the PhD.

Chapter Six – Scientific Research

Chapter six presents the findings of the studies, analyses the study's results and discusses the mechanisms that cause CIED malfunctions and or failure. In reporting CIED malfunctions and failure the effect of radiotherapy treatment and the clinical impact to the patient will be discussed. Recommendations regarding radiotherapy tolerance doses to all CIEDs will be made.

Chapter Seven – Research outcomes

Chapters five and six discussed the results and conclusions from the PhD research project. This chapter details how the results from these studies informed recommendations and guidelines for the management of patients with CIEDs receiving radiotherapy treatment. A multidisciplinary working party was then established to publish evidence-based guidelines for the management of such patients. This chapter documents the theoretical background upon which the national guidelines are based and presents the guidelines developed and published based on this research.

Chapter Eight – Final remarks

Chapter eight summarises the key findings of the research, relates these findings to the implications for theory and practice, outlines the limitations of the research and offers recommendations for future work.

Chapter Two

Cardiovascular disease, the cardiovascular system and CIEDs.

2.1 Introduction

CIED implantation is indicated for the treatment of a number of cardiovascular diseases. This chapter describes the nature of cardiovascular disease, the range of cardiovascular diseases and the symptoms related to these conditions. This research investigated whether ionising radiation and / or EMI can have an adverse effect on the CIED implanted in patients being treated for cancer and cause subsequent damage to their cardiac conduction system. This chapter outlines the components and functions of the cardiovascular system and discusses the role of the heart, blood vessels and blood within this system. It details the sequence of the mechanical and electrical events that make up the cardiac cycle and how this is represented in a normal electrocardiogram (ECG) trace.

CIEDs aim to maintain the patient's heart rate based on circulatory needs and pacing in a manner that mimics the natural physiology of the cardiac conduction system. This chapter explores the clinical indications for CIED implantations and how these conditions are represented on abnormal ECG traces. CIEDs provide electrical stimuli to cause cardiac contraction during periods when intrinsic cardiac electrical activity is inappropriately slow or absent. The type of CIED implanted depends on the patient's symptoms and their specific heart condition. Research has shown, that in clinical practice, there are two main types of programming for CIEDs; demand pacing and rate-responsive pacing (Dell'Oca et al, 2004).

The remainder of this chapter describes the CIED hardware and provides a basis to compare any damage to this hardware as a result of ionising radiation and / or EMI; this being one of the main aims of the research.

2.2 Cardiovascular disease

Cardiovascular disease is a collective term for conditions affecting the heart or blood vessels and comprises many conditions including coronary heart disease, heart failure, heart rhythm problems (arrhythmias), cardiomyopathy, congenital heart disease, peripheral vascular disease and stroke (Mendis et al, 2017).

Coronary heart disease (CHD)

CHD also known as ischaemic heart disease is a major cause of death both in the UK and worldwide (Shepard et al, 2015). CHD is the term that describes what happens when the heart's blood supply is blocked or interrupted by a build-up of fatty deposits (atheroma) in the coronary arteries. Over time, the walls of the arteries can become ‘furred up’ with these fatty deposits (Mendis et al, 2017). The two major forms of CHD are angina and heart attack (acute myocardial infarction). Angina is a chronic condition where short episodes of chest pain occur periodically, caused by a temporary shortage of blood supply to the heart. While it is not usually life threatening it can be associated with increased risk of heart attack. A heart attack is caused if a piece of atheroma breaks off, this leads to a blood clot (blockage) forming. Should this clot block the coronary artery and cut off the supply of oxygen-rich blood to the heart muscle, the heart may become permanently damaged and suffer a loss of function (Romero et al, 2015). A CIED is inserted if the patient is at risk of a cardiac arrest, as the heart’s electrical signals cause the heart to stop beating altogether.

Heart failure and cardiomyopathy

Heart failure is a life-threatening condition that occurs when the heart is unable to maintain a sufficient enough blood flow to meet the body's needs (McMurray, 2012). Heart failure can result in shortness of breath, chronic tiredness and a reduced ability to carry out physical activity (Fox et al, 2001). A study in 2008 by Epstein et al, showed that there is considerable evidence that the use of biventricular pacing, by providing cardiac resynchronisation therapy (CRT), reduces heart failure symptoms and lowers heart failure mortality with or without an ICD. The New York Heart Association classification system (The Criteria Committee of the New York Heart Association, 1994) also recommends that patients who have symptoms and are classified as class III or class IV undergo CRT implantation. At classification III patients have a marked limitation of physical activity, comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnoea. At classification IV patients are unable to carry out any physical activity without discomfort. Symptoms of heart failure at rest and if any physical activity is undertaken, discomfort increases.

Cardiomyopathy is a general term for diseases of the heart muscle and occurs when the heart muscle (walls of the heart chambers) becomes stretched, thickened, enlarged or stiff (NHLBI.nih.gov, 2018). Consequently, there is a reduction in the effectiveness of the heart as it impairs the heart's ability to pump blood around the body. Cardiomyopathy and heart failure commonly occur together. Guidelines published by Gersh et al in 2011, document the indications for CIED implantation for patients with cardiomyopathy depending on the classification of the disease. For patients with Class I, and Class II, CIED implantation is indicated.

Congenital heart disease

Congenital heart disease is a general term for a range of birth defects that affect the heart or blood vessels that is present from birth (NHLBI.nih.gov, 2018a). It is one of

the most common types of birth defect, affecting up to nine in every one thousand babies born in the UK (Nhs.uk, 2018b). It may include abnormalities of the heart or heart valves, such as a hole between chambers of the heart, or narrowing of major blood vessels, or a combination of disorders.

Peripheral vascular disease

Peripheral vascular disease is a blood circulation disorder that causes the blood vessels outside of the heart to narrow, block or spasm. This can be caused by blockage of arteries due to cholesterol or fatty substances or caused by widening of the arteries such as the aorta, which in severe cases can lead to rupture of the arterial wall (NHLBI.nih.gov, 2011). Peripheral vascular disease typically causes pain and fatigue, often in the legs, especially during exercise. Treatment for peripheral vascular disease includes balloon angioplasty, stent implantation or atherectomy (a catheter is used to remove plaque inside a blood vessel).

Stroke and transient ischemic attack (TIA)

A stroke occurs when the artery supplying blood to the brain either suddenly becomes blocked or begins to bleed. This may result in part of the brain dying, leading to sudden impairment of one or more capacities (for example speaking, thinking and/or movement) (NHLBI.nih.gov, 2018c). A transient ischemic attack (TIA) or ‘mini stroke’ is caused by a temporary disruption in the blood supply to part of the brain, this disruption results in a lack of oxygen to the brain. This can cause sudden symptoms similar to a stroke, such as speech and visual disturbance, and numbness or weakness in the face, arms and legs. However, a TIA doesn't last as long as a stroke, with the effects often only lasting for a few minutes or hours and can be fully resolved within 24 hours (Meschia et al, 2014).

2.3 Cardiovascular system

The cardiovascular system is the transport system of the body and is a complex network consisting of the heart, blood vessels and blood. It is responsible for transporting oxygen, nutrients, hormones, and cellular waste products throughout the body. The body takes oxygen and other nutrients from the blood, while at the same time eliminating waste products like carbon dioxide, transferring them back into the blood, so they can be removed. The heart powers the cardiovascular system, which pumps and dispenses blood to the arteries with the average heart pumping over 5 litres of blood throughout the body every minute (Menche, 2012). Within the cardiovascular system, there are several different transport circuits. The pulmonary circuit transports deoxygenated blood from the right side of the heart to the lungs, where the blood picks up oxygen and returns to the left side of the heart. The pumping chambers of the heart that support the pulmonary circulation loop are the right atrium and right ventricle. The systemic circuit carries highly oxygenated blood from the left side of the heart to all of the tissues of the body. Systemic circulation removes waste products from body tissues and returns deoxygenated blood to the right side of the heart. The left atrium and left ventricle of the heart are the pumping chambers for the systemic circulation loop (Guyton and Hall, 2000).

Functions of the cardiovascular system

The cardiovascular system has three primary functions: transportation of materials, protection from pathogens, and regulation of the body's homeostasis.

- **Transportation:** The cardiovascular system transports blood, which contains nutrients and oxygen and removes carbon dioxide and waste products. Hormones are also transported throughout the body via the blood's liquid plasma.

- **Protection:** The cardiovascular system uses white blood cells to protect the body. These cells clean up cellular debris and fight pathogens that have entered the body. Platelets and red blood cells form barriers to seal wounds and prevent pathogens from entering the body and liquids from leaking out. Blood also carries antibodies that provide specific immunity to pathogens that the body has previously been exposed to or has been vaccinated against.

- **Regulation:** The cardiovascular system contributes to the body's ability to maintain homeostatic control. Blood vessels help maintain a stable body temperature by controlling the blood flow to the surface of the skin. Blood also helps balance the body's pH due to the presence of ions, which act as a buffer solution. In addition, the albumins in blood plasma help to balance the osmotic concentration of the body's cells by maintaining an isotonic environment.

The heart

The heart is a muscular pumping organ located medial to the lungs along the body's midline in the thoracic region. The bottom tip of the heart (apex), is turned to the left, so that about 2/3 of the heart is located on the body's left side with the other 1/3 on the right side (Betts et al, 2013). The top of the heart (heart base) connects to the great blood vessels of the body: the aorta, vena cava, pulmonary trunk, and pulmonary veins. The pericardium is the fibrous covering, which encapsulates the heart, securing it in place but allowing it to move as it beats (Dorland, 2012). The wall of the heart itself is made up of a specialised muscle called cardiac muscle.

The heart has two sides, the right and left which each have two chambers, a top chamber and a bottom chamber. The two top chambers are known as the left and right atria, which receive blood from different sources. The left atrium receives blood from the lungs and the right atrium receives blood from the rest of the body. The

bottom two chambers are known as the left and right ventricles. The ventricles pump blood out to different parts of the body. The right ventricle pumps blood to the lungs while the left ventricle pumps blood to the rest of the body. The ventricles have thicker walls than the atria, which allow them to perform more work by pumping out blood to the whole body. Valves control the flow of blood, insuring that it flows in one direction. Each heartbeat results in the simultaneous pumping of both sides of the heart, making the heart a very efficient pump.

Blood vessels

Blood vessels are a series of elastic tubing that allow blood to flow quickly and efficiently from the heart to every region of the body and back again. The size of blood vessels corresponds with the amount of blood that passes through the vessel (Nichols et al, 2011). All blood vessels contain a hollow area called the lumen through which blood flows. Around the lumen is the wall of the vessel, which may be thin in the case of capillaries or very thick in the case of arteries. All blood vessels are lined with a thin layer of simple squamous epithelium known as the endothelium that keeps blood cells inside of the blood vessels and prevents clots from forming. The endothelium lines the entire circulatory system, all the way to the interior of the heart, where it is called the endocardium.

Blood

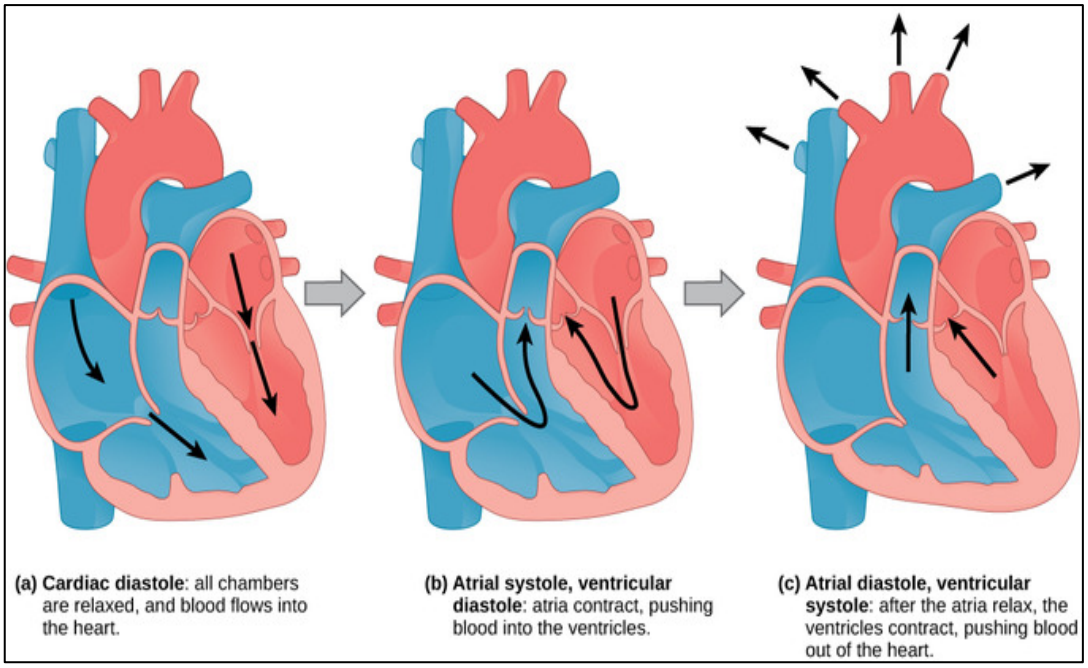
The average human body contains about 4 to 5 litres of blood. As a liquid connective tissue, it transports many substances through the body and helps to maintain homeostasis of nutrients, wastes, and gases. Blood is made up of red blood cells, white blood cells, platelets, and liquid plasma (Boron et al, 2016).

2.4 Cardiac cycle

The cardiac cycle refers to the sequence of mechanical and electrical events that repeats with every heartbeat and is measured on the basis of systole and diastole. Systole is the period in which the heart is pumping blood and diastole is the period in which the heart is resting as well as filling up with blood (Boron et al, 2016).

At the beginning of the cardiac cycle, both atria and ventricles are in diastole. During this time, all the chambers of the heart are relaxed and receive blood and the atrioventricular valves are open. Atrial systole follows this phase; the left and right atria contract at the same time and push blood into the left and right ventricles. The next phase is ventricular systole; the left and right ventricles contract at the same time and pump blood into the aorta and pulmonary trunk. In ventricular systole, the atria are relaxed and receive blood and the atrioventricular valves close immediately after ventricular systole begins to stop blood flowing back into the atria. However, the semilunar valves are open during this phase to allow the blood to flow into the aorta and the pulmonary trunk. Following this phase, the ventricles relax and ventricular diastole occurs. The semilunar valves close to stop the blood from flowing back into the ventricles from the aorta and pulmonary trunk. The atria and ventricles are in diastole together and the cycle begins again (Bloch et al, 1998). The cardiac cycle is coordinated by a series of electrical impulses that are produced by specalised pacemaker cells found within the sinoatrial node and the atrioventricular node.
The cardiac muscle is composed of myocytes, which initiate their own contraction without the help of external nerves. The duration of the cardiac cycle is the reciprocal of heart rate. Assuming a heart rate of seventy-five beats per minute, each cardiac cycle takes 0.8 seconds (Boron et al, 2016).

Figure 2.1: Diagrammatic representation of the stages of the cardiac cycle



(Macmillanhighered.com, 2018)

Components of the heartbeat

The adult heart beats around seventy to eighty times a minute at rest. On listening to the heart, with a stethoscope, the heartbeat is audible. The sound is usually described as 'lubb-dupp'. The 'lubb' also known as the first heart sound, is caused by the closure of the atrioventricular valves. The 'dupp' sound is due to the closure of the semilunar valves when the ventricles relax (at the beginning of ventricular diastole). Abnormal heart sounds are known as murmurs. Murmurs may indicate a problem with the heart valves.

2.5 The Electrocardiogram (ECG)

The heart has an inbuilt rhythm of contraction and relaxation and a small group of specialised heart muscle cells called pacemaker cells help achieve this. The pacemaker cells generate an electrical impulse, which spreads over the atria, making them contract. The impulse then spreads to the ventricles, causing them to

subsequently contract. Electrocardiography is the process of recording this electrical activity in the heart over a period of time using electrodes placed on the skin. The electrodes detect tiny electrical changes on the skin that arise from the heart muscle's electrophysiological pattern of depolarising and repolarising during each heartbeat (Ye et al, 2012).

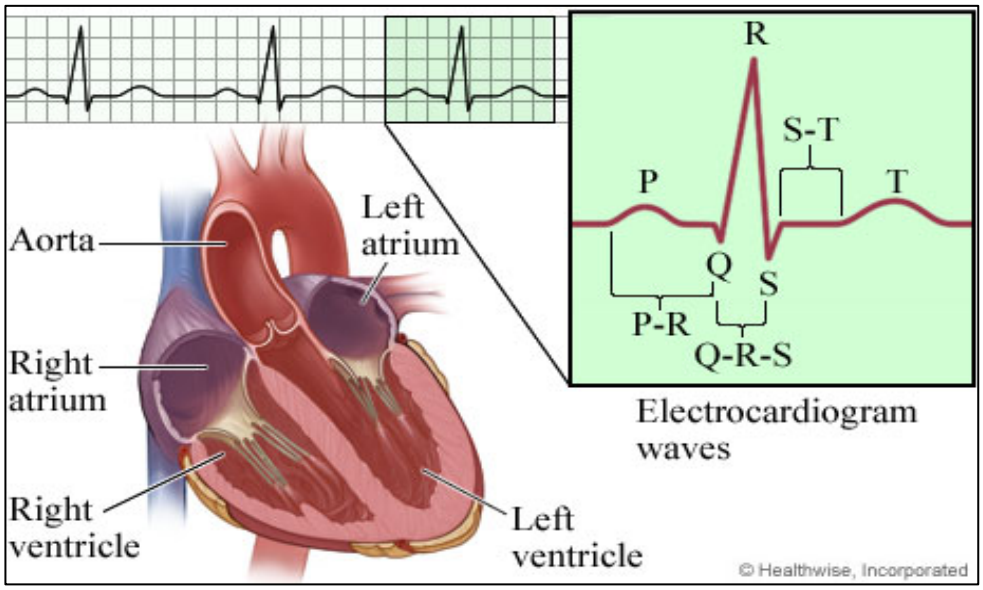
During each heartbeat, a healthy heart has an orderly progression of depolarisation that starts with pacemaker cells in the sinoatrial node, spreads out through the atrium, passes through the atrioventricular node and spreads down and throughout the ventricles. This orderly pattern of depolarisation gives rise to the characteristic ECG tracing. In a 12-lead ECG, ten electrodes are placed on the patient's limbs and on the surface of the chest. The overall magnitude of the heart's electrical potential is then measured from twelve different angles ('leads') and is recorded over a period of time (usually ten seconds). The results show the overall magnitude and direction of the heart's electrical depolarisation captured at each moment throughout the cardiac cycle (Ye et al, 2012). The graph of voltage versus time produced by this non-invasive medical procedure is referred to as an electrocardiogram (ECG).

An ECG conveys a large amount of information about the structure of the heart and the function of its electrical conduction system (Walraven, 2010). It can be used to measure the rate and rhythm of heartbeats, the size and position of the heart chambers, the presence of any damage to the heart's muscle cells or conduction system, the effects of cardiac drugs and the function of implanted pacemakers (Mabel and Braunwald, 2012).

Sinus rhythm is the name given to the normal rhythm of the heart where electrical stimuli are initiated in the sino-atrial (SA) node, and are then conducted through the

atrio-ventricular (AV) node and bundle of His, bundle branches and Purkinje fibres (Walraven, 2010). Depolarisation and repolarisation of the atria and ventricles show up as three distinct waves on ECG. A unique labelling system is used to identify each. Each ECG cycles consists of five waves: P, Q, R, S, T corresponding to different phases of the heart activities.

Figure 2.2: Diagrammatic representation of the heart (including the heart chambers) and the appearance of a standard ECG trace



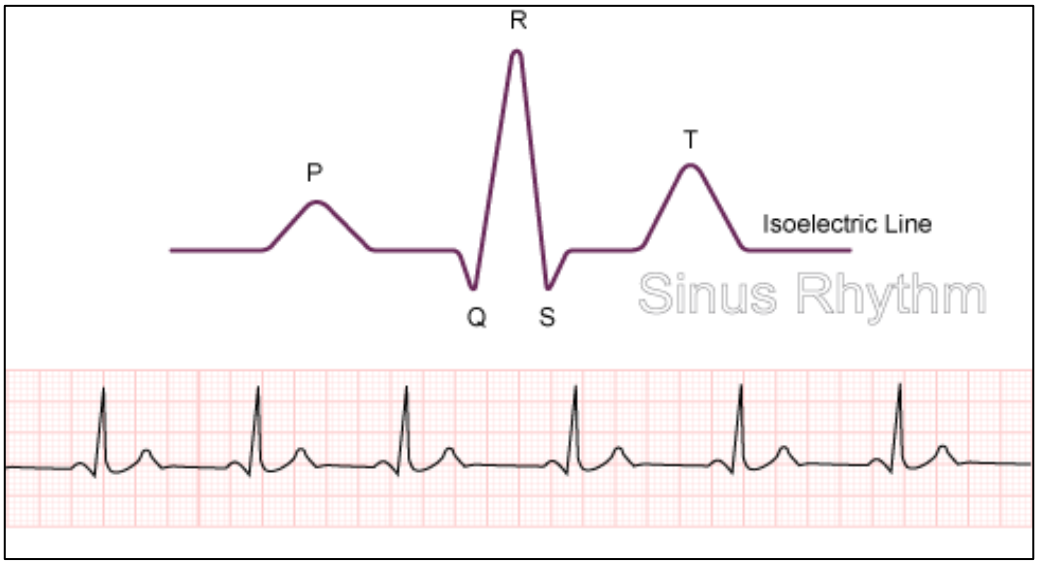
(ECG Research, 2010).

The electrocardiogram translates the heart's electrical activity into line tracings on paper. The spikes and dips in the line tracings are called waves.

- The **P wave** is a record of the electrical activity through the upper heart chambers (atria)
- The **QRS complex** is a record of the movement of electrical impulses through the lower heart chambers (ventricles) – one single heartbeat

- The **ST segment** shows when the ventricle is contracting but no electricity is flowing through it. The ST segment usually appears as a straight, level line between the QRS complex and the T wave.
- The **T wave** shows when the lower heart chambers are resetting electrically and preparing for their next muscle contraction

Figure 2.3: Diagrammatic representation of an ECG trace section, showing the P wave, QRS complex, ST segment and T wave and the ECG appearance of a patient in sinus rhythm



(EKG.Academy, 2018).

The P wave is the first ‘bump’ and is normally an upward ‘bump’ and measures atrial depolarisation. The QRS complex follows the P wave and typically starts with a negative deflection, Q; then a large positive movement, R; and next a negative movement, the S wave. The QRS complex indicates ventricular depolarisation and contraction. Following the QRS complex, the T wave is normally an upward waveform, indicating repolarisation of the ventricles. The PR interval, PR segment, QT interval and ST segment are also evaluated using the ECG analysis in order to determine if the ECG tracing represents a sinus rhythm.

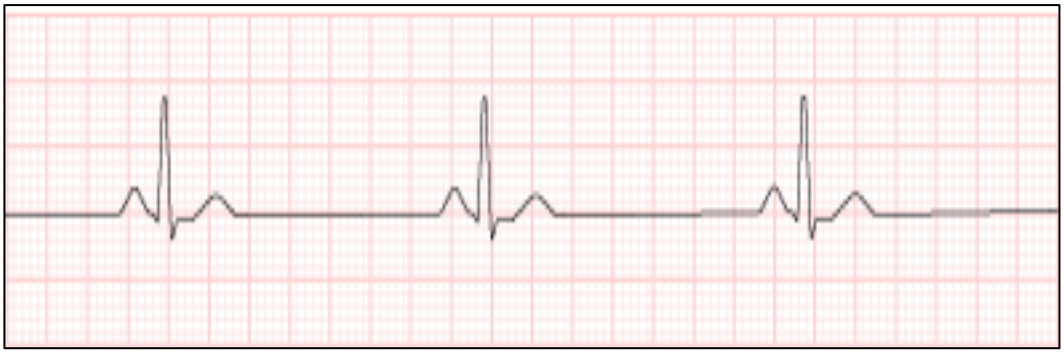
2.6 Clinical indications for CIED implantation

Approximately twenty-five thousand people in the UK have a CIED fitted each year (Townsend, 2014). However, Dr Francis Murgatroyd, Chair of the British Heart Rhythm Society Audit Committee and Clinical Lead of the Cardiac Rhythm Management audit (National Audit of Cardiac Rhythm Management Device, 2016) in 2016 said: "Pacemakers are implanted in patients to prevent the heart beating too slowly or stopping, which can cause blackouts. Although the number of pacemakers implanted has increased by 25% over the last twelve years, in line with an ageing population, the UK remains somewhat below the European average for implants, suggesting that many patients that need pacemakers are not receiving them." (British Heart Rhythm Society, 2016). CIED implantation is indicated for the treatment of a number of cardiovascular diseases for example sick sinus syndrome, heart (AV) block, cardiomyopathy and cardiac arrhythmias.

Sinus bradycardia

Sinus bradycardia defined as a sinus rhythm with a resting heart rate of 60 beats per minute or less. However, few patients actually become symptomatic until their heart rate drops to less than 50 beats per minute. The decreased heart rate can cause a decreased cardiac output resulting in symptoms such as light-headedness, dizziness, hypotension, vertigo and syncope (Wung, 2016). The action potential responsible for this rhythm arises from the sinus node and causes a P wave on the surface ECG that is normal in terms of both amplitude and vector. The presence of sinus bradycardia in itself does not cause a change in the QRS complex and T wave. For this condition a pacemaker will stimulate the heart to speed up when it beats too slowly or it will substitute for the natural pacemaker cells of the heart (SA node) or the heart tissue that regulates the beating of the ventricles (AV node).

Figure 2.4: ECG trace of a patient with sinus bradycardia



(Practical Clinical Skills, 2017)

Heart block

Heart block,is the second most common reason for pacemaker implantation (NHS.uk, 2017). Heart block, also called atrioventricular block (AV block) is a common problem affecting the heart's electrical system and is one of the two major causes of bradycardia (slow heart rate). In heart block, the heart's electrical impulses (responsible for telling the heart when it is supposed to beat) are partially or completely blocked as they attempt to travel from the atria to the ventricular chambers of the heart. If heart block is severe, it may slow the heart rate to dangerously low levels (Fuster et al, 2006).

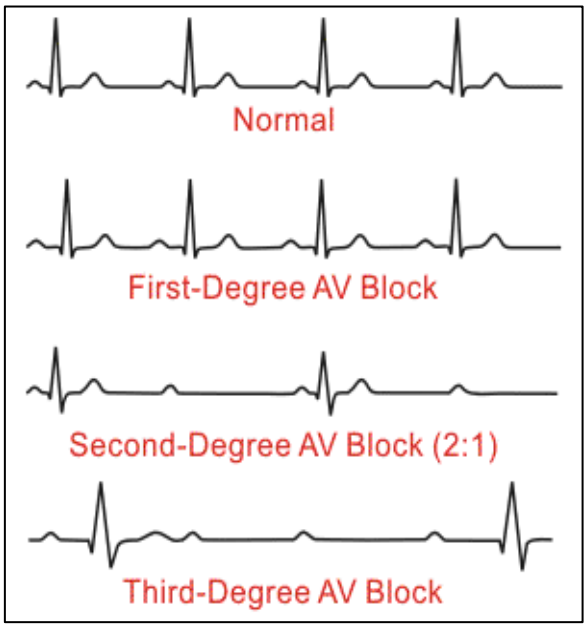
The three types of heart block are first degree, second degree and third degree, with first degree the least severe and third degree the most severe.

- **First-degree heart block -** The heart's electrical signals are slowed as they move from the atria to the ventricles resulting in a longer, flatter line between the P and the R waves on the ECG. First-degree heart block may not cause any symptoms or require treatment.

- **Second-degree heart block –** The heart's electrical signals between the atria and ventricles are slowed to a large degree with some signals not reaching the ventricles. On an ECG, the pattern of QRS waves doesn't follow each P wave. If an electrical signal is blocked before it reaches the ventricles, they won't contract and pump blood to the lungs and the rest of the body.

- **Third-degree heart block –** None of the heart's electrical signals reach the ventricles and this can be deemed as complete heart block or complete AV block. In this instance, certain areas in the ventricles may create electrical signals to cause the ventricles to contract. However, this natural backup system is slower than the normal heart rate and isn't coordinated with the contraction of the atria. On an ECG, the normal pattern is disrupted.

Figure 2.5: Diagrammatic representation showing the difference in appearance on ECG trace of patients with first degree, second degree and third degree heart block



(Unm.edu, 2016)

The severity of heart block can result in a range of symptoms, for example no symptoms experienced to dizziness, syncope (loss of consciousness) or even death. Heart block that is severe enough to produce symptoms, or that threatens to become that severe, can be successfully treated with a CIED. Brief episodes of heart block are not always dangerous, or even abnormal, however, heart block can occur with various cardiac diseases, especially coronary artery disease, heart failure or myocarditis. Evidence shows, when heart block is produced by heart disease, it means there is a permanent disorder of the cardiac electrical system. This kind of heart block often gets worse over time, requiring CIED implantation (Fuster et al, 2006).

Hypertrophic cardiomyopathy (HCM)

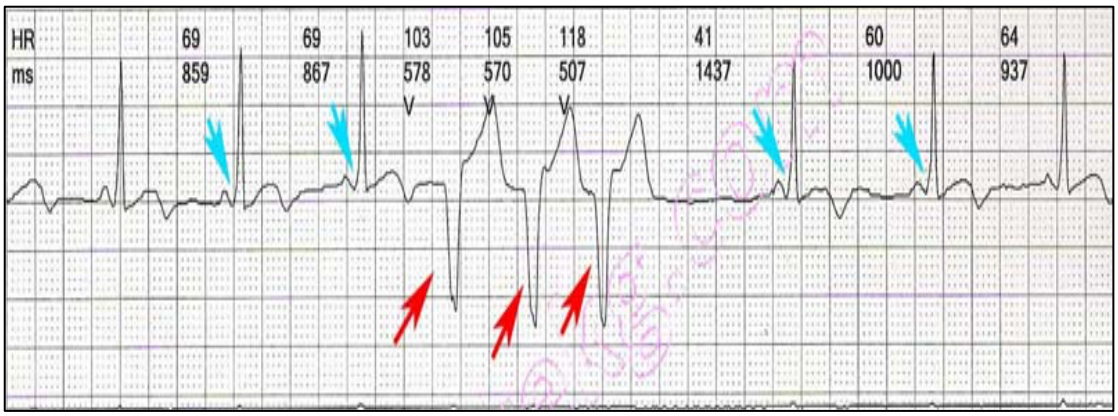
HCM is an inherited disease of the heart muscle (myocardium), where the muscle wall of the heart becomes thickened, most commonly at the septum between the ventricles, below the aortic valve. This leads to stiffening of the walls of the heart and abnormal aortic and mitral heart valve function, both of which may impede normal blood flow out of the heart. The thickness of the muscle and the extent, to which it is affected, varies from one person to another (Bhf.org.uk, 2017). In the majority of people, the left ventricle is almost always affected, and in some people the muscle of the right ventricle also thickens. The area of heart muscle that is affected by HCM and the degree of stiffening that occurs will determine the symptoms for example, shortness of breath, chest pain, palpitations, light headedness and fainting. In other cases, a number of other conditions can develop; these may include abnormal heart rhythms, or arrhythmias, including heart block and endocarditis.

Treatment of HCM depends on whether there is narrowing in the path that blood takes to leave the heart (called the outflow tract); how the heart is functioning; and if arrhythmias are present (Elliott et al, 2016). The purpose of treatment is to prevent symptoms and

complications and these include risk identification and regular follow-up, lifestyle changes, medications, and medical procedures. Patients at risk of life-threatening arrhythmias or sudden cardiac death with HCM, require an ICD to be implanted. The ICD constantly monitors the heart rhythm and when it detects a very fast, abnormal heart rhythm, it delivers an electrical shock to the heart muscle to cause the heart to beat in a normal rhythm again.

On the ECG trace below, the red arrows show a ventricular tachycardia (VT) attack in a patient with HCM. If the patient has an ICD, the device will detect this episode and deliver the appropriate shock therapy.

Figure 2.6: ***ECG trace showing a patient with hypertrophic cardiomyopathy (HCM)***



(Metealpaslan.com, 2015)

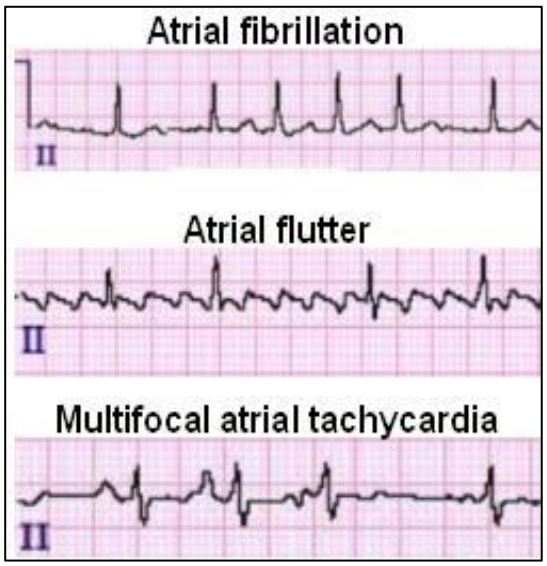
Neurocardiogenic syncope (NCS)

A drop in blood pressure quickly followed by faster then slower heart rate causes NCS. This results in poor blood and oxygen flow to the brain, which causes a temporary loss of consciousness. NCS is also referred to as vasovagal syncope or fainting. Pacemakers are indicated for patients with frequent NCS who experience bradycardia (Chen-Scarabelli and Scarabelli, 2004).

Atrial tachyarrhythmia

Arrhythmia is the most common reason for pacemaker implantation (nhs.uk, 2018b). One of the most common types of arrhythmia is atrial fibrillation (AF), which occurs in the atria of the heart. The electrical impulses normally originate at the SA node, however in AF, many electrical impulses are conducted randomly and rapidly throughout the atria to the ventricles. The resulting heartbeat is fast and irregular. When the atria are beating rapidly and irregularly (fibrillating) they are unable to completely empty all of the blood they receive into the ventricles, causing blood clots to form in some patients (Katz et al, 2015). If the patient's AF conditions has proved difficult to treat, the implantation of a pacemaker in conjunction with in atrioventricular (AV) node ablation is recommended, this will regulate the heart rate and provide symptomatic relief.

Figure 2.7: ECG trace showing patients with atrial tachyarrhythmias (atrial fibrillation, atrial flutter and multifocal atrial tachycardia)



(healio.com, 2012).

2.7 Cardiac implantable electronic devices (CIEDs)

The primary functional challenge for CIEDs is to maintain heart rate based on circulatory needs and pacing in a manner that mimics the natural physiology of the cardiac conduction system. CIEDs also maintain a minimum heart rate to avoid symptomatic or potentially life-threatening bradyarrhythmias or cardiac resychronisation between the left and right ventricles in patients with heart failure. In a healthy heart, the sinus node is controlled by the automatic nervous system and the heart rate is determined by a number of factors, such as physical activity, emotion and blood pressure. The heart rate is controlled by the CIED discharge rate and the excitation and conduction sequence are dependent on the placement of the pacing electrodes within the heart. The need for CIEDs increased as the clinical indications for implantation extended from atrioventricular (AV) disturbances to the management of people with sinus node dysfunction.

NBG Code

CIEDs are classified by the nature of their pacing mode. Classification follows the NASPE/BPEG Generic (NBG) Pacemaker Code developed by the North American Society of Pacing and Electrophysiology (NASPE) and the British Pacing and Electrophysiology Group (BPEG) but was last revised in 2002 (Bernstein et al, 2002). The code is expressed as a series of up to five letters to indicate the device pacing and sensing functions, as well as rate response and programming capabilities.

Figure 2.8: Table to show revised NASP/BPED Generic (NBG) Pacemaker Code

I	II	III	IV	V
Chamber(s) Paced	Chamber(s) Sensed	Response to Sensing	Rate Modulation	Multisite Pacing
O = None	O = None	O = None	O = None	O = None
A = Atruim	A = Atrium	T = Triggered	R = Rate Modulation	A = Atrium
V = Ventricle	V = Ventricle	I = Inhibited		V = Ventricle
D = Dual (A + V)	D = Dual (A + V)	D = Dual (T + I)		D = Dual (A + V)

Pacing Clin Electrophysiol. 2002 Feb;25(2):260-4

(Bernstein et al, 2002).

The five positions NBG Pacemaker Code:

- Position I: Chambers paced - Refers to the chambers paced
- Position II: Chambers sensed - Refers to the location where the CIED senses native cardiac electrical activity
- Position III: Response to sensing - Refers to CIEDs response to sensed native cardiac activity

  - T = Sensed activity results in triggering of paced activity

  - I = Sensed activity results in inhibition of pacing activity
- Position IV: Rate modulation - Indicates ability for rate modulation designed to alter heart function appropriately to meet physiological needs for example, during physical activity. Sensors may measure and respond to variables including vibration, respiration, or acid-base status.
- Position V: Multisite pacing - Allows indication of multiple stimulation sites within one anatomical area, for example more than one pacing site within the

atria or biatrial pacing. The fifth position is used by ICDs and their ability to pace or shock patients out of tachyarrhythmias.

2.8 Role of CIEDs

CIEDs provide electrical stimuli to cause cardiac contraction during periods when intrinsic cardiac electrical activity is inappropriately slow or absent. Pacing systems consist of a pulse generator and pacing leads. CIED output generally stimulates the cavity of the right atrium and / or right ventricle. A CIED consists of a battery, a computerised generator and wires with sensors (electrodes) at the tip. The battery powers the generator and a thin metal case surrounds both. The wires connect the generator to the heart.

Figure 2.9: Image of a CIED – Pacemaker and Lead

(Medtronic.com, 2017)

Figure 2.10: Image of a CIED – ICD and lead

(Medtronic.com, 2018)

The electrodes detect the heart's electrical activity and send data through the leads to the computer in the generator. If the heart rhythm is abnormal, the computer will direct the generator to send electrical pulses to the heart via the CIED leads. Modern CIEDs have the ability to monitor blood temperature, breathing and can adjust the heart rate to changes in activity. The CIEDs' computer can also record the heart's electrical activity and heart rhythm.

2.9 Programmable CIED functions

The two main types of programming for CIEDs are demand pacing and rate-responsive pacing. Demand pacing CIEDs monitor the patient's heart rhythm and only send electrical pulses to the heart if it is beating too slowly or if it misses a beat. A rate-responsive pacing CIED will speed up or slow down the patient's heart rate depending on how active they are (Kalahasty and Ellenbogen, 2011). The type of CIED implanted depends on the patient's symptoms and on their specific heart condition.

Pacing

Pacing refers to the regular output of electrical current, for the purpose of depolarising the cardiac tissue in the immediate vicinity of the lead, with resulting propagation of a wave of depolarisation throughout that chamber (Kusumoto and Goldschlager, 1996). A CIED will pace at a certain frequency, or rate, for example, 60bpm. This rate is programmable, that is, it can be changed by using the manufacturer's programmer.

Sensing

The heart's intrinsic electrical activity transmits a small electrical current, through the CIED leads, to the pulse generator. This current can be registered or sensed by the CIED circuitry. CIED sensing describes the response of a CIED to intrinsic heartbeats. The P waves, or atrial activity, are transmitted through the atrial lead to the atrial channel of the CIED and sensed as atrial activity. Ventricular activity (the QRS complex) is transmitted through the ventricular lead to the ventricular channel of the CIED and this is sensed as ventricular activity. For electrical activity to be transmitted from the heart to the CIED, a closed electrical circuit must be present. The programmed sensitivity setting indicates the minimum intra-cardiac signal that will be sensed (seen) by the CIED to initiate the CIED response (inhibited or triggered) (Kalahasty and Ellenbogen, 2011).

Inhibition of output

A CIED can be programmed to inhibit pacing if it senses intrinsic activity, or it can be programmed to ignore intrinsic activity and deliver a pacing stimulus anyway. If a CIED is set so that it can be inhibited by intrinsic beats, then the CIED will not deliver a stimulus if it senses an intrinsic beat at the correct time (Atlee and Bernstein, 2001). For example, if a CIED is set to pace in this way at 60bpm, it will deliver a pacing stimulus only if an intrinsic beat does not occur within one second of the last

sensed or paced beat.

Triggered pacing

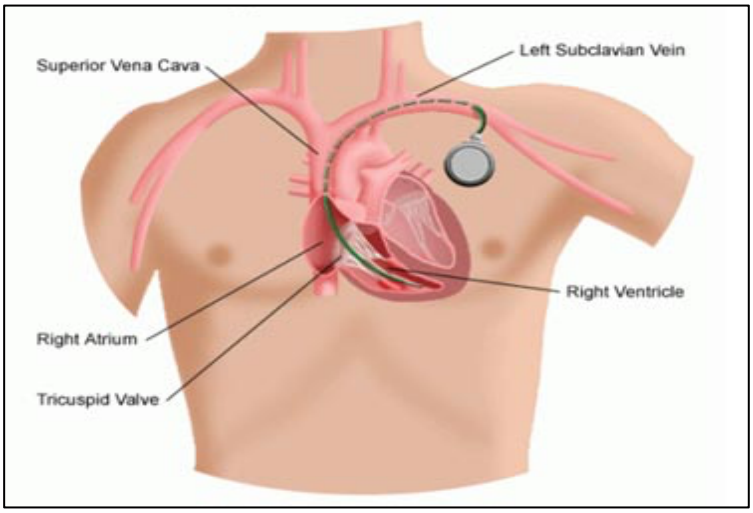
CIEDs can be programmed to deliver a pacing stimulus whenever intrinsic activity is sensed. This type of pacing is most often used in dual chamber pacemakers, that can be programmed to sense activity in one chamber (usually the atrium) and deliver a pacing stimulus in the other chamber (usually the ventricle) after a certain time delay (Atlee and Bernstein, 2001). This is known as triggered pacing. When referring to the appearance of this type of pacing on telemetry or ECGs, it is said that the ventricle is tracking the atrium, because if the atrial rate becomes faster, the ventricular pacing rate will follow faster, in a 1:1 relationship. Thus the exact rate of ventricular pacing will not be determined by any setting on the CIED, but by the patient's own atrial rate.

2.10 Types of CIEDs

Single-chamber pacemakers

Single-chamber pacemakers are the most basic pacemaker design that paces the atrium or ventricle at a fixed rate. The system includes one lead that connects the pulse generator to one chamber of the heart. A single-chamber pacemaker can be used to control heartbeat pacing by connecting the lead to the right ventricle (Zivin and Bardy, 2001).

Figure 2.11: Diagrammatic representation showing a single-chamber pacemaker and where the attached CIED lead is implanted in the heart

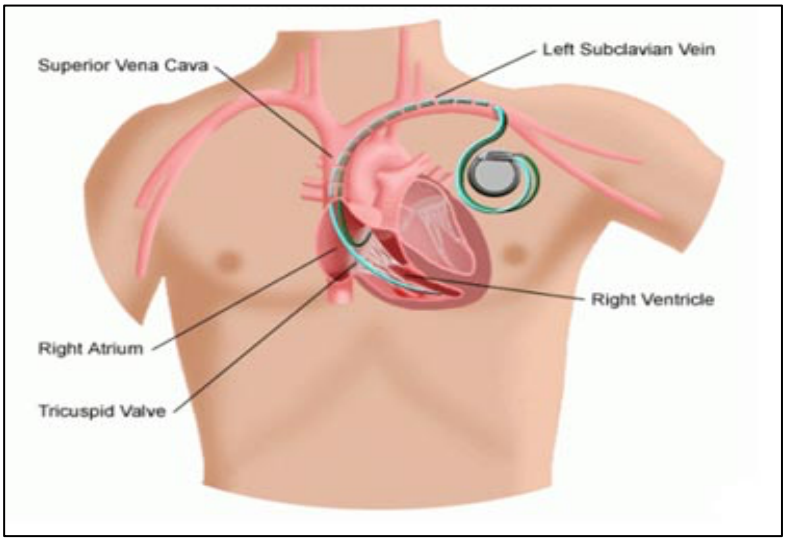


(Consultants and Implantation, 2018)

Dual-chamber pacemakers

Dual-chamber pacemakers are significantly more complex than single-chamber pacemakers; they have pacing electrodes in both the right atrium and the right ventricle. With two leads, the device connects to both chambers on the one side of the heart, allowing them to work together, contracting and relaxing in the correct cardiac rhythm. The contractions allow blood to flow appropriately between the atrium and ventricle. The device can be programmed to regulate the pace of contractions of both chambers. Dual-chamber pacemakers are the most common devices implanted in patients (Zivin and Bardy, 2001).

Figure 2.12: Diagrammatic representation showing a dual-chamber pacemaker and where the two attached CIED leads are implanted in the heart

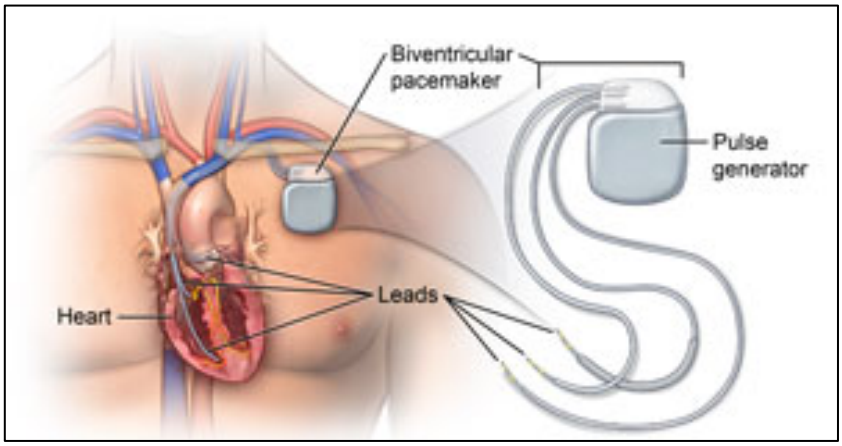


(Uchospitals.edu, 2018)

Biventricular pacemakers

Biventricular pacemakers are also known as a cardiac resynchronisation therapy (CRT) devices. These devices have three leads connected to the right atrium and both ventricles. Biventricular pacemakers are used to treat patients with arrhythmias caused by advanced heart failure, as both the left and right ventricles do not pump at the same time. The pacemaker is programmed to coordinate the contractions of the ventricles, so that they both pump together and this will allow the heart to pump blood more efficiently and can relieve heart failure symptoms. The treatment is known as cardiac resynchronisation therapy because it resynchronizes the ventricles' pumping action (Asirvatham et al, 2007).

Figure 2.13: Diagrammatic representation showing a biventricular pacemaker and where the three attached CIED leads are implanted in the heart



(Baylor College of Medicine, 2014)

Implantable cardioverter defibrillators (ICDs)

ICDs have the ability to defibrillate and pace the heart and have the capability of correcting most life-threatening cardiac arrhythmias. ICD implantation is the first-line treatment and prophylactic therapy for patients at risk for sudden cardiac death due to ventricular fibrillation and ventricular tachycardia. Modern ICDs can be programmed to detect abnormal heart rhythms and deliver therapy via programmable antitachycardia pacing in addition to low-energy and high-energy shocks (Epstein et al, 2008).

The ICD constantly monitors the patient's heart rhythm through the electrodes and if it detects a dangerous or abnormal heart rhythm it can deliver the following therapies:

- **Pacing** - a series of low-voltage electrical impulses (paced beats) at a fast rate to try and correct the heart rhythm
- **Cardioversion** - one or more small electric shocks to try and restore the heart to a normal rhythm

- **Defibrillation** - one or more larger electric shocks to try and restore the heart to a normal rhythm

Rate-response activated CIEDs

One form of cardiovascular disease is chronotropic incompetence, which is the inability of the heart to increase heart rate in line with increased activity or demand. Rate adaptive pacing is a treatment-pacing mode, that has been shown to improve exercise capacity in patients with chronotropic incompetence (Diaz et al, 2005).

A person's normal heartbeat fluctuates depending on activity. When at rest, the heart rate normally slows and then speeds up during times of activity or stress, to meet the increasing demands on the body. Individuals with this abnormality of the cardiac conduction system may be unable to properly speed up the heart rate during activity. This can result in fatigue, shortness of breath, and / or activity intolerance. Rate-adaptive pacing has been designed to increase heart rate according to metabolic needs during physical, mental or emotional activity. Rate responsive CIEDs control heart rate by sensing physiological or non-physiological signals other than atrial rate (Duru et al, 2000).

A rate response activated CIED comprises:

- A sensor for sensing cardiac activity and generating a corresponding cardiac sense signal
- A pace generator for generating pacing signals in response to a command signal
- A metabolic demand sensor for sensing a metabolic demand and generating a corresponding metabolic signal
- A noise sensor for generating a noise signal when sensing noise

- A controller receiving the sensor, metabolic and noise signals and generating a command response

Rate response activated CIEDs have specialised sensors built into the pulse generator that can sense increasing activity by means of increased body movement (vibrations) and / or increased rate of breathing. The sensors will automatically increase or decrease the heart rate according to the body's needs. Rate responsive pacing closely mimics the normal heartbeat and the sensors should reproduce the sinus node as close as possible.

All rate adaptive CIEDs should:

1. Program the rate adaptive response output to respond as promptly as the normal sinus node
2. Have sensors which detect of the need of increasing heart rate
3. Increase the heart rate in proportion to the metabolic demand
4. Control the rate decay during recovery after exercise to match metabolic needs
5. Operate in a closed loop system - making rate adaptive pacing also insensitive to inputs not heart related
6. Have dedicated sensors avoiding unwanted over pacing and requiring complex programming

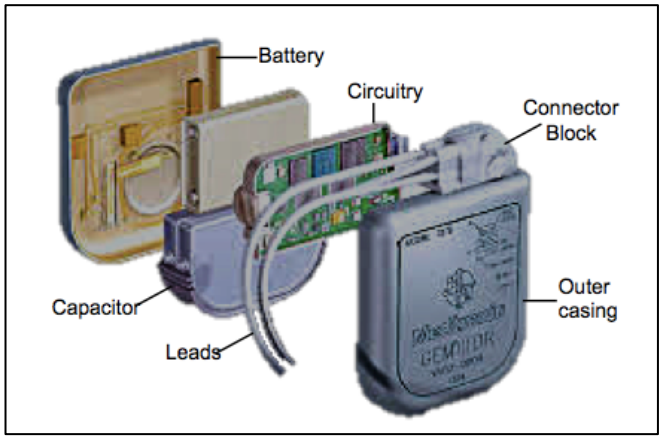
2.11 CIED hardware

A CIED comprises a pulse generator and lead(s) which all have the same basic components (Kalahasty and Ellenbogen, 2011):

- A power source in the form of a battery

- Circuitry (output, sensing, telemetry, microprocessor or micro sequencer, memory)
- A metal casing (can) welded shut to keep out fluids
- A feed through (a piece of wire surrounded by glass or sapphire) that maintains a hermetic seal to provide an electrical connection through the can
- A means of connecting a pacing lead to the header of the CIED
- Sensors (for example, sense acceleration, vibration and impedance)

Figure 2.14: Diagrammatic representation of the CIED hardware enclosed in the outer casing

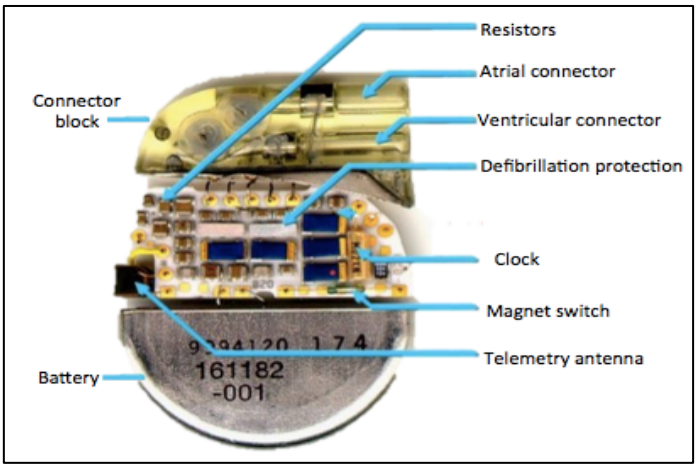


(Clinical Gate, 2015a)

The CIED unit delivers an electrical pulse with the correct intensity to the appropriate location to stimulate the heart at a desired rate. Electrical impulses are transmitted to the heart through the lead, which is attached to the pulse generator via the connector block. A lead is either unipolar or bipolar; a unipolar lead contains one insulated coil, whereas a bipolar lead contains two coils, separated by an inner insulation. An outer insulation shields a lead from the environment. The tip of a lead, which contains an electrode, is implanted into the inner, endocardial surface of the heart. The CIED is usually implanted in the pectoral region, with the lead running through the right subclavian vein to the internal surface of the heart. The casing of

the pulse generator functions as housing for the battery and all other electronic and electrical circuits. A connector block, made of polyurethane is located at the top of the CIED and attaches the CIED to the CIED lead(s).

Figure 2.15: Image of the CIED hardware



(Clinical Gate, 2015)

Pulse generator

The pulse generator is made of a header block, which contains the setscrews for lead connection and a radiofrequency antenna and the device enclosure, which houses the electrical components responsible for generating the pulse (via output circuits) at the required time (via timing and control circuits) based on events sensed (via sensing circuits). It also contains a power supply (battery) and may include components such as telemetry for testability and programmability and memory (random access memory - RAM) to store data for diagnostic purposes (Kalahasty and Ellenbogen, 2011).

Microprocessors

Microprocessors are the standard control circuits of CIEDs, as they have a greater circuit density and greatly reduced current drain than the previously used bipolar devices. Microprocessors allow sophisticated algorithms, requiring multiple

calculations, to be incorporated into implantable devices, and have vastly increased data storage. The microprocessor is constantly accessing its memory for instructions on what to do next. The microprocessor can respond to changes in programming instructions that allow functions to be added or changed after implantation (Kalahasty and Ellenbogen, 2011).

The integrated circuit of pulse generators may contain both read-only memory (ROM) and random access memory (RAM). Almost all manufacturers offer fully RAM-based pulse generators. RAM is used to store diagnostic information regarding pacing rate, intrinsic heart rates, sensor output and intracardiac electrograms from episodes of high atrial or ventricular rates and mode-switching events. The rapidly expanding diagnostic capabilities of CIEDs has allowed for improved assessment of the physiological condition of the patient, including stored information about heart rate variability, respiration, intracardaic pressure, patient activity, lung water and arrhythmia logs.

Circuitry

CIEDs incorporate some of the most advanced, high-reliability electronic circuitry available. The basic building block is the integrated circuit (IC), which starts as a silicon wafer and has a number of miniaturized circuit elements etched into its surface during the manufacturing process. Modern pulse generators incorporate custom-designed, very large-scale integrated circuits. ICs are built up layer by layer and can incorporate millions of electronic elements. The elements are so fine that they can barely be seen with an optical microscope (Kalahasty and Ellenbogen, 2011).

Output circuit

Output circuitry is usually composed of capacitors and electrical switches controlled

by the microprocessor. Output circuitry can deliver voltage in excess of the battery voltage, generally through the use of a charge pump. A charge pump provides the flexibility to program many discrete voltages and also allows for voltage regulation.

Sensing circuit

The sensing circuitry of a pulse generator is used for both the amplification and filtering of intracardiac signals. The intracardiac electrogram is conducted from the electrodes to the sensing circuit of the pulse generator where is it amplified and filtered. The intracardiac electrogram is filtered to remove unwanted frequencies, a process that markedly affects the amplitude of the processed signal. Following filtering of the intracardaic signal, the processed signal is compared with a reference voltage to determine if the signal exceeds a threshold detection level (programmed sensitivity). Signals with amplitudes greater than the sensitivity threshold levels are sensed as intracardiac events, whereas signals of lower amplitude are discarded as noise. Signals that exceed the threshold levels are sent to the timing circuit and logic circuits (Kalahasty and Ellenbogen, 2011).

Most CIEDs also contain noise reversion mode circuits that change the pulse generator to an asynchronous pacing mode when the sensing threshold level is exceeded at a rate faster than the noise reversion rate. The noise reversion mode prevents inhibition of pacing in the presence of electromagnetic interference. The electronic circuitry of the pulse generator must also be protected from the damage caused by overwhelming electrical energy generated in the clinical environment.

Timing circuit

The pacing cycle length and the timing circuit of the pulse generator regulates pulse duration and AV interval. The timing circuit of a pulse generator is a crystal oscillator that generates with a frequency in the kilohertz range. The output of the crystal

oscillator is sent to the digital timing and logic control circuit that operates internally generated clocks at divisions of the oscillator frequency. The output of the logic control circuit is a pulse that triggers the output of the pacing pulse, the blanking and refractory intervals and the AV delay. The timing circuit also receives input from the sense amplifier to reset the escape intervals of an inhibited pacing system or trigger initiation of an AV delay for triggered pacing modes. The pulse generator also contains a rate-limiting circuit that prevents the pacing rate from exceeding the upper limit in the case of a random component failure (Kalahasty and Ellenbogen, 2011). This runaway protection rate is typically in the range of 180 to 220ppm.

Telemetry circuit

Telemetry is the word used to describe measurement at a distance. Programmable pulse generators have the capability of responding to radiofrequency signals emitted from the programmer as well as sending information in the reverse direction, from the pulse generator to the programmer. The pulse generator is capable of both transmitting information from a radiofrequency antenna and receiving information with a radiofrequency decoder (Kalahasty and Ellenbogen, 2011). Telemetry information must be sent as radiofrequency signals or as a pulsed magnetic field. Information is sent from an external programmer to the pulse generator in coded programming sequences with a preset frequency spectrum. Most pulse generators require the radiofrequency signal to be pulsed with a specific frequency in a sequence that is typically sixteen pulses in duration. Thus, the radiofrequency signal is quite precise, decreasing the likelihood of inappropriate alteration of the program by environment sources of radiofrequency energy or magnetic fields. The detected telemetry bursts from the programmer are sent as digital information from the radiofrequency demodulator to the telemetry control logic circuit of the pulse generator. This logic circuit also provides for properly timed pulses to be sent from the antenna of the pulse generator to the programmer. ‘Real-time telemetry’ is the

term used to describe the capability of a pulse generator to transmit information to the programmer regarding measurements of pulse amplitude and duration, lead impedance, battery impedance and delivered current, charge and energy.

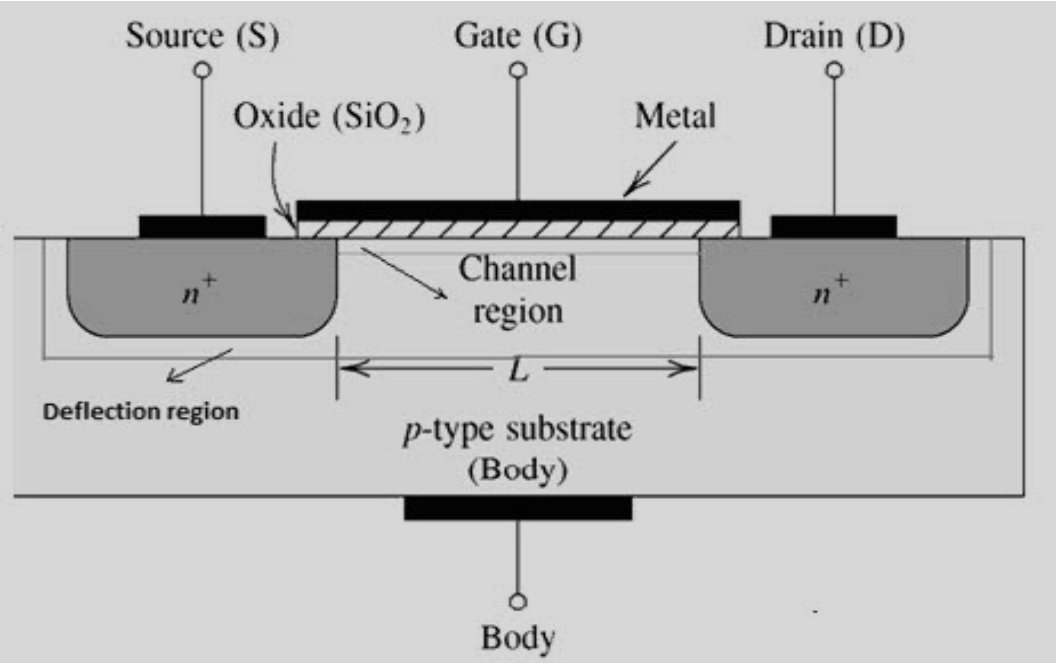
CMOS and MOSFET technology

CMOS and MOSFET technology work on the principle that signals (digital or analogue) are controlled by voltage and charge. This is in contrast to BJT devices that control signals through current flow. A CMOS device generally has a Gate, Source and Drain. The Gate is the terminal that controls the ON or OFF state of the Drain-Source switch. In the steady state, no power is dissipated by the gate and therefore is favourable for low power consumption applications. The conduction channel in a CMOS device is also very thin and can in some cases be approximated by a 2 dimensional electron gas (2DEG). Switching currents in a BJT occupy bulk regions of a semiconductor. CMOS technology is more sensitive to ionising radiation damage. This is because, as already stated, the control of signals as defined by the ON or OFF state of the switch is determined by the presence or absence of charge. A key feature of the Gate is the very thin but highly insulating gate oxide below the gate metal contact. This can be perturbed by ionising radiation in a number of ways:

1. The conductivity of the gate oxide can increase due to defects caused by radiation damage. This induces leakage currents that can impair the performance of the switch.
2. The gate oxide can accumulate embedded charge that, over time, can lock the switch open or closed, independently of applied gate voltage.
3. Embedded charge and increased leakage can increase the time taken to change the state of the switch. Furthermore, the conduction channel relies on a very high degree of purity and crystallinity, of the silicon material. This implies a high mobility for the electrons and holes that traverse this channel. If

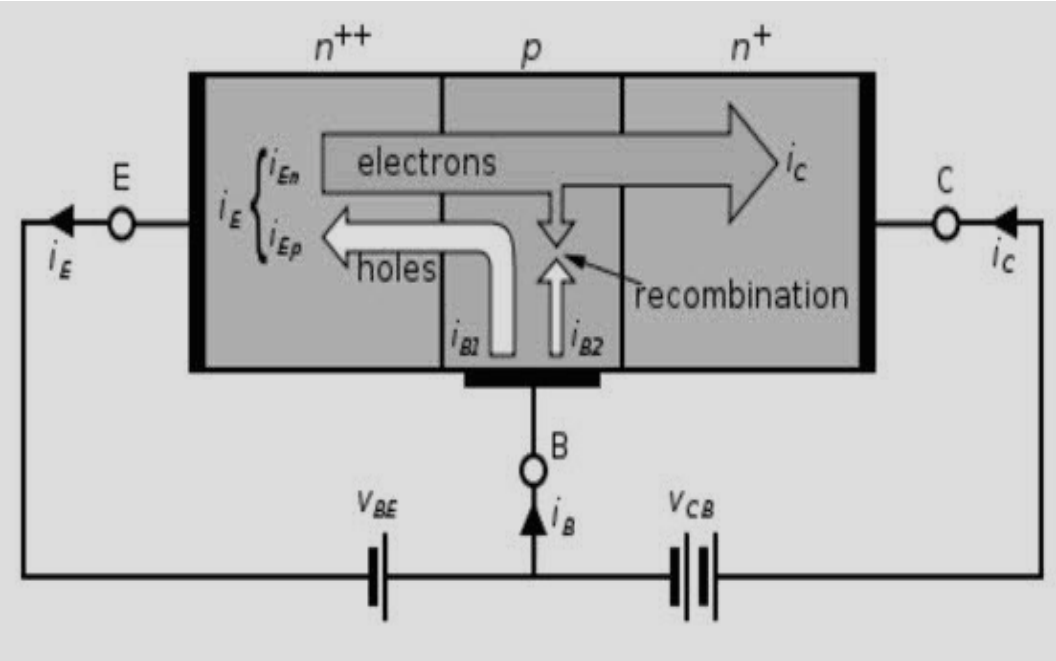
the ionising radiation causes defects to occur in this region, the conductivity of the channel may be impaired.

Figure 2.16: Schematic representation - Showing the working principle of a MOSFET



(Electronic Projects for Engineering Students, 2017)

Figure 2.17: Schematic representation - Showing the working principle of a BJT



(Electronic Projects for Engineering Students, 2017)

Power source (battery)

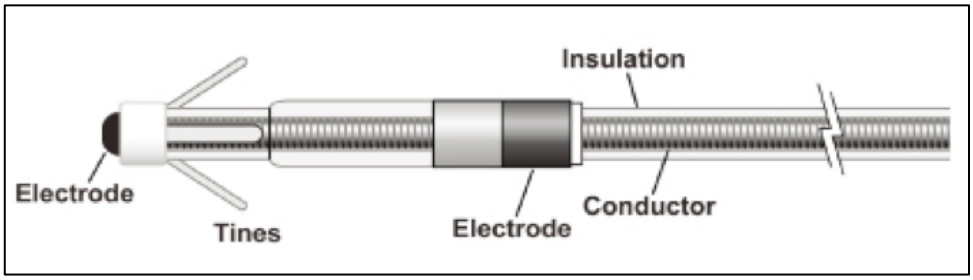
The power source for most CIEDs today is a solid chemical battery, the most commonly used battery chemistry today remains lithium-iodine. However, as CIEDs have become more complicated, their power needs have grown. As a result, the demands on the power source have increased exponentially. Lithium-carbon monofluroide, lithium manganese dioxide and hybrid batteries are increasingly being used in pacemakers (Greatbatch and Holmes, 1992). It is also important to consider the battery as part of the pacemaker and ICD system. The longevity of the battery is dependent on the usage conditions, but also the number and efficiency of the associated components of the integrated circuit boards. Clinically, once a system is implanted, it is important to maximise the longevity of the device by careful programming of outputs and selection of options. The use of capture management features, reducing the frequency of capacitor reformations (ICDs), and programming outputs to clinically safe margins is essential. Disabling unused features, such as

pre-detection electrogram storage, can help preserve battery longevity. All modern devices have an end-of-service indicator that alert the clinicians to impeding battery depletion and allows adequate time for replacement of the device. These indicators include monitored battery voltage, battery impedance and capacitor reformation times (ICDs only) (Boston Scientific, 2012).

2.12 CIED leads

A CIED lead is an insulated conductor cord for transmitting electrical impulses. In a standard pacing or defibrillation lead there are four basic components: conductor elements, insulations, electrodes (screws, rings, dots, coils), and connector pieces.

Figure 2.18: Image showing the components of a CIED lead



(Thoracic Key, 2016)

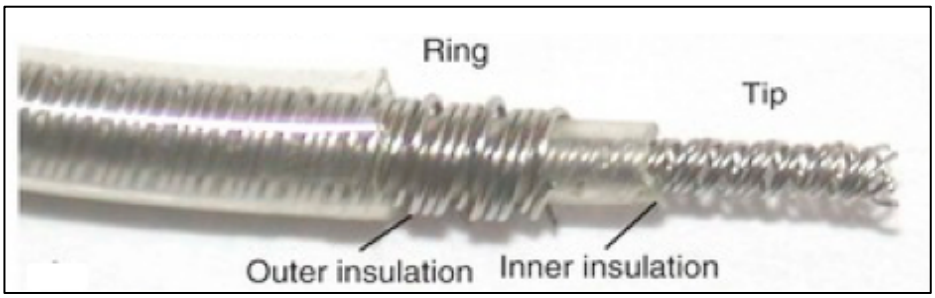
The conductor elements are made of multiple metal wires (fila) wound into interweaving helices (coils) or braided into wire ropes (cables) (Meagher and Altman, 1997). The insulations are made of polymers: silicone (polydimethylsiloxane), poly(ether) urethane, fluoropolymers such as ethylene tetrafluoroethylene (ETFE) and polytetrafluoroethylene (PTFE), and silicone-polyurethane copolymers. The electrodes are made of inert metals (for example iridium, tungsten, platinum) (Lau et al, 2008).

CIED lead design

Unipolar pacing leads have the simplest lead design of all CIED leads. Once unipolar leads was the only option for CIED lead implantation, however, these have been primarily replaced by bipolar CIED leads. Unipolar leads have only one conductor surrounded by insulation. The tip of the lead is the cathode and the CIED generator completes the circuit as the anode (Kalahasty and Ellenbogen, 2011).

In a bipolar pacing CIED lead, the pulse generator is not part of the pace/sense circuit. Both the ring electrode (anode) and the tip electrode (cathode) are in contact with the myocardium. There are two main bipolar CIED lead designs: co-axial and co-radial.

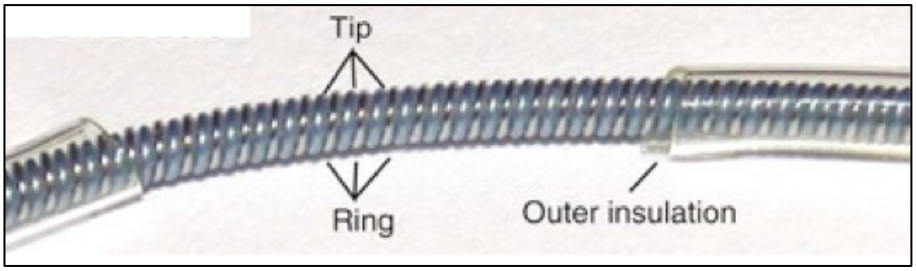
Figure 2.19: Image showing the design of a co-axial CIED lead



(Clinical Gate, 2015b)

In a co-axial lead design, the inner conductor is arranged in a coil and has a central lumen to allow passage of a positioning stylet during the implantation procedure. A layer of insulation covers the inner coil, electrically separating it from the other coil in the lead. The number of metal wires used in the inner and outer coils can be variable, depending on the specifications of the CIED manufacturer. This lead design is an industry standard for most pacing leads (Kalahasty and Ellenbogen, 2011).

Figure 2.20: Image showing the design of a co-radial CIED lead



Clinical Gate, 2015b)

In a co-radial lead design, two conductor strands are coiled in parallel around a central lumen. These strands terminate at the ring and tip electrodes, respectively, and are individually coated with a bonded layer of ethylene tetrafluoroethylene (ETFE) fluoropolymer insulation. The coils are then typically covered with a polyurethane outer layer of insulation (Lau et al, 2008).

ICD leads are more complex and require multi conductors and use a multilumen design with the conductors arranged in parallel rather than co-axial. The components of an ICD lead include the conductors, insulation materials, defibrillation coils, lead electrodes and lead connectors (Kalahasty and Ellenbogen, 2011).

CIED lead materials

Materials used in pacemaker and ICD leads are similar. Although the materials used by each CIED manufacturer are similar, there are significant differences in how these materials are applied and in the construction of the CIED leads (Lau et al, 2008).

Conductors

The primary conductors used in most pacemaker and ICD leads are MP35N and silver (Kalahasty and Ellenbogen, 2011). MP35N is a superalloy that is double melted to remove impurities and it is characterised by biocompatibility, high tensile strength, and resistance to corrosion. Single wires are combined together into

strands and then wound into cables for use as cable conductors. The number of wires used in a cable is directly related to its intended use, with larger cables used for high voltage applications, for example ICDs. Cables can be coated in ETFE fluropolymers before being coiled into co-axial radial lead designs, this coating protects the silicone or polyurethane insulation.

Electrodes

The pacing electrode is the interface between the lead and myocardium. Its design and composition greatly influence the overall electrical performance of the pacing system. The complex, textured surface of current pacing leads minimises the polarisation effect and improves both sensing and stimulation efficiency. The ability to differentiate a true myocardial electrogram from polarisation induced after potentials has dramatically improved with the development of these low-polarisation electrodes (Kalahasty and Ellenbogen, 2011).

Insulation

The materials used in CIED leads for insulation play a vital role in their durability and reliability. The optimal insulation material should be biologically inert and exhibit no surface erosions, no molecular chain disruptions, no uptake of low-molecular-weight biological materials and no tendency to calcifications, while retaining stable mechanical properties. There is no one specified CIED lead insulation material, and some CIED leads use multiple materials. Pacemaker leads are generally made of one insulation type but ICD leads are more complex, utilising a combination of insulation material (Lau et al, 2008).

Fluropolymers are fluorocarbon-based polymers that are characterised by high resistance to solvents, acids and bases. Therefore, they have maximum biocompatibility and tensile strength, but their stiffness limits their use to thin layers of

insulation coating. This coating on the conductors prevents adverse interaction with silicone tubing. Examples of fluoropolymers are PTFE (polytetrafluroethylene) and ETFE (ethylenetertrafluroethylene).

Silicone rubber is a polymer that is made up of silicone-oxygen linkages, that is both biostable and biocompatible. Its main disadvantage is its low tensile strength, making it prone to tearing and abrasion wear. Abrasion wear comes from lead-to-generator and lead-to-lead interactions within the implantation pocket (Himes and Wilson, 2013). Silicone also has a high co-efficient of friction, making it difficult to pass alongside other CIED leads.

CIED developments

In the last decade, CIED technology evolved rapidly with the development of lithium-iodide batteries that have greater longevity (Schmidt and Skarstad, 2001). The need to noninvasively change CIED rate and sensing and pacing parameters led to the development of CIEDs whose functions could be altered with an external programmer using radio-frequency to communicate with the CIED. Further electronic advances led to the development of smaller CIEDs, which utilise integrated circuits as opposed to the discrete components used previously. The advantage of these devices to the patient, is that is occupies a smaller area in the chest cavity. The CIED leads are subject to millions of flexures during their lifetime, therefore the lead materials use silicone and / or polyurethane, which are more biocompatible and reliable than earlier materials. As a result of technical advances, CIEDs are relatively small in size (8-10cc) and can pace reliably for eight to ten years before generator replacement is needed (Zivin and Bardy, 2001).

2.13 Chapter conclusion

This chapter explained the nature and range of cardiovascular diseases and the clinical indications of CIED implantation for patients with cardiac conditions. In discussing CIEDs and their functions, this chapter provides an understanding of the different types of CIED in clinical use and their specific roles. This chapter concluded by detailing the CIED hardware, to provide an understanding how the hardware can be damaged by ionising radiation and EMI in future chapters when the patient receives radiotherapy as part of their cancer treatment.

Chapter Three

Cancer and the effect of ionising radiation and EMI on CIEDs

3.1 Introduction

Cancer is a broad term for a class of diseases characterised by abnormal cells that grow and invade healthy cells in the body. Based upon an overview of current literature, scientific studies and current clinical guidelines for the management of patients with a CIED receiving radiotherapy treatment, this chapter aims to put into context the effect of ionising radiation and / or EMI on CIEDs and CIED leads. It will outline the role and function that radiotherapy plays in the management of patients with cancer and details the radiotherapy planning and treatment delivery process. It then analyses how ionising radiation and / or EMI cause cardiac device malfunctions and discusses the effect and impact on both the CIED and the patient.

In 2013, there were no UK guidelines on the safe use of radiotherapy in patients with CIEDs. Research has shown that patients with a CIED and receiving radiotherapy treatment are at risk of CIED malfunction. This chapter explores the safety recommendations and guidelines that have been issued for treating these patients and shows that the policies that in place are based on evidence which is more than two decades old and does not reflect subsequent advances in CIED or radiotherapy technology and treatments.

3.2 Cancer

Cancer is the name given to a collection of related diseases that involve abnormal cell growth and results from a series of molecular events that alter the normal properties and functions of cells (World Health Organisation, 2018). Typically,

human cells grow and divide to form new ones as the body needs them, as well as replacing older or damaged cells as they die. The normal control mechanisms that prevent cell overgrowth and the invasion of other tissues are disabled in cancer cells, leading to cell mutations. These mutated cells divide and grow as a result of signals that normally impede cell growth. Therefore, they no longer respond to the signals that induce cell growth and division. With growth, these cells acquire new characteristics, for example changes in cell structure, decreased cell adhesion and production of new enzymes. These new characteristics allow the cancer cells to spread and invade other normal tissues (Klein, 2008).

3.3 Management of patients with cancer

As a greater understanding of the underlying biological processes has increased, the treatment of cancer has evolved. As new information about the biology of cancer emerges, treatments will be developed and modified to increase effectiveness, precision, survivability, and quality of life. The general principles for the treatment of cancer are the same, i.e. interruption in function followed by eradication of tumour cells, albeit cancer can develop at many different sites around the body. There are a range of treatments including surgery, chemotherapy, radiotherapy, hormonal therapy and targeted therapy (including immunotherapy, for example monoclonal antibody therapy) (Enger et al, 2006). The choice of treatment is dependent upon the stage of the disease, the location and grade of the tumour and the general medical performance status of the patient, as well as treatment availability and patient choice.

The fundamental aim of treatment is the complete removal of the cancer without damage to the rest of the body, thereby, achieving a cure with minimal adverse side effects to the patient. This can be accomplished by surgery only, but the propensity of cancers to invade adjacent tissue or to spread to distant sites by microscopic

metastasis often limits its effectiveness. Therefore, a variety of treatment modes and techniques are used. The three main techniques used to treat cancer are surgery, chemotherapy, and radiotherapy. They can be used as a single treatment modality or used in conjunction with each other.

Treatment option - Surgery

The aim of surgery can be either the removal of only the tumour, or the entire organ (Subotic et al, 2012). For early stage cancer, surgical removal of a solid tumour is the main treatment. As part of the surgical procedure, some of the normal tissue surrounding the tumour is removed, in order to increase the chances that all cancerous cells are removed from the body. In some cases, the lymph nodes near the tumour are also removed as the cancer can spread to these nodes first. Less frequently, surgery is used to remove tumours that have spread to more distant sites in the body. Examples of surgical procedures for cancer include mastectomy for breast cancer, prostatectomy for prostate cancer, and lung cancer surgery for non-small cell lung cancer. In addition to removal of the primary tumour, surgery is often necessary for staging of the disease and to inform further management and treatment options.

For patients with CIEDs requiring surgery as part of their cancer treatment plan, the primary concern is the management of EMI during the surgical process and the potential damage to the CIED. Madigan et al (1999) published a paper on the surgical management of the patient with a CIED. The aim of the study was to identify the sources of EMI that may alter the performance of CIEDs and develop strategies to minimise their effects on a patient during surgery. The authors stated that all devices should be evaluated pre and post surgery to determine if its function has been damaged or failed. They recommend that if electrocautery is used during surgery, CIEDs should be placed in a triggered or asynchronous mode. Triggered

mode is a pacing mode in which a sensed beat triggers a paced beat. This is most commonly used in dual chamber pacemakers, so that a sensed atrial beat triggers a paced ventricular beat, after an adjustable delay. Asynchronous mode, is a pacing mode that is not inhibited by intrinsic beats. Activating triggered or asynchronous mode, will avoid inhibition due to EMI that could lead to a cardiac arrest rhythm in pacemaker-dependent patients (Madigan et al, 1999). ICDs should have arrhythmia detection suspended prior to surgery and if external defibrillation is to be used placement of the paddles should be kept as far away from the leads as possible. They concluded that patients with CIEDs could safely undergo surgery as long as previously stated precautions are taken (Madigan et al, 1999).

Treatment option - Chemotherapy

Chemotherapy uses one or more anti-cancer drugs as part of a standardised regime to kill cancerous cells. It may be given with a curative intent (which involves a combinations of drugs), or it may aim to prolong life and/or to reduce symptoms (palliative chemotherapy). Conventional chemotherapeutic agents are cytotoxic by means of interfering with cell division and cell growth (mitosis) but cancer cells vary widely in their susceptibility to these agents. The side effects vary with the type of drug used but can include nausea and vomiting, temporary alopecia, constipation, diarrhoea, tiredness, or anaemia (Takimoto and Awada, 2008). The duration of chemotherapy treatment varies depending on the type of cancer and the aim of the treatment.

For patients with CIEDs requiring chemotherapy as part of their cancer treatment plan, the primary concern is the management of cardiotoxic chemotherapeutic agents that may cause an elevation in the cardiac stimulation threshold. That is an elevation in the minimum electrical stimulus needed to consistently elicit a cardiac depolarisation. Each cycle of chemotherapy may cause further increases in the

cardiac stimulation threshold and even cause loss of capture and device failure. CIED manufacturer (St. Jude Medical, 2013) recommends that patients with CIEDs, undergoing chemotherapy with cardiotoxic chemotherapeutic agents should be monitored. If the patient is pacemaker dependent, a full assessment of the cardiac stimulation threshold should be performed. Following completion of chemotherapy a CIED check should be carried out to determine any damage to the CIED.

Treatment option - Radiotherapy

Radiotherapy is the use of ionising radiation to kill cancer cells and shrink tumours. Ionising radiation is directed at cancerous cells and tissue to destroy them or slow their growth and is used in 50-60% of cases where the cancer is cured (National Radiotherapy Advisory Group, 2007). Radiotherapy treatment impairs or destroys cells in the area being treated by either damage to DNA directly or creates charged particles (free radicals) within the cells that can damage the DNA. As a result, it is impossible for these cancer cells to continue to grow and divide. Radiotherapy can be administered externally via external beam radiotherapy (EBRT) or internally by inserting a radioactive source via brachytherapy. There are a variety of options when using radiotherapy. It may be used to shrink a cancer before surgery, or to reduce the risk of a cancer recurring after surgery, and to complement or enhance the effects of chemotherapy or as palliation to relieve symptoms.

3.4 Radiotherapy treatment (External beam radiotherapy treatment - EBRT)

Although ionising radiation damages both cancer cells and normal cells, the majority of normal cells can recover from the effects of ionising radiation and function appropriately. The aim of radiotherapy treatment is to damage as many cancer cells as possible, while limiting harm to nearby healthy tissue. Ionising radiation can

damage cell DNA and result in cell death or inability to reproduce. Normal cells are more able to withstand the damage of ionising radiation, than cancerous cells. By splitting radiotherapy treatments into treatment 'fractions', it is possible to take advantage of the normal cell repair mechanism and inflict damage on the cancer cells while minimising damage to the normal cells. Fractions of radiotherapy are usually delivered in a daily basis with rest days to allow for the healthy tissue to repair and for the patient to recover (Kian, 1998). The precise fractionation of the radiotherapy treatment is vital to the overall radiotherapy prescription. The level of radiation dose to each tumour site depends on the radiosensitivity of the cancer type and whether there are tissues and organs nearby that may be damaged by ionising radiation. There are side effects to radiotherapy treatment but they are localised and confined to the region being treated.

Radiotherapy planning

In the delivery of radiotherapy treatment, there is a compromise between the likelihood of controlling the tumour and cancer cells and the likelihood of causing damage to normal tissues. Individual patient radiotherapy treatment plans are produced to enable the delivery of prescribed ionising radiation to the tumour and the planned radiotherapy treatment site. During the radiotherapy treatment planning process every patient will undergo a planning CT scan or MRI scan. Using these scans, medical physicists and/or therapeutic radiographers will outline the radiotherapy treatment site, anatomical structures, organs of importance and the presence of CIEDs. Certain organs that are in close proximity to the radiotherapy treatment site are designated 'organs at risk' (OARs); these organs need to receive as low an ionising radiation dose as possible to avoid long-term side effects. If the presence of a CIED has been identified from the planning scan, medical physicists will need to adhere to departmental protocols to limit the ionising radiation dose to the CIED. On completion of the radiotherapy treatment plan, verification and

approval by the clinical oncologist, the patient can receive the prescribed radiotherapy treatment.

Linear accelerator (LINAC)

For most patients radiotherapy is administered using a linear accelerator, a machine which uses high-frequency electromagnetic waves to accelerate charged particles such as electrons to high energies through a linear tube. The high-energy electron beam itself can be used for treating superficial tumours, or it can be made to strike a target to produce x-rays for treating deep-seated tumours (Williams and Thwaites, 1995).

Figure 3.1: Image showing a linear accelerator (radiotherapy treatment machine)

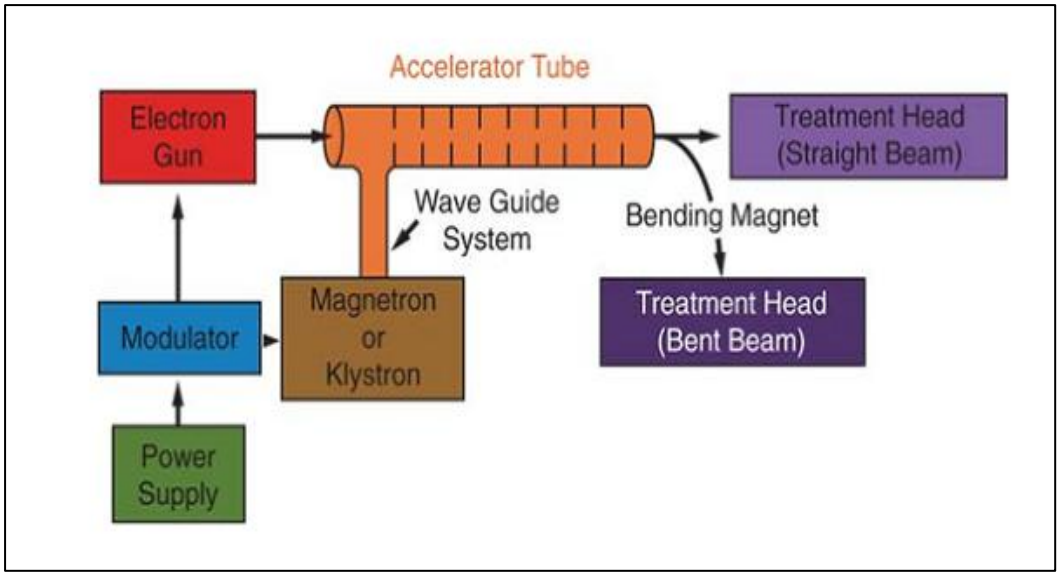
(Varian.com, 2017)

A linac has a power supply that provides DC power to the modulator, which contains a pulse-forming network, which stores electrical energy to provide DC pulses to the thyratron. The thyratron uses these pulses as a switch and delivers the pulses to the electron gun and simultaneously to the magnetron or klystron. The electron gun

produces a stream of electrons that enter the proximal part of the wave-guide with energy of approximately 50keV. The magnetron or klystron produces pulsed microwaves, which are directed into the wave-guide by a hollow rectangular copper piping system, which is filled with SF_6 (Mayles et al, 1999).

The wave-guide is a copper tube with the interior divided by copper discs or diaphragms, and is evacuated to a very high vacuum by an ion pump. Ejected electrons interact with the microwaves produced by the magnetron or klystron, absorb energy and are subsequently accelerated. The wave-guide has side pockets, which have the effect of continuously accelerating the electron down the entire 1-1.5m length of the wave-guide. High velocity energy electrons then exit the thin ceramic window at the end of the wave-guide in the form of a 3 mm 'pencil beam'. If the linac is only required to produce a 4MeV or less photon beam, a short wave guide is required and is vertically mounted so that the exiting beam is directed down onto the patient. For photon beams above 6MeV or higher photon energy, the wave-guide is too short, therefore a longer waveguide is needed which is mounted horizontally, parallel to the patient, thus requiring the beam to be bent in order for it to be focussed onto the patient. Most linacs have a 'bending magnet' to change the electron beam's direction and it does this by applying a magnetic field. After exiting the bending magnet within the linac treatment head, the electrons continue in a straight line. At this point, if electrons are required, the electrons will collide with the scattering foil, which will spread the electron 3mm pencil beam into an electron beam. If photons are required, the electron beam will collide with the tungsten target and because of the velocity of the accelerating electrons, the resulting bremsstrahlung x-ray production will be projected forward (Mayles et al, 1999).

Figure 3.2: Diagrammatic representation showing x-ray production



(Radccore.org, 2015)

It is necessary to shield the linac treatment head with lead to minimise radiation exposure to the patient because of photons that are projected and scattered laterally. Following collision with the scattering foil or tungsten target, two ion chambers are placed to monitor the beam's dose rate, integrated dose and field symmetry. This is to prevent the use of too much radiation and radiation beams that do not meet expected profiles. Below these chambers are the primary, secondary and sometimes tertiary collimators. The primary and secondary collimators are large lead blocks approximately 15cm thick that move on tracks to open a rectangular aperture for the radiation to escape. In addition to these beam-defining devices, the treatment head also has a field light system, which duplicates the radiation beam size, to enable patient set up. There is also an optical distance indicator, which is used to define skin source distance. This is mounted on the gantry, which can rotate around the patient. The patient lies on a moveable treatment couch, which can move in many directions and setups are used to ensure the patient is in the correct position. The ionising radiation beam exits from the gantry of the linear accelerator; this can be rotated around the patient, as documented in the radiotherapy treatment plan. Radiation can

be delivered to the tumour from any angle by rotating the gantry and moving the treatment couch. Engineers have deliberately designed these three movements to occur around axes that all intersect at a common point, which is situated 100cm from the source (the focal point of the radiation beam). This point is called the isocentre (Williams and Thwaites, 1995).

Radiotherapy treatments

The two essential characteristics of a radiotherapy treatment are the localisation of the radiation beam to within the radiotherapy target volume and the amount of radiation dose delivered to this volume. The radiation beam is localised within the radiotherapy target volume using image-guided radiotherapy (IGRT). IGRT is enables the radiographers to visulaise the tumour before treatment commences and uses a cone-beam CT scan with an x-ray tube and detector mounted onto the linear accelerator gantry. This scan will show the size, shape and position of the tumour as well as the surrounding tissues and bones in relation to the radiotherapy treatment field. A comparison is made before each treatment between the scan taken from the radiotherapy planning process and the radiotherapy treatment cone beam CT scan. Treatment cone beam scans can be used to check if the target volume has moved since the previous treatment. Should changes have occurred, the patient can be repositioned so that the radiation treatment is more accurate (Cancerresearchuk.org, 2016).

There are no published guidelines that make recommendations on the potential contribution of imaging techniques to the cumulative ionising radiation dose to the CIED. Murphy et al reported that the dose from a kilovoltage cone beam CT scan is likely to be in the region of 10-80mGy (Murphy et al, 2007). Kan et al reported mean skin doses of 6.4cGy per kilovoltage cone beam CT chest scan (Kan et al, 2008). Even using the lower limit of 10mGy from Murphy et al, it is possible that daily cone

beam CT in a 20-fraction radical lung treatment may contribute as much as 0.2Gy. Using the Kan et al skin dose estimates, it is possible the CIED may receive more than 0.2Gy.

With advances in radiotherapy treatment techniques and equipment, the use of intensity-modulated radiation therapy (IMRT) for treating certain patients with cancer is increasing. IMRT allows for improved 'shaping' of radiation dose profile conformity around the tumour and at-risk nodal structures while sparing adjacent normal tissue structures. IMRT refers to a specific technique of linear accelerator-based radiotherapy whereby radiation beams are modulated in a way to produce highly conformal dose distributions. The intensity of the radiation beam in IMRT can be changed during treatment for the primary objective of reducing radiation dose to selected normal tissue structures in an effort to preserve function, while maintaining full radiation dose to tumour targets. Linear accelerator manufacturers utilise different techniques and methods to achieve particular intensity-modulated fields (Varian.com, 2014).

If the ionising radiation dose to the CIED is within the tolerance dose limits, the main concern for patients receiving IMRT with a CIED is the effect of EMI on the device. A CIED response to EMI is observed clinically when patients experience CIED mediated tachycardia. This effect is primarily observed when the ionising radiation beam is switched ON and OFF. IMRT utilises a greater number radiotherapy treatment beams than conformal radiotherapy treatment. Therefore, advances in radiotherapy treatment machines and radiotherapy planning and treatment techniques have resulted in more patients receiving IMRT as the standard treatment delivery. As a result, the effect of EMI on CIEDs is likely to be clinically observed more frequently. There is a need therefore, to investigate these effects.

Quality assurance (QA)

Within a linear accelerator there are several built-in safety features and measures. These ensure that the linear accelerator will not deliver a higher ionising radiation dose than prescribed, with the machine routinely checked by medical physicists and technicians to ensure it is working correctly. It is a sophisticated piece of equipment that requires several months for installation, acceptance testing and commissioning. The manufacturer's personnel carry out installation, but the acceptance testing and commissioning are the responsibility of the radiotherapy department physicists (Quality Assurance and Radiotherapy, 1996). Patients' treatments do not begin until the unit has been commissioned, that is, the machines performance has been tested and proven to be acceptable, and baseline readings have been taken that will be used as part of the QA programme. Only then can treatment planning and dose calculations for patients' treatments begin (Quality Assurance and Radiotherapy, 1996).

All radiotherapy departments are required to deliver a radiotherapy service to a consistent standard. In the UK this standard complies with the Ionising Radiations Regulations 1999 and the Ionising Radiation (Medical Exposure) Regulations 2000 (Department of Health, 2017). Departments must implement a quality system, which conforms to the EN ISO 9001:2000 (ISO, 2012) international standards. A quality standard is the set of accepted criteria against which the quality of the activity in question can be assessed. Various national and international organisations, such as the World Health Organisation in 1988, American Association of Physicists in Medicine in 1998 (AAPM, 1998), European Society of Therapeutic Radiation Oncology (ESTRO, 1995) in 1995 and Clinical Oncology Information Network (COIN, 1999) in 1999, have issued recommendations for standards in radiotherapy.

The procedure of quality assurance (QA) is defined generally as all those planned and systematic actions necessary to provide adequate confidence that a product or service will satisfy given requirements for quality (Guidance for the commissioning and quality assurance of a networked radiotherapy department, 2006). QA in radiotherapy is defined by all those procedures that ensure consistency of the radiotherapy prescription and the safe fulfilment of that prescription, with regard to the dose to the target volume, together with a minimal dose to normal tissues, minimal exposure of personnel and adequate patient monitoring aimed at determining the end result of treatment (WHO, 1988). It must be stressed that quality assurance in radiotherapy is concerned with all aspects of the radiotherapy process and should involve all groups of staff in a cooperative approach, since quality activities are interdependent (Barrett et al, 1999). Quality control is one part of overall quality assurance. It is concerned with operational techniques and activities used. Its aim is to check that quality requirements are being met and to adjust and correct performance if the requirements are not (AAPM, 1998).

Specific Quality Control protocols are written for each linear accelerator. They have a common basis in that they specify the method of testing and test equipment, the parameters to be tested and the frequency of testing, the responsibilities of different members of staff, the baseline values and tolerances for these values, action levels and documentation guidelines (Leer et al, 1995). A clinical linear accelerator must in all circumstances function within the very narrow tolerances obtained at the time of acceptance testing. The quality of treatment of a patient can be compromised by gross equipment failure as well as by undetected deviation of a single parameter (Williams and Thwaites, 1995). To achieve this, regular quality assurance tests consisting of a variety of mechanical and dosimetric checks are performed. Radiotherapy departments should carry out this programme at the recommended

frequency to maintain conformity with the national standards (Department of Health, 2017). The frequency of testing encompasses daily, weekly and monthly checks as well as extended tests performed annually. Some tests or their frequency may have to be modified to take into account certain unique characteristics of a given linear accelerator. However, these modifications should be made with the intention of improving the QA programme rather than cutting corners (Horiot et al, 1997). All QA measurements must be entered in departmental logbooks. This is important not only in following machine performance over the years but also because it is a legal record that documents the operational health of the machine for any time in which patients were treated. QA programmes should be adapted when the accuracy requirements change, for example in the case of a radiotherapy department deciding to participate in a clinical trial (Horiot et al, 1997).

Patient safety

Patient safety is of paramount importance. Before treatment is delivered to the patient, a treatment plan is developed and approved by the clinical oncologist in collaboration with the medical physicists and/or therapeutic radiographers. The plan is verified and approved before treatment is given and quality-control procedures ensure that the treatment is delivered as planned. The internal checking system within modern linear accelerators does not allow the machine to be turned on unless all the prescribed treatment requirements and parameters are met. During the patient's radiotherapy treatment, the therapeutic radiographer continuously observes the patient using a closed-circuit television monitor. Imaging modalities, for example x-rays or cone beam CT, are taken regularly to ensure that the radiation beam position doesn't change from the original treatment plan. Safety of the staff operating the linear accelerator is also taken into consideration. The linear accelerator is situated in a room with lead and concrete walls so that the high-energy x-rays are shielded. The therapeutic radiographer must turn on the linear accelerator from

outside the radiotherapy treatment room, thereby eliminating the risk of accidental exposure to ionising radiation.

3.5 CIEDs and radiotherapy treatment

Although most medical treatments pose little danger to the functioning of CIEDs, radiotherapy has the potential to alter CIED function. CIEDs may be affected in two ways: direct damage via ionising radiation and by / via EMI, both of which may cause temporary or permanent CIED malfunction (Last, 1998).

Before the 1970's, pacemakers were made up of bipolar semi-conductor devices, which when exposed to therapeutic doses of ionising radiation, were resistant to radiation damage (Sundar et al, 2005). The demand for smaller, reliable and more energy efficient devices has led to the replacement of the bipolar transistors with CMOS components, which have a potential for increased damage and CIED failure (Little, 1994 and Mouton et al, 2002).

3.6 Effect of ionising radiation on CIEDs

Ionising radiation is used in the treatment of cancer. This radiation deposits energy in tumour cells and it directly or indirectly damages the genetic material (DNA) in the individual cells, making it impossible for them to continue to grow.

Ionising radiation can be categorised into two types:

1. **Photon radiation** – x-rays and gamma rays
2. **Particle radiation –** electrons, protons, neutrons, carbon ions, alpha particles and beta particles

Photon radiation is the most common form of ionising radiation used for cancer treatment. Photons, which are 'packets' of energy, destroy cancer cells on the surface of an area or penetrate to tissues deeper in the body, depending on the amount of energy they possess. The higher the energy of the photon beam, the deeper the distance at which the ionising radiation is delivered to the radiotherapy treatment area.

Ionising radiation interferes with the electrical circuits in CIEDs. Modern CIEDs incorporate CMOS circuitry. These circuits comprise doped semiconductor silicon terminals (either negatively or positively doped), with silicon dioxide used as an insulating layers between the various circuitry components. The most sensitive parts of the CMOS structure to ionising radiation are the silicon dioxide layers (Rodriguez et al, 1991). High energy particles and electromagnetic radiation possess enough energy to break atomic bonds and create excess electron-hole pairs in both the silicon semiconductor and silicon dioxide insulator. Within a silicon semiconductor, excess electrons created in the so-called 'conduction band' and the corresponding holes in the so-called 'valence band' rapidly recombine when irradiation stops. In the silicon dioxide insulator, however, the excess electrons in the conduction band soon leave by flow towards the adjacent metal case or the silicon semiconductor, but the holes in the so-called 'valence band' are not very mobile and only respond slowly to an electric field. These holes tend to be attracted to any structural defects within the silicon dioxide and remain there, leading to a build-up of trapped positive charge in the insulator. This leads to the formation of aberrant electrical pathways in the insulator, which may be temporary or more permanent, resulting in a variety of minor or significant malfunctions (Last, 1998). These malfunctions may include altered sensitivity, amplitude changes of electrical signal, telemetry and programming defects preventing reprogramming, or adjustment of function or complete loss of functioning (Hurkmans et al, 2012). In some cases, CIEDs may return to normal

functioning within seconds to days after irradiation (device recovery), but often these changes become permanent if continually exposed to ionising radiation (Last, 1998). ICDs have also proven to be more sensitive to radiation than pacemakers due to the effect of scatter radiation on the RAM (Frizzell, 2009).

Various theoretical mechanisms of malfunction due to ionising radiation have been proposed. All depend on aberrant accumulation of electrical charge and / or abnormal current flow within the semiconductor material inside the device.

Last (1998) stated:

i. Trapped charge in the insulation layer leads to alterations in the current-voltage characteristics of individual semiconductor devices, with changes in threshold voltages and amount of bias required to produce changes in current.
ii. The build-up of positive charge in the insulator can cause the formation of aberrant electrical pathways, which may be transient or permanent.
iii. The metal case of the pacemaker is used as one electrode and will be at a different potential from the other parts of the circuit. Like an ionised chamber, the material within the pacemaker body can be ionised with radiation. These ions can then polarise between the pacemaker body and the integrated circuit creating a static field, which disperses slowly by leakage currents inside the CMOS itself, leading to failure of the various components in the circuitry.
iv. Photocurrents generated by very high dose rate radiation may have transient effects on a CMOS device. Such effects only become appreciable for high instantaneous dose rates and thus are unlikely to be significant at the relatively low dose rates occurring during each pulse from a linear accelerator.

In 2013, Munshi et al discussed the interaction of ionising radiation with CIEDs and carried out a review of literature and recommendations regarding CIEDs exposed to ionising radiation and subsequently suggested three reasons for the damage to them:

1. Destruction of electrical components, most often with direct ionising radiation
2. Effects on the random access memory - RAM (which hold patient-related data), most often secondary to scatter ionising radiation or EMI. RAM is an array of transistors in the device; low voltage RAM stores programmed data and software algorithms. Low voltage makes the data more volatile compared with the older bipolar transistor-based data storage. For example, in cases of single-bit errors in CMOS, the microprocessor should have the ability to repair the minor malfunctions by built-in error correction algorithms. However, a more pronounced malfunction in the RAM will result in the reset of the device.
3. Loading of the silicon dioxide insulator with excess of electron-hole pairs, which may persist to accumulate a net positive charge on the insulator. The resultant formation of aberrant electrical pathways within the insulator leads to transient or permanent changes in the CIED function

3.7 Observed types of CIED malfunction

CIED malfunction is defined as failure to capture or sense electrical impulses or both and will require cardiac intervention, for example CIED reprogramming (Last, 1998). CIED failure is defined as the inability of a CIED to perform its intended function of regulating the beating of the heart and the requirement of repeat surgical CIED-related procedures after the initial CIED implantation (Maisel et al, 2006).

Causes of CIED failure include lead related failure, unit malfunction, problems at the insertion site and failures related to exposure to ionising radiation, EMI, high voltage electricity or high intensity microwaves. CIED malfunction has the ability to cause serious injury or death, but if detected early enough, patients can continue with their needed therapy once complications are resolved.

Last, (1998) used clinical observations and in vitro studies to classify two main types of pacemaker malfunction induced by ionising radiation:

1. **Minor malfunctions –** Posing little risk to the patient, for example, transient or prolonged change to interference or safety mode pacing, increases in pulse width, small changes in paced rate and programming and telemetry function defects. Such changes have been detected at doses as low as 2Gy;
2. **Significant malfunctions –** Posing a definite risk to the patient such as extreme fixed rate output, prolonged pacemaker inhibition or total shutdown. Such malfunctions require immediate replacement of the damaged pacemaker generator. These can occur in the range of 15-36Gy.

In 2015, Zeremba et al stated the mechanism of CIED malfunctions could be categorised broadly, into three groups:

1. Transient effects due to interference, manifesting during exposure to ionising radiation only
2. Reverting to backup settings (reset), recoverable after reprogramming the CIED
3. Permanent damage to the CIED

Hashii et al, 2013. further catergorised CIED malfunctions during radiotherapy:

- **Hard errors -** relates to damage to the hardware of the CIED
- **Soft errors -** relates to software alterations of the CIED

1 - Severe - reset requiring reprogramming of the CIED

2- Moderate - reset not requiring correction by the programmer

3 - Minor - not detectable at interrogation and only recorded in the data log of the CIED

It is not possible to predict the exact behaviour of any given CIED when it is in, or in close proximity to the radiotherapy treatment field. Solan et al (2004) published a paper, which detailed the potential life-threatening malfunctions of CIEDs when exposed to EMI and ionising radiation. He concluded that major discrepancies exist among CIED manufacturer guidelines and recommendations regarding the management of patients with CIEDs receiving radiotherapy treatment.

3.8 Effect of electromagnetic interference (EMI) on CIEDs

EMI is the term used to describe combined electric and magnetic fields in the electromagnetic field. Electric fields exist whenever electric charges are present and a magnetic field is produced when an electric current flows in a conductor with magnetic field lines perpendicular to the current flow. Electromagnetic radiation is the term used to describe electromagnetic energy radiating away from its source and can be described as ionising or non-ionising radiation. Ionising radiation is made up of very short wavelengths and has sufficient power to move electrons from their nuclear orbits. Non-ionising radiation is made up of longer wavelengths, which are less powerful and are not able to move electrons off their orbit around the nucleus. Electromagnetic fields are characterised by wavelength, frequency and field strength. EMI occurs when electromagnetic waves emitted by one electrical source or device impedes the normal function of another electronic device. In relation to CIEDs, EMI is defined as interference of CIED function by any signal generated by an external source, that falls within a frequency spectrum being detected by the sensing circuitry of the CIED (Munshi,et al, 2013). CIEDs rely on complex microcircuitry and use

electromagnetic waves in order to communicate. EMI can interfere with the optimal function of the CIED. EMI can occur from multiple sources and can induce voltages within the CIED circuit. This might occur if the patient comes into direct contact with a source, or if the CIED enters an electromagnetic field, with the CIED leads acting as an antenna (Pinski and Trohman, 2002).

There are three elements that contribute to any EMI compatibility issues. There must be an electromagnetic source (linear accelerator environment / radiotherapy room), a receptor (CIED) that cannot function appropriately due to EMI and an environment between them that allows the source to interfere with the receptor. The factors affecting EMI can be categorised into properties of the emitting device (operating frequency), the physical relationship between the devices (distance) and the susceptibility of the affected device (electromagnetic shielding).

1. **Emitting device (linear accelerator environment / radiotherapy treatment room)**

The frequency (which is inversely proportional to wavelength) of the electromagnetic radiation emitted from the linear accelerator environment is a significant factor in relation to the physical length of various electric components in the susceptible device. These act as antennae to receive interfering signals. Long wavelengths (low frequencies) transfer minimal energy to small electronic components, and very short wavelengths (extremely high frequencies) are easily shielded. Frequencies between 10 kHz and 1GHz are generally the most problematic.

2. **Affected device (CIED)**

Electromagnetic compatibility (EMC) refers to the ability of electronic devices of different types to operate in an electromagnetic environment without loss of intended

function. The EMC of the affected device affects the degree of malfunction that may occur.

3. **Distance and environment**

Electromagnetic field energy decreases as the distance from the source increases (inverse squared function of distance from the source). Therefore, doubling the distance from the source results in a four-fold exposure reduction. For example in the setting of static magnetic fields created by linear accelerators, the intensity of static magnetic fields decreases as a function of distance from the source and creates a spatial gradient magnetic field.

3.9 CIEDs response to EMI

Currently in radiotherapy, much of the research has examined the effects of ionising radiation dose on CIEDs, and malfunction only occurs due to cumulative ionising radiation dose and dose rates (Mouton *et al* 2002), suggesting that EMI is not a concern. However, EMI can enter the sensing circuits and mimic the heart's intrinsic rhythm as well as influencing timing cycles. The impact of EMI on CIEDs, depends upon the frequency and intensity of the signal, duration of exposure to EMI during radiotherapy treatment and the presence of noise reversion filters in the CIEDs. Modern CIEDs utilise shielding, filters, and bipolar leads to mitigate EMI (Beinart and Nazarian, 2013), yet it can occasionally result in harmful consequences, for example pacing inhibition or inappropriate tachyarrhythmia resulting in shock therapy in ICDs (Pinski and Trohman, 2002).

Historically authors contend that CIEDs are extremely resistant to any sort of EMI found in a hospital and that the only sources of concern should be defibrillators and possibly arc welding (Grant 1993). Others say that CIEDs are shielded from frequencies above 1 kHz and that only ultra high frequencies, 300 MHz–3 GHz, can

affect them (Smith and Aasen 1992). Electromagnetic compatibility (EMC) describes efforts to minimise the possibility of EMI. Internally CIEDs are protected from EMI in that the circuitry is shielded, the distance between the electrodes and the antenna is minimised and incoming signals are filtered to exclude non-cardiac signals. CIED generators are typically shielded by hermetically sealed titanium or a stainless steel case. Insulation surrounds the CIED leads to improve shielding from radiofrequency and magnetic fields and the pulse generator is shielded to reject electric fields above 2MHz. However, if EMI does enter the CIED, noise protection algorithms integrated in the timing circuit aim to reduce its effect on the CIED. Incorporation of bandpass filters allows rejection of frequencies outside the range of interest. EMI signals between 5Hz and 100Hz are not filtered because these overlap the frequency range of intracardiac signals (Pinski and Trohman, 2002). Therefore, EMI in this frequency range may be interpreted by the CIED as intracardiac signals, causing CIED malfunction and a clinical reaction in the patient. The noise reversion mode on CIEDs is activated when signals are detected in the noise-sampling period. It is stated that cardiac pacemaker programming could be affected by EMI, but only if the magnitude of the electric field strength exceeds 200 V m^{-1} or the magnetic field strength exceeds 10 Gauss (Smith and Aasen, 1992). However, other authors contend that the complete inhibition of pacemaker functioning could be achieved with electric field strengths as low as a few volts per meter (Venselaar, 1985).

In 2009 Burke et al (2009) published a paper regarding radiofrequency noise from clinical linear accelerators. The purpose of this paper was to report on the measurement of the RF emissions from the treatment rooms of three different clinical linac configurations. This data was then used in the program to help develop an integrated linear-accelerator-magnetic resonance system. The results showed that RF noise emanating from medical linacs are not specific to one system but their data

outlining the field strengths surrounding clinical linacs could be applied to EMI testing of modern CIEDs.

The most frequent responses to EMI are inappropriate inhibition or triggering of pacemaker stimuli, reversion to asynchronous pacing, and spurious ICD tachyarrhythmia detection. Reprogramming of operating parameters and permanent damage to the device circuitry or the electrode to tissue interface are much less frequent (Pinski and Trohman, 2002).

Possible CIED responses to EMI are:

1. Stopping the CIED from delivering the stimulating pulses that regulate heart rhythm
2. Triggering the CIED to deliver stimulating pulses irregularly
3. Triggering the CIED to ignore the heart's own rhythm and deliver pulses at a fixed rate
4. Asynchronous pacing
5. Mode resetting
6. Damage to the pulse generator circuitry
7. Triggering of unnecessary ICD shocks (Pinski and Trohman, 2002).

The linear accelerators used in radiotherapy treatment, can emit various sources of EMI, for example couch drive motors, shutters, x-ray tube rotors, x-ray transformers, power supplies, magnetrons, klystrons, waveguide assemblies and beam pulse forming circuits, all potentially leading to pacing inhibition, fixed-rate pacing, or reprogramming of CIEDs (Hurkmans et al, 2012). However, these effects are usually transient and are observed when the ionising radiation beam is turned on or off (Munshi et al, 2013). However, the consequences could be serious and permanent. For example, severe circuitry damage can potentially lead to CIED reprogramming

and / or device failure (Solan et al, 2004; Hurkmans et al, 2005; Hoecht et al, 2002 and Niehaus and Tebbenjohanns, 2001). Modern linear accelerators are sufficiently shielded, but there is limited literature to identify and quantify the risk of EMI to CIEDs during radiotherapy treatment (Pinski and Trohman, 2002).

3.10 Observed clinical cardiac responses to EMI

Pacing Inhibition

CIEDs can be programmed to withhold electrical stimulus and inhibit pacing if it senses intrinsic activity (heart contractions). This CIED response is limited to a heart rate range up to approximately 300 pulses per minute or 5 Hertz (Pinski and Trohman, 2002). However, EMI that is detected by the CIED in this rate range can cause the CIED to incorrectly withhold the electrical stimulus and therefore inhibit pacing. In pacemaker dependant patients, sustained pacing inhibition could have serious consequences. Depending on the duration of pacing inhibition, light-headedness, syncope, or death could result (Last, 1998).

ICDs may be more vulnerable to consequences of pacing inhibition from EMI, as the programmed settings of the ICD can influence the response of the device to EMI. ICDs are required to be programmed at a high sensitivity setting in order to sense cardiac arrhythmias and deliver the appropriate therapy, however, this increased sensitivity makes the ICDs more susceptible to EMI and can cause oversensing of the extracardiac signals (Pinski and Trohman, 2002). Asynchronous pacing will not occur due to lack of reliable ICD noise reversion modes. Therefore, EMI induced prolonged inhibition and spurious tachyarrhythmia detection become likely.

Triggering of rapid or premature pacing

Oversensing of EMI by the atrial channel of a pacemaker programmed to a tracking mode can trigger ventricular pacing at or near the upper tracking rate limit (Last,

1998). Rapid pacing due to atrial oversensing is observed when the CIED is placed in an electromagnetic field. As the electromagnetic field becomes stronger, the period of atrial oversensing is followed by a period of ventricular oversensing in the CIED. Patients who experience this are typically symptomatic and complain of rapid palpitations. If sustained, inappropriate CIED acceleration induced by atrial oversensing may cause palpitations, hypotension, or angina. Very rapid pacing could induce ventricular fibrillation (Pinski and Trohman, 2002).

Noise reversion mode

CIEDs incorporate protective algorithms against prolonged inhibition from spurious signals. A common response is transient reversion to asynchronous pacing (Strathmore, 1995). Within the CIED, a safety feature identifies and classifies EMI that is outside of the cardiac rate range (5 Hertz). On identifying and classifying EMI, the CIED delivers pacing stimuli to the heart and CIED noise reversion mode is activated. CIED noise reversion minimises the types of EMI that can cause the CIED to be inhibited. The CIED will continuously pace the heart at the programmed low rate of the CIED in the presence of EMI.

Hudson et al (2010) used the study by Souliman et al in 1994 to report that EMI had no impact on pacemaker malfunction. A further study by Hurkmans et al (2012) stated that EMI effects are mainly temporary or reversible and they concluded that EMI did not seem to be of clinical relevance. In 2015, Zaremba et al stated that the effects of EMI are usually transient and EMI typically does not pose any threat to the function of CIEDs, as in his study no events of symptomatic inhibition or rapid pacing was observed during radiotherapy treatment.

3.11 Rate response activated CIEDs

As a result of the development and improvement in CIED technology, rate response activated CIEDs are increasingly being implanted in patients for the management of their cardiac conditions. However, there is no research into the effect of ionising radiation and / or EMI on these devices.

Rate-adaptive pacing is designed to increase the heart rate according to metabolic needs during physical, mental or emotional activity. Rate responsive CIEDs control heart rate by sensing physiological or non-physiological signals other than the patient's atrial rate. Rate response activated CIEDs have specialised sensors built into the pulse generator that can sense increasing activity and / or increased rate of breathing. The sensors will automatically increase or decrease the heart rate according to the body's needs.

Activity-driven (accelerometer) rate response activated CIEDs

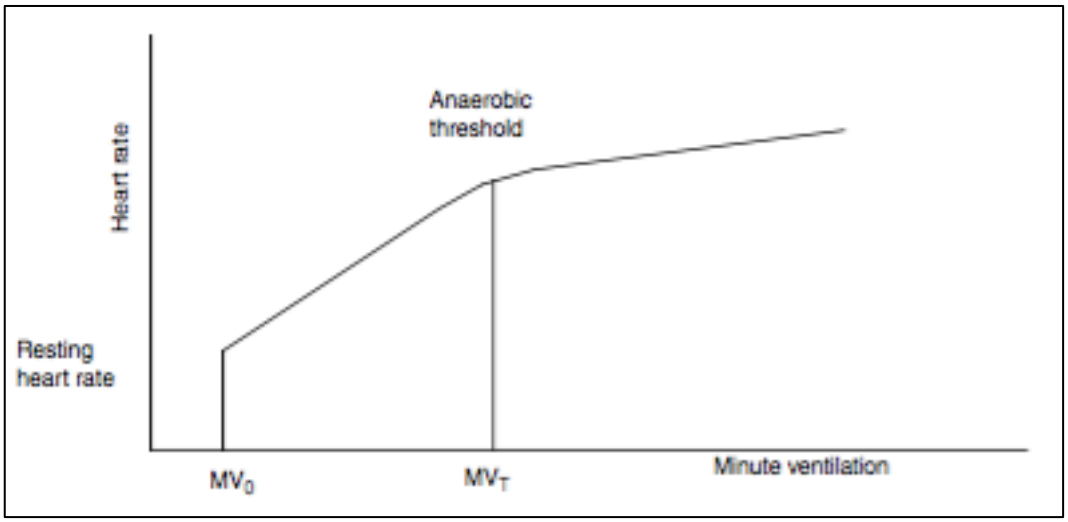
Accelerometer rate-adaptive CIEDs are non-physiological and non-specific because they do not respond to an increased metabolic demand unrelated to exercise. The devices sense body motion by means of an integrated circuit accelerometer located on the circuit board. The accelerometer responds to activity in the frequency range of typical physiological activity (1–10 Hz). An algorithm translates the measured acceleration in this range into a rate increase above the lower rate limit set.

Minute ventilation rate response activated CIEDs

Minute ventilation CIEDs are highly physiological as they react to the patient's metabolic demand and therefore are also highly specific. These devices use impedance minute ventilation sensors to change the pacing rate in response to variations in the patient's minute ventilation. Minute ventilation is the product of respiratory rate and tidal volume. Up to the anaerobic threshold, minute ventilation is

approximately linearly related to heart rate. At exercise levels beyond the anaerobic threshold, the relationship is still approximately linear but at a reduced slope.

Figure 3.3: Graph to show rate response activated CIED (minute ventilation) – Response of device



(Bostonscientific.com, 2017).

The minute ventilation sensor for rate adaptation is derived by means of transthoracic impedance measurement. Approximately every 50ms (20 Hz), the device will drive a current excitation waveform between the selected (atrial or ventricular) lead ring electrode and the pacemaker case (Boston Scientific, 2012).

EMI can trigger rapid pacing (up to the sensor-triggered upper rate limit) by activating the sensor in minute ventilation pacemakers. Minute ventilation CIEDs may also erroneously interpret the signals generated by a range of hospital equipment, such as respiratory monitors, diagnostic echo imaging and surface ECG monitors (Bostonscientific.com, 2017). Pacing returns to normal once the minute ventilation sensor in the CIED is deactivated. CIED manufacturer, Boston Scientific (Bostonscientific.com, 2017). issued the following caution:

"electrical signals introduced into the body by some hospital monitoring and / or diagnostic equipment may result in accelerated pacing, possibly up to the maximum sensor-driven rate, when minute ventilation is programmed ON. Examples of this equipment include, but are not limited to, respiratory monitors, diagnostic echo imaging, surface ECG monitors, and hemodynamic monitors. Therefore, deactivation of the minute ventilation sensor is required when interaction with this equipment is suspected".

3.12 Effect of ionising radiation and EMI on CIED leads

As discussed in Chapter Two, CIED leads are insulated flexible wires that conduct electrical signals from the generator to the heart muscle and relay information concerning the heart's intrinsic electrical activity back to the CIED pulse generator. Although ionising radiation may affect the function of the CIED, CIED leads are considered to be resistant to these effects. None of the CIED manufacturers have issued any ionising radiation tolerance doses for CIED leads. CIEDs are afforded some protection against exposure to ionising radiation and EMI, however, the CIED leads still remain vulnerable to noise pickup and the effects of EMI.

CIED lead malfunction and failure

CIED lead malfunction is defined as not performing according to specifications or intentions and it is the most common cause of CIED therapy failure. Even when all the electrical parameters are within normal limits, structural compromises in a lead may still pose dangers to the patient through cardiac perforation, thrombogenesis, bacterial infection, interference with adjacent leads, and difficulty in extraction (Maisel et al, 2009 and Hauser et al, 2013). Pacemaker or ICD lead failure in patients, can result in morbidity in the form of symptomatic bradycardia, inappropriate ICD shock therapy, arrhythmias, as well as mortality due to failure to pace or deliver therapy.

Lead failure can have more serious and immediate consequences than failure of the CIED pulse generator. The consequences of CIED lead failure include high pacing or shock impedance, over-sensing, under-sensing, failure to capture and a failure to defibrillate. The most common clinical presentation of lead failure is over-sensing; resulting in delivery of multiple inappropriate shocks and is the most serious cause of lead failure. CIED malfunction can be managed by the surgical replacement of the device, but the management issues are more complex in the case of lead failure.

3.13 Previous studies

Various studies have been undertaken to consider the implications of level and rate of radiation doses delivered during radiotherapy treatment, as well as the risk of EMI upon the CIED. There is limited research undertaken on the impact reported on CIED leads. Previous studies have either used laboratory-based (in vitro) methods where exposure occurs only to the pacemaker itself on the bench, or 'live' (in vivo) studies, which investigated the effects caused by radiation and EMI, directly or indirectly, to the implanted device in the patient during their radiotherapy treatment.

3.13.1 In vitro studies: Effect of ionising radiation and EMI on pacemakers (see Appendix A – Table 1)

The majority of cancer patients receive their radiotherapy treatment via external megavoltage photon beams with a daily radiotherapy treatment dose of 1.5 – 2Gy to the tumour per fraction up to a total dose of between 50 – 60Gy given in 20 to 30 fractions over five to six weeks. For the treatment of breast cancer, patients receive a radiotherapy treatment dose of 40Gy in 15 daily fractions over 3 weeks and for the treatment of lung cancer, patients receive a radiotherapy treatment dose of 55Gy in 20 daily fractions over 4 weeks (Royal College of Radiologists, 2006).

The earliest pacemaker in vitro study was carried out by Souliman and Christie in 1994, in which eighteen multi-programmable pacemakers were irradiated to a total dose of 70Gy (2.8Gy per fraction) using 8MeV photons. Results showed that no pacemakers failed at a dose less than 16.8Gy. Eleven of the eighteen pacemakers failed between doses of 16.8Gy and 70Gy, with no device recovery observed. Five of the eighteen pacemakers experienced device malfunctions, such as loss of atrial pacing combined with a decrease in pulse rate and increased pulse interval and corresponding pulse rate reduction. Two pacemakers showed no failure before reaching 70Gy. Souliman and Christie (1994), concluded that pacemakers could temporarily or permanently fail at radiation dose levels commonly used in radiotherapy treatment and in this study they deemed that EMI had no effect on the devices. They reinforced the need that all patients with a pacemaker should be monitored closely during their radiotherapy treatment.

In 2002, Mouton et al. conducted an in vitro study, which provided data on radiation tolerance doses and the effect of dose rates on pacemaker function. In this study they used explanted pacemakers. Explanted pacemakers are devices which have been surgically removed from the body as a result of infection around the implantation site of the device, battery depletion requiring a battery change within the device generator, the device reaching the end of its 'working life' and needing to be replaced by a more modern device or the death of the patient. Ninety-six explanted pacemakers were irradiated to a total dose of 200Gy (ranging from scatter radiation to four times the normal dose rate for direct irradiation), using a range of dose rates. Results showed that a number of pacemakers could withstand a radiation tolerance dose of up to 140Gy but some pacemakers failed at very low radiation dose levels. For example, one pacemaker exhibited clinically significant disturbances at a cumulative dose of only 0.15Gy. Two pacemakers exhibited defects at a dose of 1Gy and nine pacemakers failed at a cumulative dose of 2Gy. A further thirteen

pacemakers failed at a cumulative dose of 5Gy. This study found pacemakers to be more sensitive to ionising radiation than previous studies that had defined the maximum tolerance dose to be as high as 5–10Gy. Mouton et al (2002), concluded that the maximum radiation tolerance dose of 2–5Gy quoted by the pacemaker manufacturers is not reliable in all situations. They concluded that there is no safe ionising radiation dose level due to pacemaker failures appearing at doses equivalent to scatter radiation. They proposed that pacemaker manufacturers should redesign devices with radiation-hardened circuitry, or at the very least specify safe ionising radiation doses for each individual pacemaker.

CIED manufacturers have since updated their recommendations and guidelines. However, the recommendations are not consistent for all manufacturers. Boston Scientific (Boston Scientific, 2012) state that no level of cumulative ionising radiation dose is 'safe' to both pacemakers and ICDs. Medtronic (Medtronic, 2013) state that for pacemakers, tests have revealed minor radiation damage at doses as low as 5Gy. Therefore, they recommend monitoring after each radiotherapy treatment when this limit is reached. They also list specific, ionising radiation tolerance doses for its eleven various models of ICD, in two of these models the radiation tolerance dose is 5Gy and in the remaining nine ICD models the radiation tolerance dose is 1Gy. St. Jude Medical (St. Jude Medical, 2013) states that its pacemakers have been tested to 30Gy cumulative ionising radiation dose without adverse effect. They reinforce Last's (1998) comments regarding the patient management during radiotherapy treatment. Biotronik's (Biontronik, 2011) product information sheet states that pacemakers have functional disturbances at 20Gy cumulative ionising radiation doses and less severe damage at 5Gy.

Hurkmans et al, in 2005 irradiated nineteen pacemakers to a total dose of up to 120–130Gy (end point failure) with 6MeV photons. Results showed that malfunctions

varied from 10Gy to 120Gy, while five pacemakers irradiated to 130Gy exhibited no malfunctions. Hurkmans et al (2005), classified these failures into five groups; changes in pacing pulse, pacing frequency, sensing threshold changes, telemetry and miscellaneous (battery problems and lead impedance changes). Five pacemakers exhibited no errors and some experienced a combination of device malfunctions. In seven pacemakers, a complete loss of signal was observed. Three pacemakers showed an amplitude deviation >25%. Eight pacemakers experienced pacing frequency inhibition during irradiation, but stopped when the radiation beam was switched off. Three pacemakers experienced temporary or permanent loss of telemetry. The researchers proposed that the AAPM guidelines (Marbach et al, 1994) were still valid; but more studies were needed to quantify pacemaker malfunctions and issue further guidelines when treating patients with pacemakers. This is therefore, one of the factors leading to this current study.

Zaremba et al (2014), conducted an in vitro study to compare the effect of high-energy and low-energy photon beams on modern CIEDs. They irradiated ten pacemakers with a dose of 2Gy per fraction to a cumulative dose of 150Gy using 6MeV and 18MeV photon beams. Results showed that in the 6MeV group, one episode of pacemaker malfunction was detected after 150Gy. In the 18MeV group, a total of fourteen episodes of malfunction were detected starting at 30Gy in all five pacemakers. They concluded that photon beam energy plays a considerable role in inducing pacemaker malfunctions. Low-energy radiotherapy may be safer in CIED patients despite relatively high ionising radiation dose to the devices.

3.13.2 In vitro studies: Effect of ionising radiation and EMI on ICDs (see Appendix A – Table 2)

The majority of in vitro studies observing the effects of radiotherapy focus on the effect of ionising radiation and EMI on pacemakers. Understanding of the relevant

data on the effects of ionising radiation and EMI on ICDs is limited. However, Hurkmans et al (2012) in vitro study on patients with ICDs and radiotherapy, irradiated eleven new ICDs exposed to a total dose of up to 120–130Gy (end point failure) with 6MeV photons induced malfunctions which varied from 0.5Gy to 120Gy. The study by Hurkmans et al (2012) found that malfunctions and / or failures were observed in all ICDs. The first malfunctions were observed at 0.5Gy, with shock energy deviations >25%. Four ICDs reached their point of failure at 2.5Gy. A fifth ICD reached the end point failure dose of 120Gy. No other ICD failed at doses less than 10Gy. Sensing interference was observed in all of the ICDs, in four ICDs, VT or VF detection occurred. This would trigger the ICD to deliver an inappropriate shock. No significant changes in pulse amplitude, pulse frequency and telemetry problems, were recorded. The researchers concluded that EMI did not have any effect on the ICDs but recommended management and monitoring protocols for patients with ICDs receiving radiotherapy treatment.

Uiterwaal et al (2006) reported a study on ICD irradiation in 2006. Eleven new ICDs were irradiated to 20Gy in a fractioned regime, in order to assess EMI interference. Interference was observed in all ICDs that were placed inside the irradiation field, this interference caused pacing inhibition or rapid ventricular pacing. Four out of the eleven ICDs incorrectly detected VT or VF, which would have caused tachycardia-terminating therapy and lead to an inappropriate shock therapy. No interference was observed in all the ICDs placed outside the irradiation field. The researchers made recommendations for the management of ICD patients, including the need to reprogram the ICD to ‘monitor only’ to avoid inappropriate delivery of a shock. They also emphasised the need for access to emergency resuscitation equipment, including an external defibrillator when treating these patients.

In 2008, Kapa et al, irradiated twelve ICDs and eight CRT-ICDs to 4Gy of scattered ionising radiation from a 6MeV photon beam. The ICDs were interrogated prior to radiation exposure, after each fraction, on completion of the radiation course and one-week post completion. Interrogation reports showed there was no evidence of device reset or malfunction during or after radiation. Kapa et al (2008), concluded that there was no clear contraindication to radiotherapy in patients with ICDs or CRT-ICDs. However, they stated that ICDs should not be exposed to direct ionising radiation and there is a need for patients to be monitored during their radiotherapy treatment.

In contrast, the Mollerus et al*,* study in 2014, showed that modern ICDs can withstand a greater cumulative ionising radiation dose than the 4Gy dose investigated by Kapa et al (2008). Mollerus at al (2014) irradiated four modern ICDs and four older generation ICDs to escalating doses of ionising radiation from a 6MeV photon beam. Results showed that the four modern ICDs remained functional at a cumulative ionising radiation dose of 131.11Gy but three of the ICDs exhibited minor memory faults. All four of the older generation ICDs failed to deliver shock therapy after 41.11Gy and exhibited changes in lead impedance. The researchers therefore, concluded that modern ICD design might be more robust than earlier generation ICDs.

The 2014 in vitro study, conducted by Zaremba et al (2014), compared the effect of high-energy and low-energy photon beams on modern CIEDs. They irradiated two ICDs with a dose of 2Gy per fraction to a cumulative ionising radiation dose of 150Gy using 6MeV and 18MeV photon beams. Results showed that no episodes of device malfunction occurred in either groups and concluded that photon beam energy plays a considerable role in inducing device malfunctions. Low-energy radiotherapy may

therefore be safer in CIED patients despite relatively high radiation dose to the device.

3.13.3 In vivo studies: Effect of ionising radiation and EMI on pacemakers (see Appendix A – Table 3)

In the period 2000 to 2012, five studies produced case reports for patients with a pacemaker receiving radiotherapy and documented the effect of ionising radiation and EMI on the devices. Tsekos et al. in 2000 irradiated a pacemaker that was located in the lower lateral quadrant of the treatment field to treat a neuroendocrine carcinoma to 50.4Gy in 28 fractions. During treatment, there was a decrease in magnet rate of the pacemaker, which returned to normal four months post radiotherapy treatment. Results showed that no malfunction was evident. In 2001, Nibhanupudy et al. reported on a patient with left breast carcinoma, where the pacemaker was re-sited, away from the radiotherapy treatment field, to the contra lateral pectoral pocket, and the pacemaker received a total ionising radiation dose of 1.8Gy during treatment. No malfunction was recorded in this case. Mitra et al. (2006) reported a similar case where pacemaker relocation was contra indicated due to patient instability. The pacemaker was situated just inside the radiotherapy treatment field and the device received a total dose of 1.66Gy. No malfunction was recorded in this case. In 2013, Munshi et al reported that when treating a left breast carcinoma, the pacemaker was originally directly in the radiotherapy treatment field. This required medical physics to optimise the radiotherapy treatment plan to minimise the ionising radiation dose to the pacemaker of 4.3Gy. This device exhibited no malfunction. In 2012, Kesek et al, documented the treatment of a patient with left sided lung cancer. The device could not be re-sited as this would require either use of a lead extender and tunnelling or implantation of a third electrode through the right subclavian vein already occupied by a venous port. Radiotherapy proceeded and the pacemaker received a total dose of 48Gy and no

malfunction was observed.

During the period 2002 – 2012, five studies investigated the effects of ionising radiation on pacemakers. These studies irradiated the pacemakers to a range of ionising radiation doses and all reported that the pacemakers exhibited no malfunctions. In 2002, Santhanam et al presented the results of their study of six patients with pacemakers receiving radiotherapy. In five patients, no malfunctions were recorded in radiotherapy doses ranging from 0.5Gy to 1.3Gy. One patient, whose pacemaker was situated within the radiotherapy treatment field, received a total dose 26.7Gy and no malfunction was recorded. In 2014, Ampil et al produced a study on the use of radiotherapy for the palliation for lung cancer patients with compromised hearts. They reported that the devices received a negligible dose of ionising radiation and no malfunctions were detected. Croshaw et al, in 2011 reported that in three patients having radiotherapy for the treatment of breast cancer, the pacemakers received doses ranging from 0.23Gy to 0.73Gy with a 6MeV photon beam. No malfunctions in these devices were observed. In Wadasadawala et al, 2011 study of eight patients receiving radiotherapy, with a total dose ranging from 0.14Gy to 60Gy to the pacemaker, the devices exhibited no malfunctions. They concluded that radiotherapy could be safely delivered in patients with pacemakers. However, the dose to the pacemaker needs to be kept as low and possible and close liaison with the cardiologist before, during and after the course of radiotherapy treatment is essential to ensure patient safety. Makkar et al, in 2012 found no device malfunctions after irradiating fifty pacemakers. They concluded that pacemaker malfunction due to indirect ionising radiation is uncommon.

From 2011 to 2015, three studies investigated the effects of ionising radiation on pacemakers. In these studies, pacemakers were irradiated with a range of ionising radiation doses and all reported device malfunctions. Soejima et al (2011), reported

on sixty patients with pacemakers receiving radiotherapy to a variety of different treatment sites. One patient, who was receiving radiotherapy for prostate cancer exhibited a device malfunction as the device reset during their radiotherapy treatment. This device required reprogramming. The researchers concluded that pacemaker malfunctions can occur when the pacemaker is away from the radiotherapy treatment site and receiving a negligible dose of ionising radiation. EMI could be the causal factor for the device malfunction. In 2014, Gossman et al irradiated sixty-seven pacemakers where malfunctions were observed in four devices. One pacemaker failed at 0.3Gy, one pacemaker exhibited an increased sensor rate during ionising radiation delivery, one patient had an irregular heartbeat leading to device reprogramming, and one patient complained of 'twinging' in the chest wall that resulted in a respiratory arrest. However, the researchers do not detail the nature of the clinical consequences. The most recent study by Zaremba et al in 2015, irradiated three hundred and nighty-four pacemakers. Ten pacemakers exhibited device malfunctions. Nine of which were reset or deprogrammed during their radiotherapy treatment and one device showed an increase in atrial pacing threshold from 1.25V to 2.75V. These pacemakers required reprogramming by the Cardiology department. Zaremba et al (2015), concluded that the damaging effects of radiotherapy on pacemakers seem to be transient and indicates that beam energy has a pivotal role in inducing impairments.

3.13.4 In vivo studies: Effect of ionising radiation and EMI on ICDs (see Appendix A – Table 4)

From 2004 to 2015, out of the nine in vivo studies investigating the effect of ionising radiation and EMI on ICDs, only three reported that no malfunctions were observed in ICDs during radiotherapy treatment (Sepe et al, 2007; Croshaw et al, 2011 and Soejima et al, 2011). In 2007, Sepe et al, published a case report, where an ICD received a total dose of 2.5Gy when treating a patient with head and neck cancer.

The ICD was deactivated during each radiotherapy treatment and the device was checked by their Cardiology department and no malfunction was recorded at any stage during their radiotherapy treatment. Croshaw et al, in 2011 reported that in two patients having radiotherapy for the treatment of breast cancer, the ICDs received a total dose of 1.01Gy and 1.68Gy with a 6MeV photon beam. No malfunctions in these devices were observed. Soejima et al (2011) reported on two patients with ICDs receiving radiotherapy. The ICDs were away from the treatment sites, so received a negligible dose of ionising radiation and no device malfunctions were detected.

In comparison, Thomas et al (2004) and Nemec (2007) published case reports where malfunctions were observed in ICDs during radiotherapy treatment. Thomas et al. (2004) reported a patient receiving radiotherapy to the right lung. As the ICD was away from the treatment site, it received a negligible dose of ionising radiation. During the post radiotherapy cardiology follow-up, it was discovered that an electrical reset of the ICD had occurred during the patient's radiotherapy treatment. The patient who was not ICD dependent, had not shown any physical symptoms, and the reset of the ICD had gone undetected. Nemec (2007) published a case report for a patient being treated for lung cancer and documented the potentially lethal effect on the patient due to ICD failure. An ionising radiation dose to the ICD could not be obtained, as the incident occurred during the third fraction (this dose would have accumulated to <5Gy). During the radiotherapy planning process because the ICD was not in the treatment field it was not re-sited. However, the patient collapsed during their third fraction of radiotherapy treatment requiring cardiopulmonary resuscitation. Therefore, the ICD was removed and the patient continued radiotherapy treatment. Following a cardiology investigation there was found to be no fault with the ICD. This malfunction could be as a result of random access memory (RAM) damage.

Between 2009 and 2015, four studies investigated the effects of ionising radiation on ICDs. In these studies, ICDs were irradiated with a range of ionising radiation doses and all reported device malfunctions. Gelblum and Amols (2009) irradiated thirty-three ICDs with a radiation dose ranging from 0.1Gy to 2.99Gy. Two patients who were receiving radiotherapy to the pelvic region using a 15MeV photon beam (rectal cancer and prostate cancer) experienced a reset of the ICDs back to its factory settings and required cardiology intervention to re-programme the devices. In both these patients the ICDs were away from the radiotherapy treatment site. The researchers suspect that both device resets were caused by neutron radiation. In 2012, Makkar et al. irradiated nineteen ICDs using a 16MeV photon beam. Two patients' ICDs displayed a partial reset with the loss of historic diagnostic data after exposure to 0.04Gy and 1.23Gy. In a study by Elders *et al (2013),* fifteen ICD patients received radiotherapy treatment with 6 to 8MeV photon beams. All ICDs received a total ionising radiation dose of <1Gy. During irradiation, the researches noted disturbances in the memory data, inappropriate VF detection due to external noise and a device data error. Upon interrogation, the ICDs of two patients showed invalid data retrieval, one patient's ICD reset during radiotherapy treatment and one patient's ICD reset and nine months later a trend data error was reported. They concluded that there is a possible correlation between the beam energy and the malfunctions displayed by the ICDs. This correlation may be due to an interaction between neutrons produced in the head of the linear accelerator at beam energies ≥10MeV. The most recent study by Zaremba et al in 2015, irradiated seventy-three ICDs and four devices exhibited malfunctions. Three ICDs were reset or deprogrammed during their radiotherapy treatment and one device showed an increase in pacing threshold. These devices required reprogramming by their Cardiology department.

3.13.5 In vivo studies: Effect of ionising radiation and EMI on CIED leads

There is limited literature and no research into the effects of ionising radiation and EMI on CIED leads. From 2004 to 2012, four case reports were published, with one recording malfunction to the CIED and CIED leads (John and Kaye, 2004). In 2004, John and Kaye reported an ICD malfunction after radiotherapy treatment for left sided breast cancer. While the ICD had been shielded, the leads received a full dose of ionising radiation with partial exposure of the ICD. At the post radiotherapy cardiology follow-up appointment it was deemed that a new ICD was required due to battery depletion. During the procedure it was discovered that the shock impedance had increased, suggestive of shock coil failure, possibly due to structural damage to the leads. The leads were tested four times and similar values were obtained, consequently a new lead was implanted. The researchers concluded that it was likely that damage to the shock coil during high dose irradiation resulted in high shock impedance and caused a malfunction in the ICD and the leads. In 2008, Munshi et al published a case report for a breast cancer patient where their CIED leads were in the radiotherapy treatment field. The patient was monitored throughout their radiotherapy treatment and the cardiologist documented that there was no malfunction to their CIED. The researchers concluded that the dose to the CIED and leads should be kept as low as possible. In 2011, Dasgupta et al published a case report for the successful radiation treatment of anaplastic thyroid carcinoma metastatic to the right cardiac atrium and ventricle in a pacemaker dependent patient. The cumulative ionising radiation dose to the CIED was 0.37Gy and the cumulative radiation dose to the CIED leads was 5Gy. The patient was monitored throughout the radiotherapy treatment and a single episode of ventricular under-sensing with pacing stimuli during T-waves was successfully addressed by the reprogramming of the CIED. In 2012, Kirova et al published a case report for a patient receiving palliative radiotherapy to the thoracic spine. The cumulative ionising radiation dose to the CIED was 0.1Gy and the cumulative ionising radiation

dose to the CIED leads was 5Gy. No change in CIED function was observed during and after the radiotherapy treatment. The researchers concluded that all patients with CIEDs, especially ICDs should be monitored during their radiotherapy treatment.

3.14 Safety measures

The major manufacturers of CIED devices (Biotronik, 2011; Boston Scientific, 2012; Medtronic, 2013 and St. Jude Medical, 2013) do not provide specific guidelines on the safe management of patients with a CIED who are receiving radiotherapy treatment but some issue recommendations in relation to ionising radiation tolerance doses to the CIEDs. However, these recommendations differ considerably. Medtronic state that their pacemakers should be able to tolerate cumulative ionising radiation doses of 1-5Gy depending on the model (Medtronic, 2013). Boston Scientific and St. Jude Medical cannot rule out that their devices might fail even at low ionising radiation doses, stating that no dose limit be regarded as safe Boston Scientific, 2012 and St. Jude Medical, 2013). Boston Scientific further state that there is no safe ionising radiation dose to their devices due to the random nature of scatter ionising radiation and the effect this may have on RAM which is a common element in all devices (Lau et al, 2008).

The CIED manufacturers state that previous research has shown EMI to have an insignificant effect on CIEDs, as EMI is only present briefly when the radiation beam is turned on or off. With advances in radiotherapy treatment technology and delivery, for example IMRT and IGRT, there is an increased presence of EMI, therefore there may be a more significant effect on CIEDs than previous conventional radiotherapy treatments. Additionally, Biotronik and Medtronic highlight the importance of beam energy, due to the damaging effects of secondary neutrons with a recommendation to limit photon energy to 10MeV (Medtronic, 2013 and Biontronik, 2011). While CIED

manufacturers give different recommendations, all state that the CIED should not be located in the radiotherapy treatment field (Biotronik, 2011; Boston Scientific, 2012; Medtronic, 2013 and St. Jude Medical, 2013).

The American Association of Physicists in Medicine (AAPM) (Marbach et al,1994) published a report on the safe use of radiotherapy in patients with permanent pacemakers. The AAPM report is the basis of most of the CIED departmental radiotherapy policies used in the UK before 2015. Frizzell (2009) published a more contemporary review and a distinction was made between pacemakers and ICDs. Both the AAPM and Frizzell reports are widely referenced in the literature and appear to have the most robust evidence base to support them. Despite this, the AAPM report is now twenty-four years old and does not reflect advances in CIED or radiotherapy technology.

Summary of the AAPM (Marbach et al, 1994) and Frizzell (2009) recommendations:

AAPM Recommendations (pacemakers):

1. Pacemakers should not be placed in the direct (unshielded) radiotherapy beam
2. The absorbed dose to be received by the pacemaker should be estimated before treatment and limited to 2Gy
3. If the total estimated dose to the pacemaker might exceed 2Gy, pacemaker function should be checked before radiotherapy and possibly at the start of each following treatment week by a cardiologist
4. Patients should be closely observed during the first radiotherapy treatment on a linear accelerator

Frizzell Recommendations (ICDs):

1. The absorbed dose to be received by the ICD should limited to 0.5Gy
2. A magnet should be placed over an ICD when a patient is exposed to radiation
3. Notify all patients about the possibility of ICD malfunction, failure or both

Monitoring recommendations:

1. Patients should be monitored with a continuous electrocardiogram (ECG) strip during the first radiotherapy treatment. This strip should then be reviewed for any evidence of pacing disruption when radiotherapy is being administered
2. ICD patients should undergo daily monitoring and staff should document any changes in the patient's physical status and any changes in the ECG trace
3. Monitoring should be carried out by fully trained and competent health professionals. If therapeutic radiographers are monitoring patients, they should receive specific training on the management and monitoring of these patients
4. If at any point malfunction is suspected or detected, the clinical oncologist and cardiologist should be immediately informed

Consent recommendations:

1. The patient is aware of potential adverse effects of radiotherapy on CIEDs
2. The patient is aware the ICD will be deactivated during radiotherapy

3.15 Chapter conclusion

In discussing the role that radiotherapy plays in the management of patients with CIEDs, this chapter provides the theoretical background, clinical observations and study results of the effects of ionising radiation and EMI on CIEDs and CIED leads.

Chapter Four

Research Methods

4.1 Introduction

The overall aims of the research were to determine the effect of ionising radiation and EMI on CIEDs and CIED leads and to provide UK guidelines for the safe management of cancer patients with CIEDs receiving radiotherapy treatment. The review of current literature and scientific studies were discussed in previous chapters. This information led to the formulation of the research questions and objectives and the development of the research design and the studies undertaken within the context of this PhD project.

The specific research questions and objectives as discussed in chapter one are:

- To establish current UK practice regarding the management of patients with CIEDs receiving radiotherapy treatment
- To determine the effects of ionising radiation and EMI on patients with CIEDs receiving radiotherapy treatment at a RCW
- To evaluate the relationship between cumulative ionising radiation dose and EMI and damage sustained to CIEDs
- To evaluate the relationship between cumulative ionising radiation dose on the physical condition of the CIED leads
- To determine whether there is a safe minimum radiation tolerance dose to CIEDs and CIED leads
- To determine the effect of ionising radiation and EMI on rate response activated CIEDs

These research questions and objectives are discussed in six studies, under three headings:

1. **Test compliance, knowledge, understanding and perception**

   - ***Study 1:***

     To establish current UK practice regarding the management of patients with CIEDs undergoing radiotherapy treatment and to compare this practice with current 'gold standard' evidence-based guidelines.

   - ***Study 2:***

     To conduct clinical audits to determine the effects of ionising radiation and EMI on patients with CIEDs receiving radiotherapy treatment at a RCW

2. **Scientific research**

   - ***Study 3:***

     To investigate and evaluate the relationship between cumulative ionising radiation dose and the damage sustained to CIEDs (pacemakers and ICDs).

   - ***Study 4:***

     To investigate and evaluate the relationship between cumulative ionising radiation dose and / or EMI and the damage sustained to CIED leads.

   - ***Study 5:***

     To investigate and evaluate the relationship between EMI and the damage sustained to CIEDs (pacemakers, ICDs and rate response activated CIEDs).

3. **Research outcomes**

- ***Study 6:***

  To provide evidence based guidelines for the safe management of cancer patients with CIEDs receiving radiotherapy treatment.

The purpose of this chapter is to outline and explain the reasoning and approach by which the research was undertaken. This chapter addresses the research questions and the development of the research methodology and method for each study, which is explained in detail.

Firstly, this chapter will explain the choice of research approach and research method to establish current UK practice regarding the management of patients with CIEDs undergoing radiotherapy treatment. Secondly, this chapter will detail the choice of research approach and present the research design, as well as the advantages and disadvantages of the research tools chosen. This will be followed by a discussion of their ability to produce valid results, therefore meeting the aims and objectives set by this work. This chapter will then discuss the preliminary study, data collection and data analysis procedures that were decided to be most suitable for addressing the formulated research questions. It concludes with addressing how the preliminary study informed the PhD research project and a discussion on the ethical considerations posed by the research methodology.

Next, this chapter will discuss the choice of research approach when conducting a systematic review to determine current 'gold standard' practice for the safe management of patients with a CIED receiving radiotherapy treatment. In conjunction with the results and findings of this PhD project, this will provide up to date, evidence based recommendations for the management of cancer patients who have a CIED and are receiving radiotherapy. Finally, this chapter outlines the

implementation of the PhD research project, detailing the research method and data collection procedures for all six studies.

4.2 Test compliance, knowledge, understanding and perception

4.2.1 Study 1

To establish current UK practice regarding the management of patients with CIEDs undergoing radiotherapy treatment and to compare this practice with current 'gold standard' evidence-based guidelines.

As part of the PhD research project, it was considered fundamental to establish current UK practice regarding the management of patients with CIEDs receiving radiotherapy treatment and compare this practice to current 'gold standard' evidence-based guidelines.

Method

Literature review

A literature search was conducted to contextualize the study aims and map them to existing research and provide an overview of the two study areas:

- The roles and responsibilities of healthcare professionals involved in the patient pathway
- The treatment and management guidelines for patients with CIEDs receiving radiotherapy treatment

The literature review was divided into two stages. The first was a broad exploratory 'Ovid Medline' search, designed to identify appropriate medical subject headings (MeSH). The keywords used at this stage were radiotherapy, pacemaker,

defibrillator, ICD and cardiac device. Hand searching of journals, relevant books, and review articles was also carried out.

The second stage of the process was the application of the generated MeSH terms and keywords in a comprehensive search of the following databases: MEDLINE, EMBASE, and Cancerlit. Subject headings were modified as required by individual databases.

The comprehensive search was limited to publications commencing 1994, the year in which the first documented guidelines (AAPM, 1994) were published. All subsequent published literature on the use of radiotherapy in patients with CIEDs was reviewed using the Critical Appraisal Skills Programme (CASP - Critical Appraisal Skills Programme, 2018) in order to define best practice (see appendix B.1)

Critical appraisal is the process of carefully and systematically examining research to judge its trustworthiness, and its value and relevance in a particular context (Burls, 2016). Critical appraisal is a formal, unbiased, systematic approach to assess the quality and relevance of evidence presented in a paper and its applicability to determine current 'gold-standard' practice for the management of patients with CIEDs receiving radiotherapy treatment. It included evaluation of the appropriateness of the study design for the research question and an assessment of information relevant to the research area.

The CASP framework and protocol was used to reduce any potential bias, in analysing the literature to eliminate any preconceived ideas about the subject area, identify literature sources and the selection of articles to include and the evaluation of the evidence (see appendix B.2)

Policy review

UK radiotherapy departments were identified using the Society and College of Radiographers' database (see appendix C). In March 2013, all radiotherapy department managers were emailed asking them to participate in a national audit. Radiotherapy departments were asked to either provide their current CIED policy or to indicate if there was no policy (seen appendix D).

A proforma was created to analyse CIED policies comprising two sections; the first section defined the roles and responsibilities of healthcare professionals involved in the patient pathway and the second section assessed the treatment and management guidelines (see appendix E). All data collected was anonymised. A spreadsheet (Microsoft Excel) was created for the entry and analysis of audit data. Guidelines were compared with current best practice. Results are presented as simple frequencies and percentages.

4.2.2 Study 2

To conduct clinical audits to determine the effects of ionising radiation and EMI on patients with CIEDs receiving radiotherapy treatment at a RCW

The first audit included all patients with a CIED receiving radiotherapy treatment. During this audit it was observed that patients with a rate response activated CIED displayed a distinct type of clinical adverse side effect during radiotherapy treatment. Consequently, a second audit was undertaken which focused on patients with a rate response activated CIED receiving radiotherapy treatment at RCW.

- Audit 1: Clinical audit – all patients with a CIED receiving radiotherapy treatment
- Audit 2: Clinical audit – patients with a rate response activated CIEDs receiving radiotherapy treatment

Audit 1: Clinical audit – all patients with a CIED receiving radiotherapy treatment

Therapy radiographers (qualified members of the CIED monitoring team) from RCW observed that an increasing number of patients with CIEDs displayed adverse cardiac side effects during and after their radiotherapy treatment. This required further investigation and as part of this work, these effects were studied in order to determine their extent and also investigate why more patients with CIEDs were thought to be exhibiting clinical adverse reactions during and after their radiotherapy treatment.

The aims of the clinical audit were to:

- Define radiotherapy induced device malfunction
- Assess device malfunction in patients with a CIED that have been exposed to ionising radiation and EMI as part of their radiotherapy treatment at a RCW
- Provide evidence and data showing that ionising radiation and / or EMI affect patient's CIEDs when receiving radiotherapy treatment.

Study Design

As part of this work, it was necessary to determine device malfunction in patients with a CIED undergoing radiotherapy treatment at a RCW. Therefore, a retrospective clinical audit was conducted, using patient information data collected after the patient had received radiotherapy treatment.

A clinical audit is a proven method of quality improvement, that seeks to improve patient care and outcomes through a systematic review of care against explicit standards and the implementation of change (NICE, 2002). Prior to commencement, audit permission was obtained from the Cardiology Department and the RCW involved. All patients were treated in accordance with departmental policies and protocols. All data was collected retrospectively from patient records, patient CIED identification cards and radiotherapy treatment documents.

Audit 2: Clinical audit – patients with a rate response activated CIEDs receiving radiotherapy treatment

Earlier chapters have documented the developments and improvement in pacing CIED technology. One such advancement is rate response activated CIEDs, which are increasingly being implanted in patients for the management of their cardiac conditions. However, there is no research into the effect of ionising radiation and EMI on these devices, hence why a clinical audit was carried out to assess device malfunction in patients with a rate response activated CIED that received radiotherapy treatment at a RCW.

As discussed in chapter three, rate response activated CIEDs can be affected by EMI from the radiotherapy treatment machine, but the reaction is highly specific to the make, model, design and CIED manufacturer. The manufacturers acknowledge that patients with a rate response activated CIED, might experience transient heart rate increases during the delivery of the radiotherapy treatment. They advise that the rate response setting on the device is switched to 'OFF' or 'PASSIVE' to mitigate any potential interference from EMI. However, there is no research into the effect of ionising radiation and EMI on rate response activated CIEDs during radiotherapy treatment.

Thus as part of this work, a clinical audit was undertaken to:

- Define CIED mediated tachycardia
- Assess device malfunction in patients with a rate response activated CIEDs that have been exposed to ionising radiation and EMI as part of their radiotherapy treatment at a RCW
- Provide evidence and data showing that ionising radiation and / or EMI affect rate response activated CIEDs when receiving radiotherapy treatment.

Materials and Methods

In order to determine device malfunction in patients with a rate response activated CIED, a retrospective clinical audit was conducted. For this clinical audit, a 'CIED mediated tachycardia' was defined as any conditions in which a CIED paces the ventricle at rates that are inappropriately fast. CIED manufacturer, Boston Scientific describe CIED mediated tachycardia as 'the repeated cycle of sensing and tracking and can continue until conduction is lost in the CIED. CIED mediated tachycardia can result in ventricular pacing rates as high as the maximum tracking rate'.

In this audit, this is observed by the patient's clinical presentation and heart rate during their radiotherapy treatment. All patients were monitored with a continuous ECG strip and observed during treatment with audiovisual monitoring and monitoring staff documented any changes in the patient's physical status and changes in the ECG trace. If at any point malfunction is suspected or detected, the clinical oncologist and cardiologist were immediately informed.

All patients from a cardiology department at a RCW, that had a rate response activated CIED implanted and presented for radiotherapy treatment at a RCW were included in this audit. These patients received radiotherapy treatment and were treated in accordance with the department's CIED policy. All data was collected

retrospectively from patient records, patient CIED identification cards and radiotherapy treatment documents.

4.3 Scientific research (Studies 3 – 5)

Research approach

These studies make use of a quantitative research strategy and adopted an experimental approach to data collection, using information obtained as a result of the preliminary study (discussed below). Due to the nature and involvement of ionising radiation in the research, at this stage it would be inappropriate to expose patients to the ionising radiation doses required to investigate the destructive effects upon the CIEDs and leads by ionising radiation and EMI. The effects of this testing has the potential to have catastrophic effects to the patient, such as inducing secondary malignancies and / or cause cardiac malfunctions and failure. The research was therefore conducted under laboratory conditions, exposing CIEDs and CIED leads (separately) to ionising radiation, EMI and physical testing. This was undertaken using a range of ionising radiation doses based upon published previous studies and the preliminary study.

Research design and method

The research design is the researcher's overall plan for obtaining answers and evidence to the research questions guiding the study. It is the set of methods and procedures used in collecting and analysing data of the variables specified in the research questions. Polit et al (2001) describe the research design as a blueprint, or outline, for conducting the study in such a way that maximum control will be exercised over factors that could interfere with the validity of the research results. Research design refers to the plan or strategy of shaping the research, that can include the entire process of research from conceptualising a problem to writing

research questions, data collection, analysis, interpretation and report writing (Creswell, 2008). This research used a quantitative experimental design to identify, analyse and describe factors contributing to the effect of ionising radiation and EMI on CIEDs and leads.

Quantitative research

Quantitative research is an objective, systematic process for obtaining quantifiable information, presented in numerical form and analysed through the use of statistics. It is used to gain information, describe and test variables and to examine the cause-and-effects of relationships and attempts to control the environment in which the data is collected (Given, 2008). The overarching aim of this research was to classify features and construct statistical models in an attempt to explain what is observed when CIEDs and leads are exposed to ionising radiation and EMI. This study aimed to quantify the factors identified as contributing to the adverse effects of the functioning of CIEDs when exposed to ionising radiation and EMI and to gather evidence that allowed conclusions to be reached.

Characteristics of quantitative research

When conducting quantitative research, the researcher should have clearly defined research questions to which objective answers are sought, obtaining numerical data in a controlled investigative setting. There are three primary types of quantitative research designs; experimental / quasi-experimental, descriptive and correlational. The research design and method should be transcribed in a systematic and logical order, which may be replicated or repeated by other researchers given its high reliability. Reliability and validity of the testing equipment and instruments are essential. Statistical analysis is conducted to organise data, determine significant relationships and identify differences and/or similarities within and between data sets. Personal bias can be avoided by following the quantitative research methodology

and using accepted computational techniques to analyse data and assess the relationship between variables.

Experimental design

An experiment tries to measure the effects of X on Y by controlling X and measuring Y, while at the same time keeping everything else constant Creswell, 2008). Experimental research has a range of definitions but in the strictest sense, experimental research is called a 'true experiment'. True experimental design is considered the most accurate and reliable form of experimental research as it uses statistical analysis to try to prove or disprove a hypothesis (Creswell, 2008).

Experimental research uses manipulation and controlled testing to understand causal processes. The experimental methodology is a systematic approach in which the researcher establishes a control group and manipulates one or more variables and measures any change in other variables. This allows the researcher to establish cause-and-effect relationships between a group of variables and assess the correlation between them. Experimental designs are developed to answer hypotheses, formulated by researchers to address specific testable questions. The researchers set up an experimental study and collect and analyse data, which will support or disprove the hypothesis. Hypotheses can be based on theory, on previous research findings, a pilot study or a theory that the researcher may wish to examine further.

Adopting an experimental approach to the research, enabled manipulation and control of the testing variables to investigate the effects of increasing the ionising radiation dose exposed to CIEDs and leads (separately) and also to investigate the effects of exposure to EMI on CIEDs. The results from these experiments enable an understanding of causal processes and possible cause-and-effect relationships as

well as assessing the correlation between them. The research design and method for each study is discussed in further detail under the sub-heading implementation of the study.

Data validity

The aim of quantitative experimental research is to gather data and evidence that allows a reasonable conclusion to be drawn as to whether or not a particular variable causes a particular effect or result. Moskal and Leydens (2002) defined validity as "the degree to which the evidence supports that the interpretations of the data are correct and the manner in which interpretations used are appropriate". Quantitative experimental research should be conducted using a representative sample under carefully controlled conditions so that the conclusion can reasonably be generalised to a larger cohort or population. In this study, a representative sample of CIEDs could not be used, due to the cost and availability of the devices within the time constraints of the research project. The CIEDs that were used in the research were all from manufacturers X, Y and Z and the same make and model which conformed to set manufacturer standards. This is a limitation of the study, however it does not appear to be detrimental to the research, as the same devices were used and the subsequent results could be compared and analysed.

According to Creswell (2008) there are several threats of validity that raise issues about the accuracy of the data or results or application of statistical tests to conclude the effects of an outcome. They are internal validity threats, external validity threats and statistical conclusion threats. For example, experimental samples may be too small or may be made up of participants that do not accurately represent the larger population. All of these threats can cast doubt upon a research study's conclusions. An experimental approach to data collection is said to be an effective means of strengthening:

- **Internal validity –** This relates to how far a study has established whether a variable under investigation has had an effect and whether there is sufficient evidence to support the claim.
- **External validity –** This relates to whether findings from a specific sample in a study can be generalised to a larger, specific population.

The basic requirement to interpret an experiment is to clearly define internal validity. Internal validity threats are experimental procedures, treatments or experiences of the participants that threaten the researcher's ability to draw correct inferences from the data in an experiment. External validity threats arise when the researcher concludes incorrect inferences from the sample data and commutates to other persons. A statistical conclusion validity threat arises when experimenters draw inaccurate inferences from the data because of the violation of the assumptions of the statistical test being used for the collected data.

The internal validity threats that could arise from data collection and the tools used for collecting the data, were clearly defined. These were:

- Changes in the instrument may produce changes in outcomes
- Measurement errors that result from changes in the calibration of an instrument or changes in the instrument itself

In order to avoid these threats, the experiment, testing equipment tools and instruments were set up by the researcher and the same testing instruments were used throughout the PhD research project. All data was stored in approved proformas in Microsoft Excel, and saved on a USB for later analysis. To mitigate the threat of external validity, all data was sorted accurately and assigned to their

particular study and results quantified to that study. This data was interrogated using statistical analysis and conclusions were subsequently drawn.

4.3.1 Preliminary Study

Introduction

A small-scale preliminary pilot and feasibility study was conducted to gather information prior to the PhD research project. It was undertaken at RCW, radiotherapy department from May 2013 to August 2013. The purpose of this study was to ensure that the ideas and methods behind the research ideas were sound, identify design issues, permit preliminary testing of the hypothesis and to identify and address any issues in the study protocol.

The feasibility aspect of the preliminary study answered whether or not the study could be done and was used to estimate important parameters that were needed to design the main study. The pilot study was a miniature version of the main study to test logistics and determine whether the components of the main study could all work together. As a result, the focus and nature of the PhD study was determined and the research questions and objectives were refined. Using results and information from the preliminary study, the design and testing protocol were evaluated and amended prior to the commencement of the full-scale PhD research project.

Preliminary study research questions (predicted measures):

The study examined 4 different predicted measures:

1. The effect of ionising radiation on CIED function
2. The effect of ionising radiation on CIED lead function
3. At what ionising radiation dose CIEDs exhibited clinical malfunctions
4. At what ionising radiation dose CIEDs failed

Hypothesis

As the level of ionising radiation dose increases, the greater the likelihood of CIED or CIED lead malfunction or failure increases.

Method

Research design

The preliminary study used a quantitative research strategy and adopted an experimental approach to data collection.

Part 1 - CIED testing - Equipment:

CIEDs

A total of six pacemakers were included in the study; two pacemakers from each of the three CIED manufacturers (Biotronik, Boston Scientific and St. Jude Medical) were tested in this study. All the devices were new (no used devices were tested, as they might have a history of use which could influence results). Inter-device reliability was tested utilising three of the same make/model devices for each of the following manufacturers - Biotronik, Boston Scientific and St. Jude Medical.

CIED programmed:

- Minimum frequency – 60bpm and maximum frequency – 120bpm
- Pulse duration – 0.5ms
- Pulse amplitude – 2.5V
- Sense threshold – 0.18mV
- Dummy load resistor of 500Ω

In order to mimic clinical practice, the CIEDs were placed in a clear plastic polymethylmethacrylate (plexiglass) block and tissue equivalent bolus material

placed on top of it, such that the middle of the device was located at the maximum dose depth for 6MeV photon beam (1.5cm). The CIED being irradiated and interrogated was positioned precisely along the projected central axis (isocentre) of the primary radiation beam.

Radiotherapy treatment room – LINAC

A standard radiotherapy unit (Varian 650c linear accelerator with 120MLC, portal imaging, beam energy 6MeV set as a dose rate of 600MU/minute) was used to deliver the ionising radiation. The x-ray field collimators were open to encompass the CIED within the primary photon beam.

Environmental conditions:

- LINAC room temperature and room pressure recorded as part of the daily QA procedure prior to data collection to ensure LINAC output was within expected tolerance
- Linear accelerator beam energy – 6MeV*

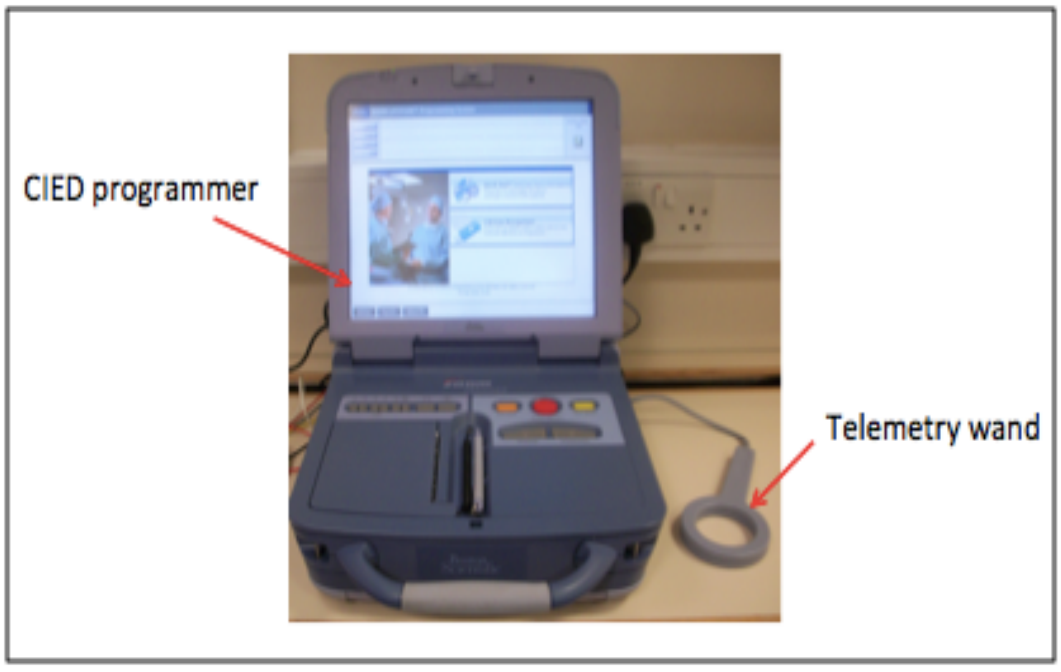
* The energy of ionising radiation is measured in electronvolts (eV). One electronvolt is an extremely small amount of energy. Commonly used multiple units are kiloelectron (keV) and megaelectronvolt (MeV).

CIED programmer and telemetry wand

A programmer is a device that communicates with the CIED with radio frequencies in the Medical Implant Communication System (MICS) band. This is a low-power, short-range (2 m), high-data-rate, 401–406 MHz (the core band is 402–405 MHz) communication network that has been accepted worldwide for transmitting data to support the diagnostic or therapeutic functions associated with medical implant devices. The programmer functions by running a user-friendly operating system to

check the integrity of the CIED system and control the functioning of the device. CIED programmers have evolved into dedicated computers, which have made possible extensive programming of CIEDs and advanced interrogation of device diagnostics. CIEDs have a micro-antenna which is able to communicate with an external transmitter via its attached telemetry wand. The programmer is able to read information stored in the logs of the CIED, interrogate its current status and to modify its settings. In this study, the programmer replicated the electrical behaviour of a paced heart and established the function of the CIED, tested electrocardiogram (ECG) parameters, differentiated between natural sinus beats and paced beats and defined the refractory period.

Figure 4.1: Photograph showing the CIED programmer and attached telemetry wand



CIED ionising radiation testing protocol:

1. **Pre-ionising radiation exposure:**

- CIED programmer telemetry wand placed around the CIED under investigation (outside of the RT treatment room)
- On the programmer, 'Quick Start' was selected, in order to run the CIED interrogation and diagnostic evaluation
- The programmer carried out the following basic tests:
  - CIED pulse rate
  - CIED pulse width
  - CIED inhibition sensitivity
  - CIED mode setting - to determine if the devices were in 'interference mode' or 'safe mode
- One completion of the device interrogation, a full service report was provided (which could either be downloaded onto USB or printed)

2. **CIED ionising radiation exposure:**

- In the radiotherapy treatment room, the CIED was placed in the phantom and tissue equivalent bolus placed on top and positioned on the treatment couch, so that the CIED was within the primary radiotherapy photon beam
- LINAC accelerator switched ON
- In order to determine at which point the CIED exhibited malfunctions, the devices were irradiated to a total dose of 50Gy in twenty-five fractions (increasing dose by 2Gy per fraction)

3. **Post-ionising radiation exposure:**

- After every five fractions (increasing dose delivered by 10Gy every five fractions) the CIEDs were subjected to functionality base-line tests to determine if the device was still operating correctly
- If these tests proved that no adverse damage had been caused to the device, they were further irradiated for another 10Gy (in five fractions)
- This process continued until the device had received a cumulative ionising radiation dose of definite point-of-failure (120Gy)

Part 2 - CIED lead Testing – Equipment:

CIED leads

- A total of twelve CIED leads were included in the study; four leads from each of the three CIED manufacturers (Biotronik, Boston Scientific and St. Jude Medical).
- All twelve leads were irradiated but only six leads (two from each manufacturer) were subjected to stress testing to determine whether this process replicated the stress placed on the lead when implanted in a patient

Radiotherapy treatment machine and environmental conditions as per preliminary study.

CIED lead ionising radiation testing protocol:

1. **CIED lead ionising radiation exposure:**

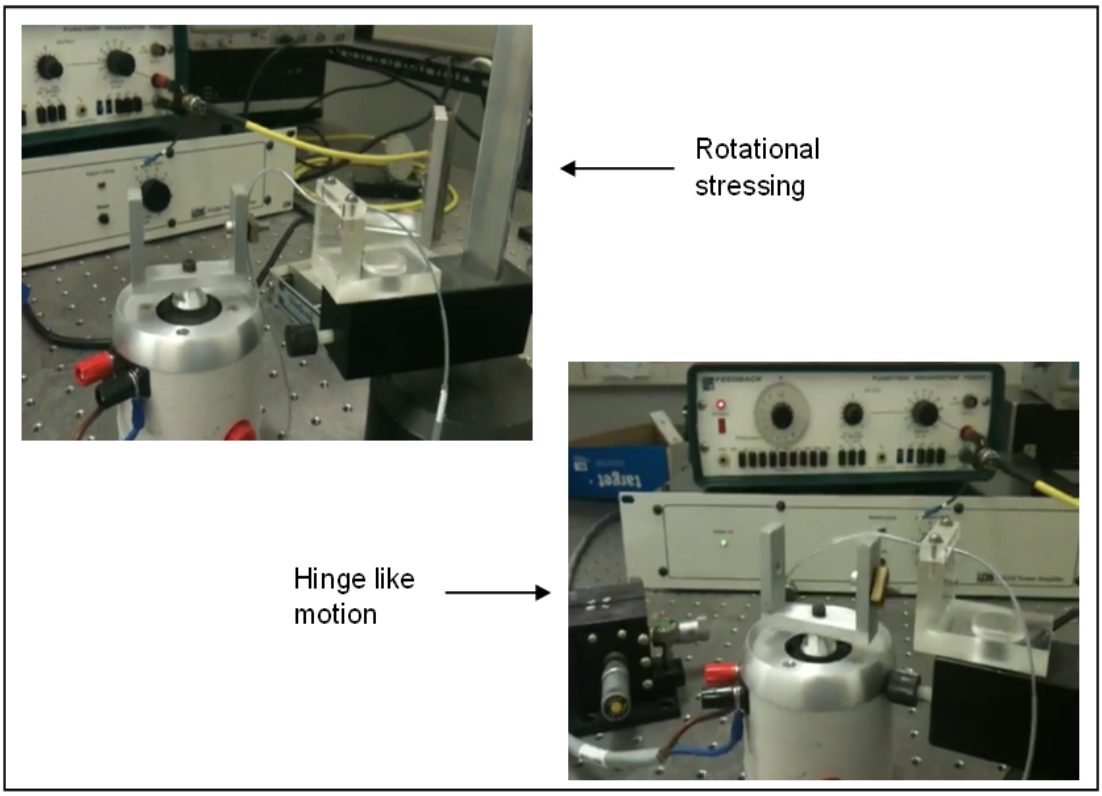
- In the radiotherapy treatment room, the whole CIED lead was placed in the phantom and tissue equivalent bolus placed on top and positioned on the treatment couch, so that the CIED lead is within the primary radiotherapy photon beam.

- LINAC accelerator switched ON
- In order to determine if ionising radiation affected the physical condition of CIED leads, they were irradiated to a total dose of 60Gy in six fractions (increasing dose by 10Gy per fraction).

2. Post-ionising radiation exposure:

To monitor the physical effects and to determine the effect of ionising radiation on the physical condition of the leads, specific testing equipment was designed. With every heartbeat, the displacement of the heart occurs in three directions; radial, long axis and rotational. The majority of displacement is radial; classically seen as systolic function on 2-D imaging. Within the equipment set-up, this will be replicated by linear vibration and rotational stressing, with a heart rate of 70bpm and a displacement in all directions of 1cm. Clinical observations showed that leads tend to stick to blood vessels and other structures at discrete places (at the junction of the superior vena cava and right atrium and in the right atrium and around the tricuspid valve), this was replicated by a hinge-like movement.

Figure 4.2*:* Photographs showing the lead testing equipment



In order to determine if ionising radiation affected the physical condition of the CIED leads, all leads (non-stressed leads and stressed leads) were subjected to electric and magnetic testing. A novel microwave experiment (see below) was used to provide measurement of the electrical conductivity of the CIED lead sheath polymer at microwave frequencies. The resonant cavity was connected to the vector network analyser (VNA) to provide data on any polymer changes in the sheath layer of the CIED leads. The electrical energy from the VNA is stored in the cavity, which resonates at a very precise frequency (analogous to striking a bell, the energy from the strike makes the bell ring at a particular note). This is the so-called un-loaded cavity resonance and serves as a reference. The sheath layer of the CIED lead was then inserted into the cavity and the electrical field at the top of the hairpin structure interacted with the CIED lead sheath material. This allowed for a direct measurement of the electrical properties of the CIED lead sheath material and any residual

conductivity in that material (in the form of free electrons liberated as a result of broken polymer bonds). This conductivity 'loads' the cavity and thus changes the characteristic resonance. (Analogous to holding the bell while ringing it, it makes a thud as opposed to a ping). Since the cavity resonance is extremely sensitive to small changes, any de-polymerisation from the radiation field should affect the cavity resonance. There are three principle changes that occur to a cavity resonance when it is loaded.

1. Shift in resonant frequency.
2. Change in the bandwidth of the resonance
3. Insertion loss; where the power entering the cavity is consumed.

Preliminary study – Data analysis

The preliminary study used quantitative methods to collate data and investigate the relationship between variables that can cause damage to CIEDs and CIED leads. Information from the CIED programmer provided raw data on the effect of ionising radiation on the CIED and data from electric and magnetic testing on the CIED leads provided information to investigate the physical condition of CIED leads when exposed to ionising radiation. The preliminary study led to the development of the research questions and research hypotheses, the results of which will underpin the testing protocol and data collection procedure for the PhD research project (studies 3-5).

Preliminary study informed PhD research project

The preliminary study revealed shortcomings in the design of the proposed testing protocol and data analysis procedure. Firstly, when conducting the CIED testing, the results from the programmer only alerted and flagged up the basic CIED parameters affected by ionising radiation. Therefore, the level of detail needed to determine if the CIED had been adversely effected by ionising radiation and at which dose this

effect occurred could not be obtained. In consultation with the CIED manufacturers, additional testing protocols, which utilised more advanced programming and functionality tests that the programmer was equipped to perform were adopted. In the PhD project, detailed tests will be conducted 'live' by interrogating the CIEDs using the programmer to pinpoint the exact ionising radiation dose at which the CIED start to exhibit clinical malfunctions. The programming tests will show if the ionising radiation has affected the hardware or software components of the CIED and the functionality tests will show any alternations in the programmed working function of the CIED. Conducting these advanced tests will allow a more detailed breakdown and analysis.

Secondly, the CIEDs were placed in a clear plastic polymethylmethacrylate (plexiglass) block and tissue equivalent bolus material was placed directly on top of it. As this was a proof of principle study, this worked as it proved that the bolus placed on top could mimic human tissue and to the depth to which the CIED would be implanted in a patient. In the resultant PhD study, a phantom will be designed using the polymethylmethacrylate block and encapsulate the CIED and lead within in. This will be achieved by channeling out a 'groove' in which the CIED lead can sit and a 'hole' that the CIED can be placed in. These will then be flush with the block and the bolus can sit directly on top with no air gaps, which could affect the distance the ionising radiation has to travel before reaching the CIED and lead. In doing this, there will be a truer representation of the clinical placement of the CIEDs and the leads when in-situ in patients.

The preliminary study, proved valuable in highlighting additional tests and changes that can be included in the PhD research project. In the preliminary study, the investigation was limited to 6MeV beam energy on a Varian linear accelerator. A study by Hurkmans et al in 2005 only irradiated their devices using a 6MeV photon

beam, as they believed that different beam energies or type (photons or electrons) would have the same effect on the pacemakers. They referenced a previous study by Rodriguez et al, in which devices were irradiated at different beam energies and they concluded that no difference to device function was determined in using the different beam energies. In clinical practice, results from study two, showed that patients receiving radiotherapy treatment at a RCW exhibited a range of cardiac and CIED changes during their radiotherapy treatment. These occurred when being treated using both 6MeV and 10MeV photon beams. Therefore, in the PhD research project the testing protocol will remain the same but this protocol will use both beam energies (6MeV and 10MeV) to irradiate the CIEDs and the CIED leads.

Conducting the preliminary study identified design issues with the testing protocol regarding the measurement of ionising radiation dose received by the CIED. To address this for the later PhD studies, in-vivo dosimetry was used to verify the planned dose was administered to the CIED. A surface thermoluminescent dosimeter (TLD) was placed on the device and this recorded the entrance ionising radiation beam dose. TLDs use small 'chips' of lithium fluoride (LiF), a material that gives off light when heated after it has been exposed to ionising radiation. The amount of light given off was measured using a photomultiplier tube while the chip was heated in an oven inside a light-tight enclosure. The amount of light given off was used to estimate the ionising radiation dose received. Medical physicists then compared this dose to the planned ionising radiation dose and verified that the correct dose was received to the CIED.

The preliminary study also identified an area of concern, as the CIEDs received a 2Gy per fraction dose of ionising radiation and there is the potential that the exact point at which the CIED first started to exhibit clinical malfunctions are not detected. Therefore, study 3 of this work will test CIEDs starting at 0.5Gy and further test

increments of 0.5.Gy per fraction, to a total cumulative ionising radiation dose whereby the device fails and onto end-point failure (test to destruction 60-120Gy). Using this low incremental value will allow accurate identification at which point any ionising radiation dose clinical defect occurs. As per the preliminary study, CIED and lead exposure to ionising radiation will occur on a daily basis to enable device and lead recovery between fractions. The preliminary study used six CIEDs from three of the CIED manufacturers. In order for a robust statistical and analytical evaluation, the preliminary study highlighted the need to test more CIEDs and CIED leads in the PhD research project.

Results from the preliminary study showed that subjecting the CIED leads to 'stressing' did not have an impact on the physical condition of the leads. Therefore, in study four of the PhD research project, the testing protocol will not include this part of the research method and protocol. When stressing the CIED lead (in the preliminary study), the whole lead was required to provide a clinical representation of the route/path the CIED lead would take when in-situ in a patient. However, as the PhD research project will be investigating the effects of physical construction, physical condition and levels of degradation as a result of ionising radiation exposure and EMI, the whole lead is not required to be tested. Liaising with CIED manufacturers and the cardiology department it was decided that CIED lead testing could proceed using 5cm sections of the CIED lead. The irradiating protocol remains the same. This would allow for an increased number of sections of the lead to be tested and improve reliability and accuracy of the results.

Significantly, the preliminary study only investigated the effects of ionising radiation on CIEDs and the leads. Results from the literature review, showed that EMI could potentially cause the CIED to exhibit clinical malfunctions and failure (Zaremba, 2015). Therefore, study five of the PhD research project, will undertake to determine

the effect of EMI on CIEDs. This will allow for a comprehensive analysis of the exact effects of both ionising radiation and EMI on CIEDs.

Summary

In this section, the methods and analysis of the preliminary study data has been discussed. The focus of the preliminary study has been maintained to determine the relationship between ionising radiation and EMI and the damage it causes to CIEDs and their leads. The experimental approach chosen for the preliminary study used a quantitative methodology of data collection to quantify the levels of damage to the CIEDs and leads caused by ionising radiation and / ore EMI. In conclusion, this preliminary study provided the framework to develop and extend the PhD research project but as a proof of principle exercise it was highly beneficial.

4.3.2 Ethical requirements

At the start of the PhD research project, the research did not include patients or patient participation; therefore formal NHS ethical approval was not required. However, during the data collection phase of the study, patient information, such as patients' medical history, CIED information and their radiotherapy treatment information was required to be included in case studies. Therefore an application was made and NHS ethical approval was granted. During the application process, strict parameters were identified; there would be no contact and communication with patients (and their families); there would be no change in any aspect of their radiotherapy or cardiology treatment and all information would be annoymised and kept confidential, in compliance with the Data Protection Act 1998. All information and data collected in the course of this research project will only be used for the purpose of the study and will remain confidential.

4.3.3 Risk review

With respect to the use of premises and equipment, the PhD research project has been subjected to risk review and peer review and been awarded R&D approval from RCW R&D Committee. Permission has also been given for access to radiotherapy machines and equipment from RCW. The study will be conducted primarily after clinical usage of radiotherapy treatment units, for example after-hours, weekends and/or planned breaks. Researchers conducted a thorough risk analysis of the effects of ionising radiation in conjunction with the Radiation Protection Advisor at RCW. All health care professionals participating in the research will be aware of the issues related to the exposure of ionising radiation, and will fully comply with the 'Ionising Radiation (Medical Exposure) Regulations 2000'.

4.4 Research outcomes

Study 6

To provide evidence based guidelines for the safe management of cancer patients with CIEDs receiving radiotherapy treatment

Research approach

Study six adopted a systematic review as the research methodology. It reviewed the evidence and literature to determine current 'gold standard' practice and provide evidence-based recommendations and guidelines for the management of cancer patients who have a CIED and are receiving radiotherapy treatment.

Systematic reviews are ranked highly in research and are considered the most valid form of medical evidence, as they provide a complete summary of the current literature relevant to a research question (Gopalakrishnan and Ganeshkumar, 2013).

Research design and method

A systematic review is designed to provide a complete, exhaustive summary of current literature relevant to specific research questions. The Cochrane Collaboration defined a systematic review as "a review of a clearly formulated question that uses systematic and explicit methods to identify, select and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review" (Higgins and Green, 2011). According to Gough, Oliver, and Thomas (2013), a systematic review is a research method that is undertaken to review research literature, using systematic and rigorous methods. Systematic reviews are often referred to as 'original empirical research' because they review primary data, which can be either quantitative or qualitative. Systematic reviews can be considered as the 'gold standard' for reviewing the current literature on a specific topic as it synthesises the findings of previous research investigating the same or similar questions (Boland et al, 2008)

The systematic review process employs literature review methods to select only those studies that meet specific criteria, which reasonably confirm the rigour of the evidence produced, by a previously published study. Essential to a systematic review, is to establish a rigorous set of criteria, to appraise the reliability and validity of published research and develop an organised method of locating, analysing and evaluating such literature.

This study reviewed the research systematically in three stages. Firstly, it identified all relevant published and unpublished evidence and research and subsequently selected the studies for inclusion in the review. Secondly, it critically appraised the research methods and assessed the quality of each study and finally it synthesised and presented the findings in an unbiased way. The research design and method for each study is discussed in further detail under the sub-heading implementation of the study.

Data analysis

Data from this study was presented narratively. Narrative methods of synthesis can be used to synthesise both quantitative and qualitative studies and can be used when the experimental and quasi-experimental studies included in a systematic review are not sufficiently similar for a meta-analysis to be appropriate (Mays et al, 2005).

Narrative synthesis is used in different ways. In this study, it was used as an overarching term to describe the method for synthesising data narratively, focusing on the application of clinical guidelines for patients with CIEDs receiving radiotherapy treatment. A narrative synthesis was used to systematically define and organise the data, highlight important characteristics of the studies and describe and comment on the methodological quality (risk of bias) of each study.

Data synthesis in this study involved the collation, combination and summary of the findings of individual studies included in the systematic review, through a narrative approach. The strength of evidence was assessed and the management guidelines and recommendations for patients with CIEDs receiving radiotherapy treatment across the studies were analysed and possible reasons for inconsistencies were investigated. This enabled reliable conclusions to be drawn from the included studies. In the data analysis phase, the strength of the evidence was assessed and used to draw conclusions and inform the development of guidelines and recommendations.

Data validity

Research can vary considerably in methodological approach and rigour. Flaws in the design or conduct of a study/report can result in bias and important themes and results can lack clarity. The strengths and weaknesses of the included studies were documented, which provided an indication of whether the results have been

influenced by the study design, analysis process and/or the researchers. Having assessed the quality of the study, results can inform the aims and protocols of the research. Quality assessment justified if the studies were robust and reliable enough to provide clinical guidelines for the management of patients with CIEDs receiving radiotherapy treatment.

Bias refers to systematic deviations from the true underlying effect brought about by poor study design or conduct in the collection, analysis, interpretation, publication or review of data. In order to mitigate the bias effect in this systematic review, the impact of search limitations and publication bias were minimised by not restricting the search to only electronic databases, which consist mainly of published journal articles. Wider searching identified articles circulated as reports, conference papers and discussion papers. Searching databases that included unpublished studies reduced the impact of publication bias.

Selection process bias was minimised by including or excluding certain studies due to pre-formed opinions. The process for study selection was documented in an explicit and objective way ensuring that this process is reproducible. In order to assess the quality of documents, a proforma and checklist was created, which ensured all the studies were assessed are critically appraised in a standardised systematic way.

4.5 Implementation of method

4.5.1 Study 3

To investigate and evaluate the relationship between cumulative ionising radiation dose and the damage sustained to CIEDs (pacemakers and ICDs).

Research questions:

- What is the relationship between cumulative ionising radiation dose and damage sustained to CIEDs (pacemakers and ICDs)?
- Is there is a safe minimum ionising radiation tolerance dose to CIEDs (pacemakers and ICDs)?
- How will any damage to the CIED impact the patient clinically?

Hypothesis:

- As the level of ionising radiation dose increases, the greater the likelihood of CIED malfunction or failure also increases.

Research design and method

Research design

The study was conducted under laboratory conditions and used a quantitative research strategy and adopted an experimental approach to data collection.

CIEDs:

- Total of thirty-three CIEDs was investigated in the study
- Twenty-one explanted fully functioning pacemakers (seven pacemakers from manufacturer X, seven pacemakers from manufacturer Y and seven pacemakers from manufacturer Z) were tested. 3 pacemakers (one from each manufacturer) were used as a control, therefore, not exposed to any ionising radiation.
- Twelve explanted fully functioning ICDs (five ICDs from manufacturer X, five ICDs from manufacturer Y and two ICDs from manufacturer Z) were tested. 3 ICDs (one from each manufacturer) were used as a control.

- Reasons for explanation – patient died, not related to CIED and at time of death CIEDs were working correctly
- All explanted CIEDs were decontaminated and suitable for safe handling
- All explanted CIEDs had not been previously exposed to ionising radiation
- Using the CIED programmer, it is vital to obtain a baseline report for the CIEDs prior to any exposure to ionising radiation as part of this study, as they are explanted devices and will each have different set parameters. Using this baseline report will allow for accurate comparison of subsequent changes

CIEDS programmed:

The CIEDs were programmed with standard settings (DDD).

- **D**ual (atrial and ventricular) pacing
- **D**ual (atrial and ventricular) sensing
- **D**ual response (inhibited and triggered) to sensing

DDD is the standard programming of dual chamber CIEDs, in this mode both atrium and ventricle are sensed and paced. For example, if both the sinoatrial node (SA) and atrioventricular (AV) node are functioning correctly, the CIED will only sense this activity and not be required to act. If the atrium does not produce a pulse/beat, the CIED will pace the atrium at a preprogramed rate. If this beat is not propagated through into the ventricles, the CIED will pace the ventricle. This mode ensures atrioventricular (AV) synchronisation at rest and during exercise. In DDD mode, the pacemaker follows the fastest rate, whether spontaneous atrial or sensor-driven. The maximum tracking rate and the maximum sensor-driven rate are independently programmable. The DDD mode is the standard setting, for all pacemaker patients. On an ECG, the tracings may show spontaneous and paced atrial events as well as spontaneous and paced ventricular events. Schematically, both chambers might be

paced, or any combination of paced and sensed events from the atrium and ventricle.

CIED programmed settings:

- Minimum frequency – 60bpm and maximum frequency – 120bpm
- Pulse duration – 0.5ms
- Pulse amplitude – 2.5V
- Sense threshold – 0.18mV
- Dummy load resistor of 500Ω

Additional programmed settings for ICDs only:

- Antitachycardia pacing and shock therapies inactivated (to avoid discharge during handling and testing)
- Ventricular tachycardia (VT) and ventricular fibrillation (VF) monitor zones were programmed active
  - VT zone from 167 bpm
  - VF zone from 214 bpm

Environmental conditions:

- In order to mimic clinical practice, CIEDs were placed in a phantom and tissue equivalent bolus material was placed on top of it, such that the middle of the device was located at the maximum dose depth to provide full backscatter conditions. In this study, the maximum depth dose for the 6MeV photon beam was 1.5cm and 2.5cm for 10MeV photon beam. The phantom had been developed as a result of the preliminary study and undergone and passed stringent quality assurance tests. The design was necessary, as no

phantom of this nature existed and it is highly adaptable and can be modified to test CIEDs and/or leads.

- A standard radiotherapy unit (Varian 650c linear accelerator with 120MLC, portal imaging, beam energy 6MeV and 10MeV set as a dose rate of 600MU/minute) was used to deliver ionising radiation. The distance from the head of the linear accelerator to the surface of the phantom including the tissue equivalent bolus was 100cm and the ionising radiation field size was set at 10x10cm^2
- LINAC room temperature and room pressure recorded as part of the daily QA procedure prior to data collection to ensure LINAC output was within expected tolerance
- Linear accelerator beam energy – 6MeV / 10MeV

CIED ionising radiation exposure:

- As in the preliminary study, the CIED programmer telemetry wand was placed around the CIED under investigation (outside of the RT treatment room)

Figure 4.3: Photograph showing the testing set-up for CIED interrogation by the CIED programmer

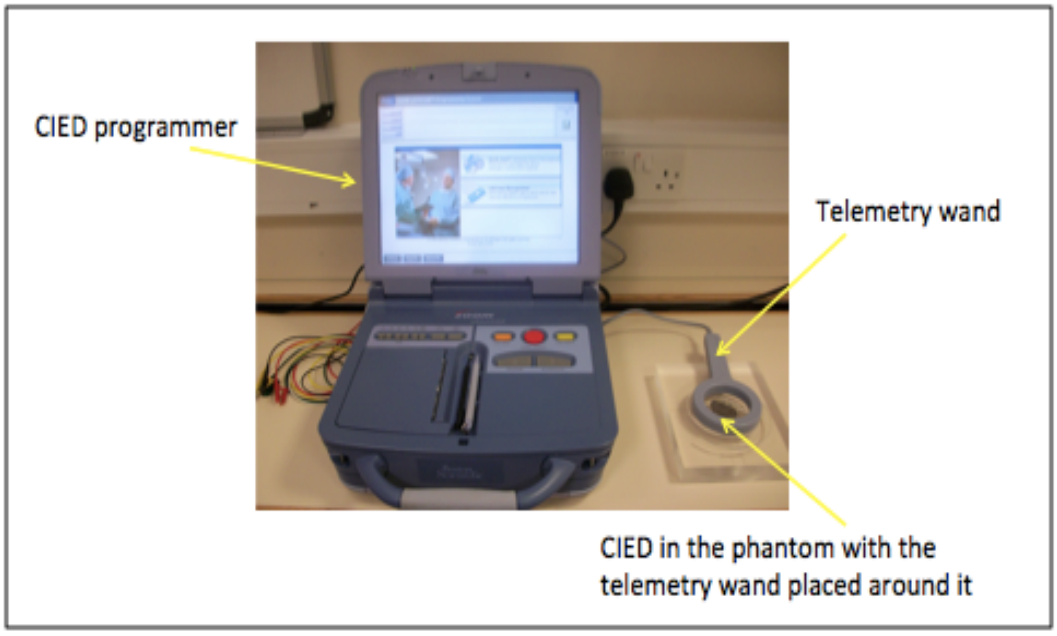
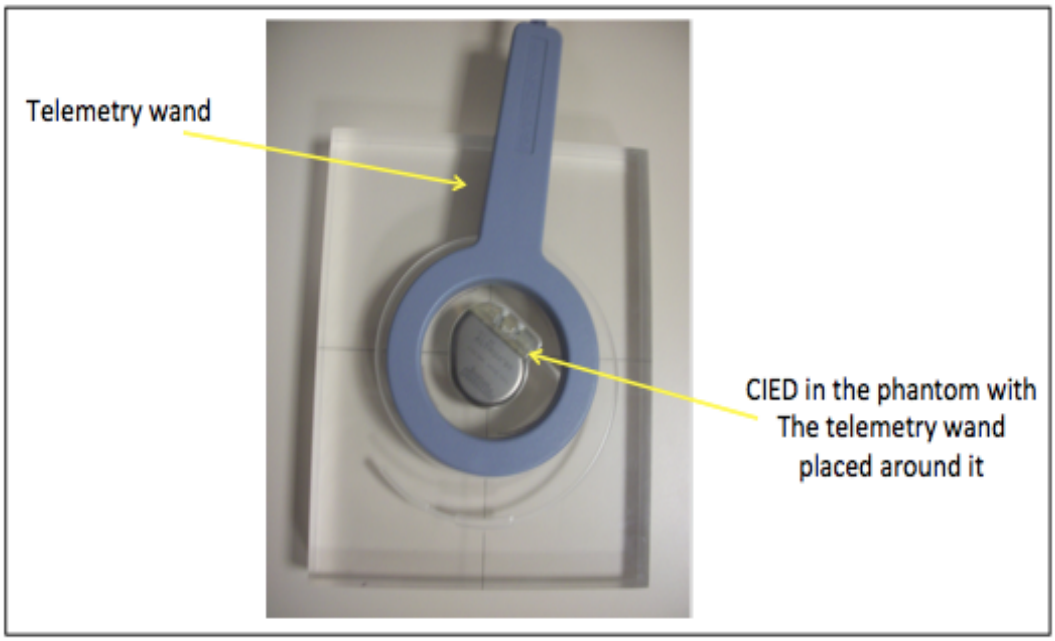


Figure 4.4: Photograph showing the telemetry wand placed around the CIED in the phantom to allow for CIED interrogation



- CIED programmer interrogated the CIED and provided a full service report
- In the radiotherapy treatment room, the CIED was placed in the phantom and tissue equivalent bolus placed on top and positioned on the treatment couch, so that the CIED is within the primary radiotherapy photon beam.
- The preliminary study identified an area of concern, as the CIEDs received a 2Gy per fraction dose of ionising radiation. Therefore, there was the potential that the exact point at which the CIED first started to exhibit clinical malfunctions were not detected. Previous studies had indicated that a dose as low as 0.5Gy, may cause clinically significant defects. Mouton et al (2002) observed small changes in pacing rate at even lower cumulative doses (<0.05Gy). However, in the preliminary study, no evidence of CIED malfunction occurred at this level. Therefore, the PhD research project tested CIEDs starting at 0.5Gy and further test increments of 0.5.Gy per fraction to

60Gy (end point failure). Using this low incremental value allowed accurate identification at which point any device malfunctions occurred.

- The CIEDs were also interrogated after every exposure to ionising radiation, using the CIED manufacturer-specific standard programmer and telemetry equipment.
- The presence or absence of the following events were recorded:
  - Noise during the radiation exposure
  - Spontaneous change in programmed device parameters without reset to backup mode
  - Reset to backup mode or other error recoverable using the programmer
  - Error not recoverable using the programmer
  - Clinically significant reduction in battery capacity
  - Inappropriate antitachycardia pacing or delivery of shock therapy in the ICDs (even though this feature of the ICDs were deactivated during irradiation)
  - Loss of telemetry
- CIEDs were irradiated to a total cumulative ionising radiation dose whereby the device exhibited failure and after reaching a cumulative ionising radiation dose of 60Gy, the dose per fraction was increased and delivered in 10Gy increments to CIED end-point failure (test to destruction 120Gy).
- The testing protocol was repeated for both 6MeV and 10MeV photon beams.

Table 4.1 : Testing protocol for CIED exposure to ionising radiation

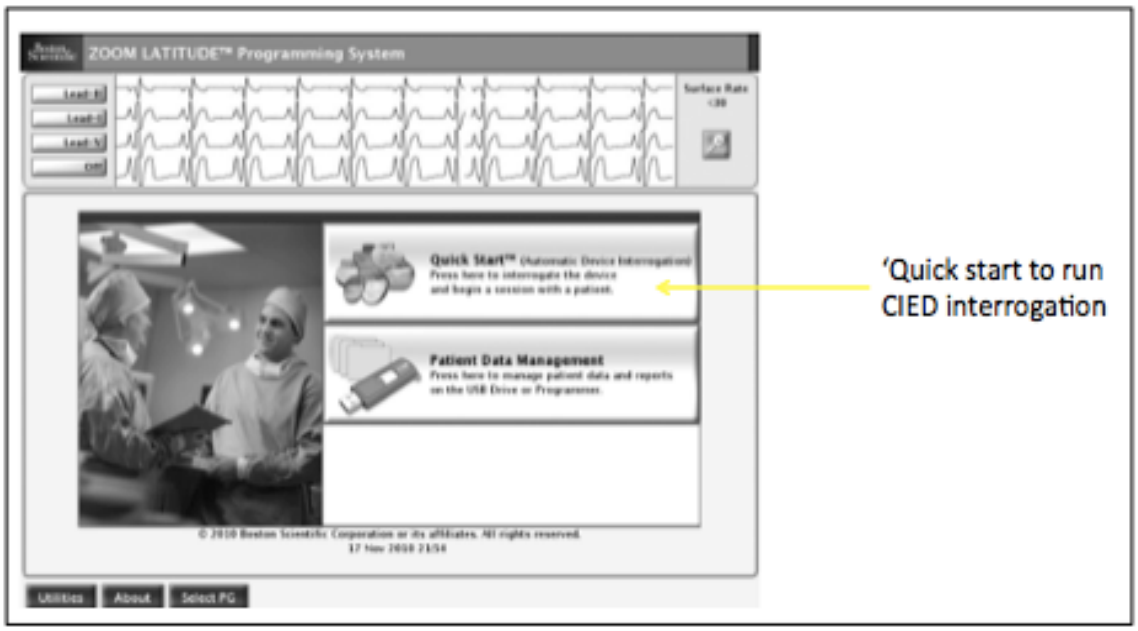
CIED type	CIED Manufact.	Control	6MeV			10MeV		
PM	**X**	PM X1	PM X2	PM X3	PM X4	PM X5	PM X6	PM X7
PM	**Y**	PM Y1	PM Y2	PM Y3	PM Y4	PM Y5	PM Y6	PM Y7
PM	**Z**	PM Z1	PM Z2	PM Z3	PM Z4	PM Z5	PM Z6	PM Z7
ICD	**X**	ICD X1	ICD X2		ICD X3	ICD X4		ICD X5
ICD	**Y**	ICD Y1	ICD Y2		ICD Y3	ICD Y4		ICD Y5
ICD	**Z**	ICD Z1	ICD Z2					

PM = Pacemaker / ICD = Implantable cardioverter defibrillator

CIED interrogation:

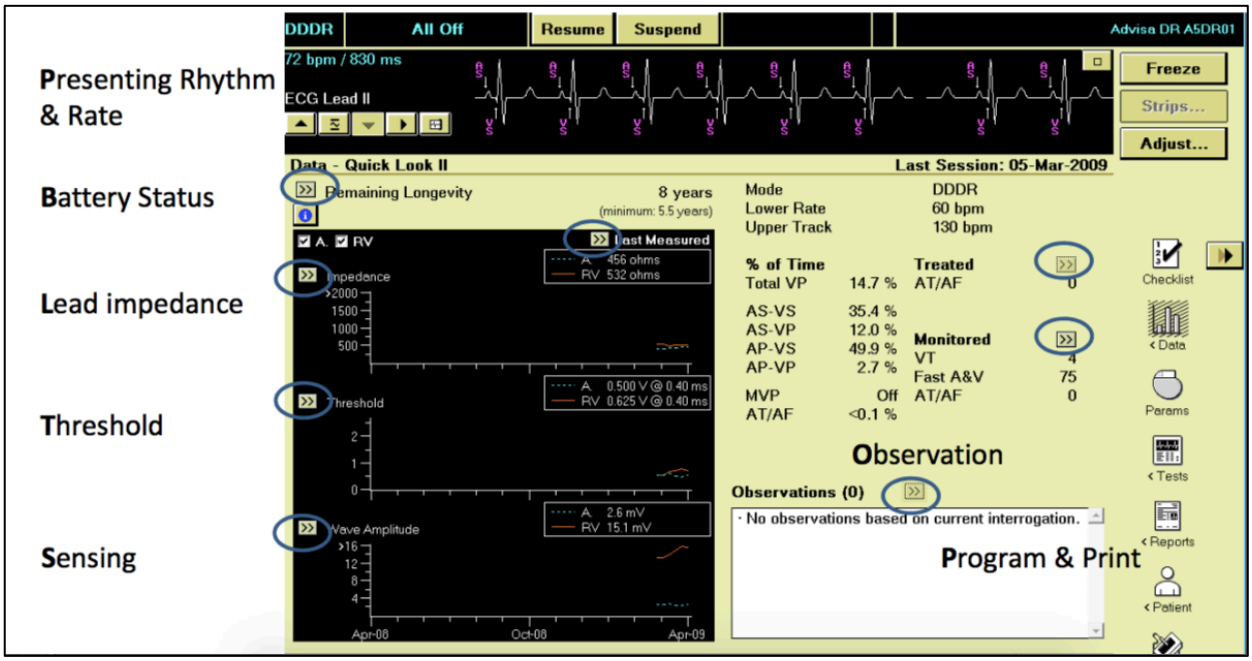
- On the programmer, 'Quick start' selected, this will automatically identify and interrogate the CIED and provide diagnostic evaluation.

Figure 4.5: Screenshot of the CIED programmer switch on 'welcome' screen



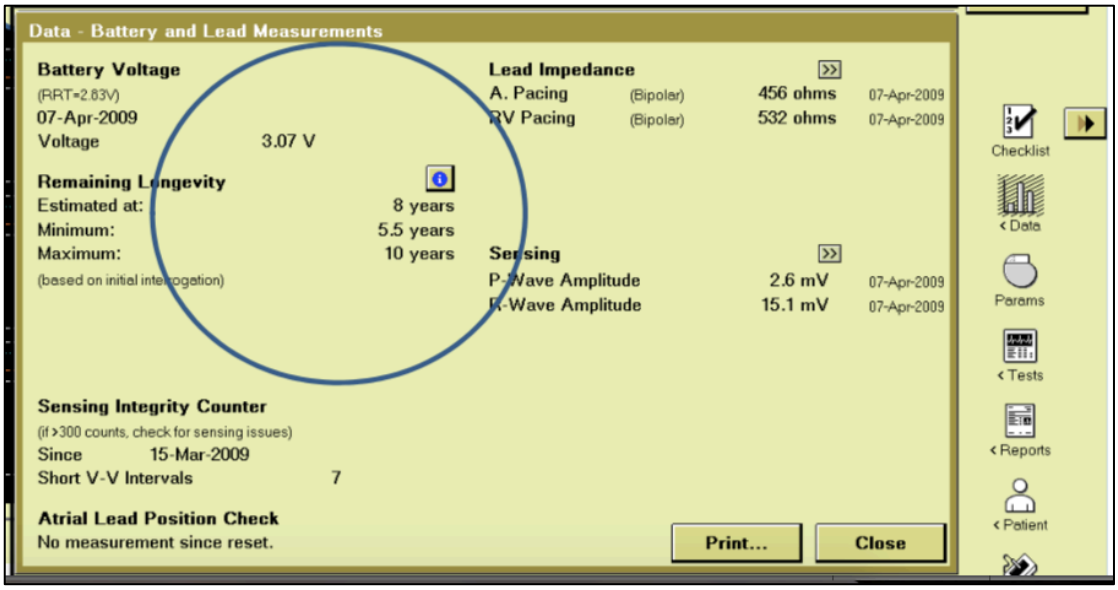
- Programmer carried out the following advanced tests, which analysed and presented data in the initial interrogation screen **(figure 4.6):**
    - CIED pulse rate
    - CIED pulse width
    - CIED inhibition sensitivity
    - CIED mode setting - to determine if the devices were in 'interference mode' or 'safe mode

Figure 4.6: Screenshot of the CIED programmer - initial interrogation screen



- The CIED programmer will then conduct the following tests and provide individual reports for analysis:
    - Determine battery status

Figure 4.7: Screenshot of the CIED programmer – battery status report (circled)



- Check lead / impedance integrity

Figure 4.8: Screenshot of the CIED programmer – lead integrity / impedance reports (circled)

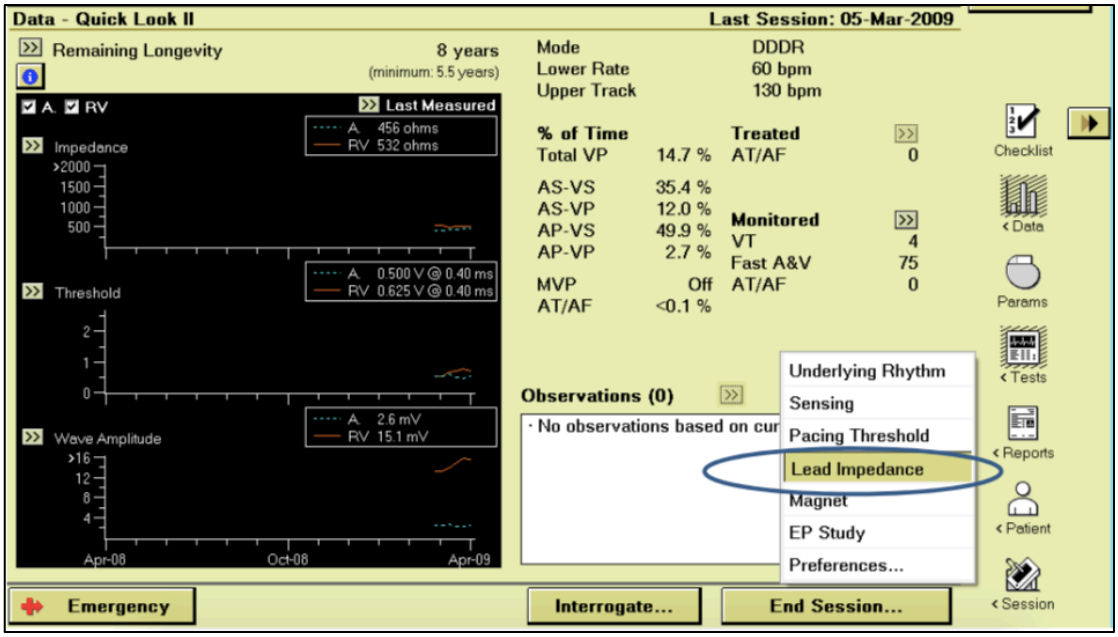
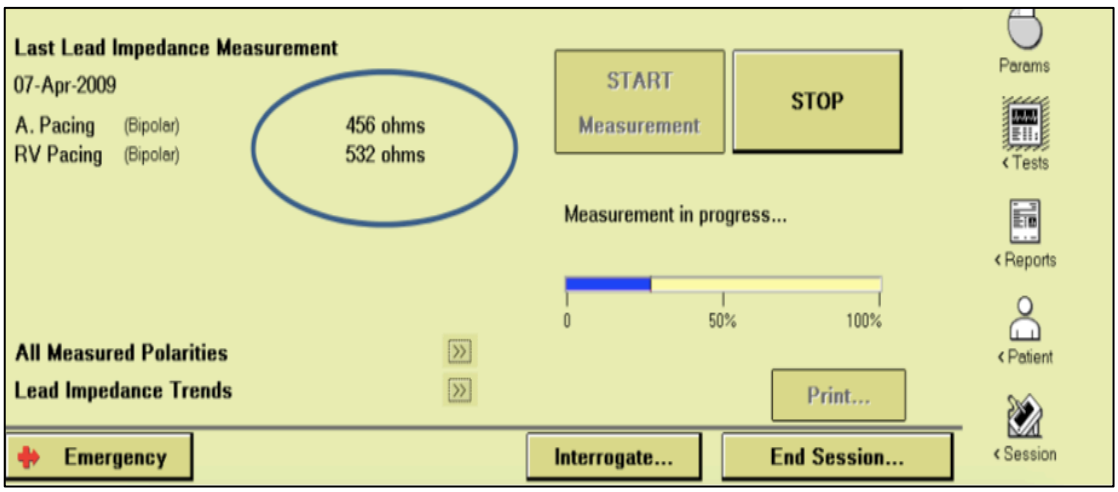


Figure 4.9: Screenshots of the CIED programmer – lead integrity / impedance report



- Check sensing threshold

Figure 4.10: Screenshots of the CIED programmer – sensing threshold reports

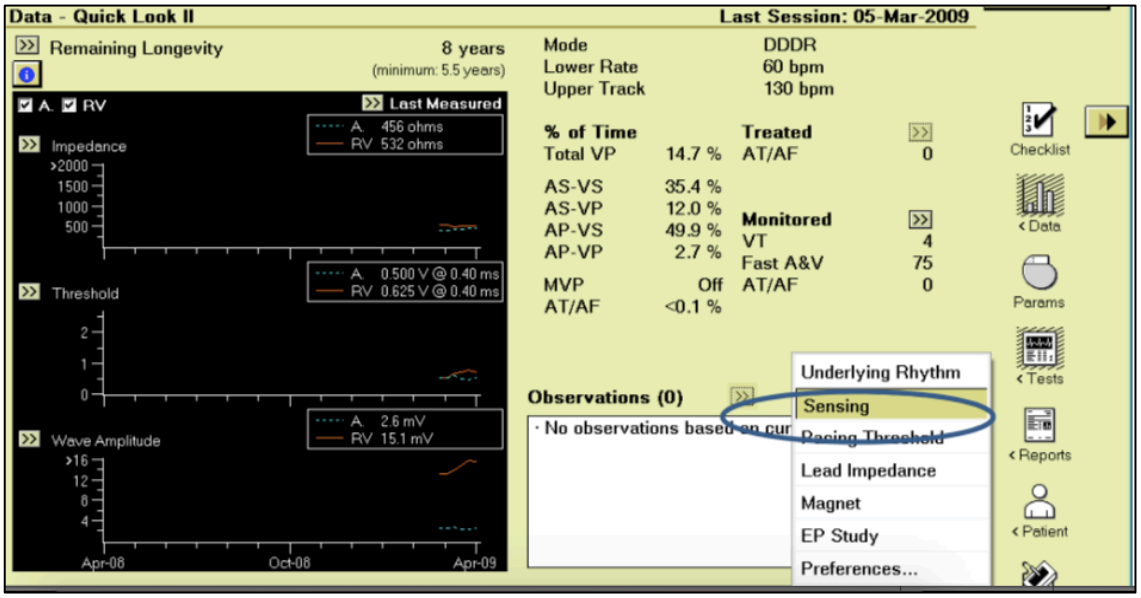
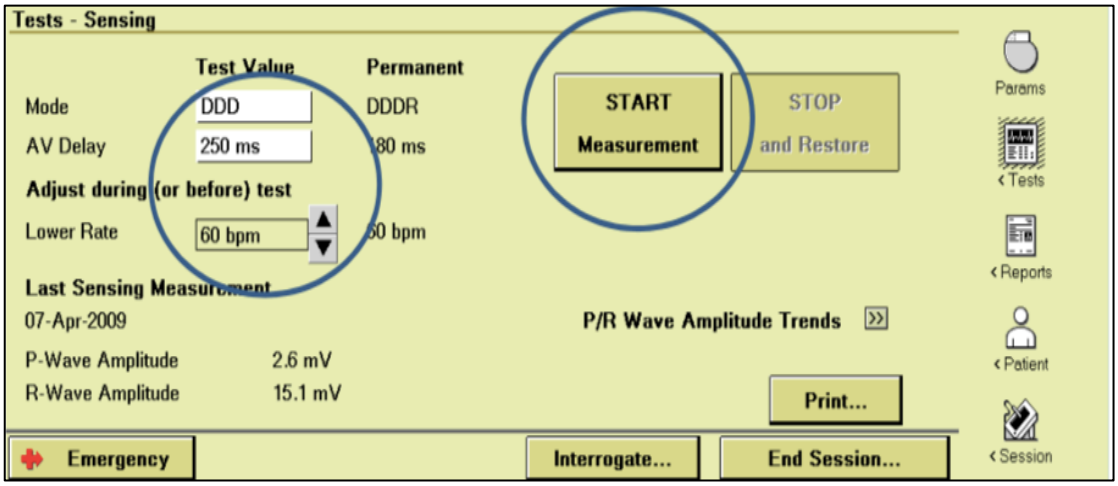


Figure 4.11: Screenshots of the CIED programmer – sensing threshold reports



- Check pacing threshold

Figure 4.12: Screenshot of CIED programmer – pacing threshold reports

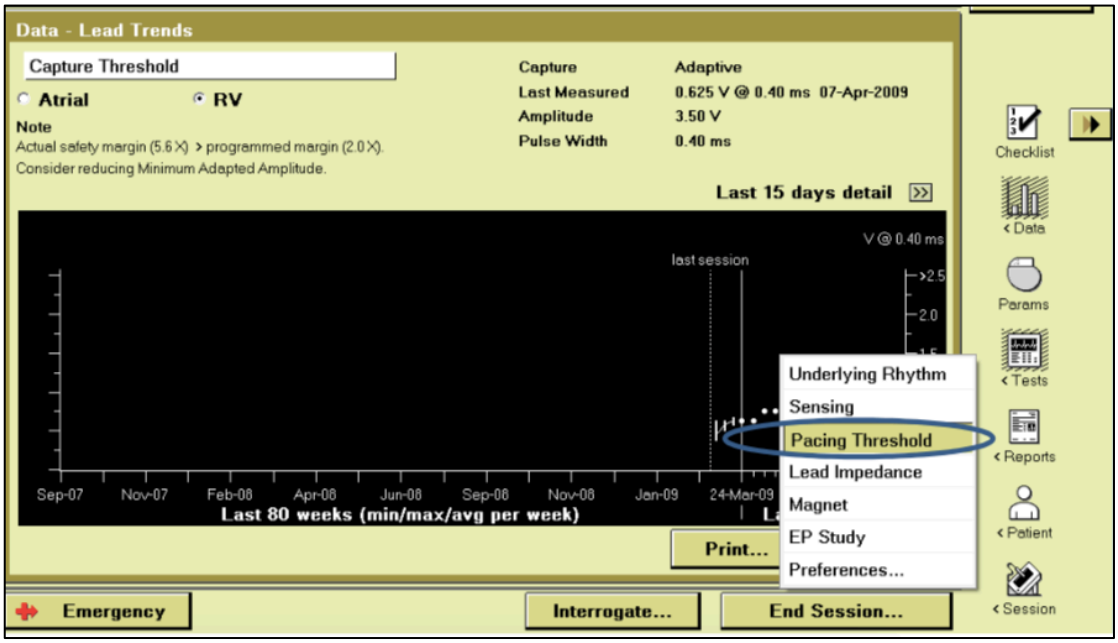
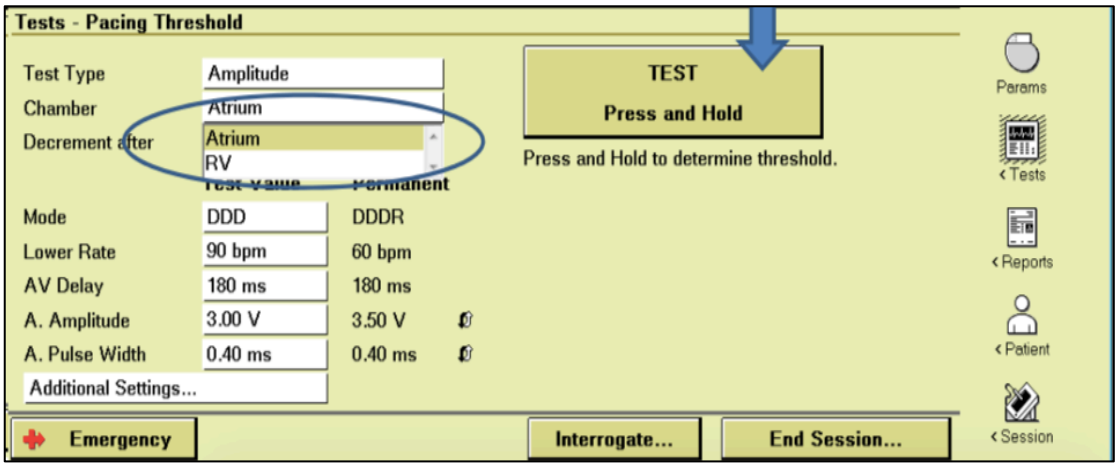


Figure 4.13: Screenshot of CIED programmer – pacing threshold reports



- Analyse diagnostics

Figure 4.14: Screenshot of CIED programmer – diagnostic report 1

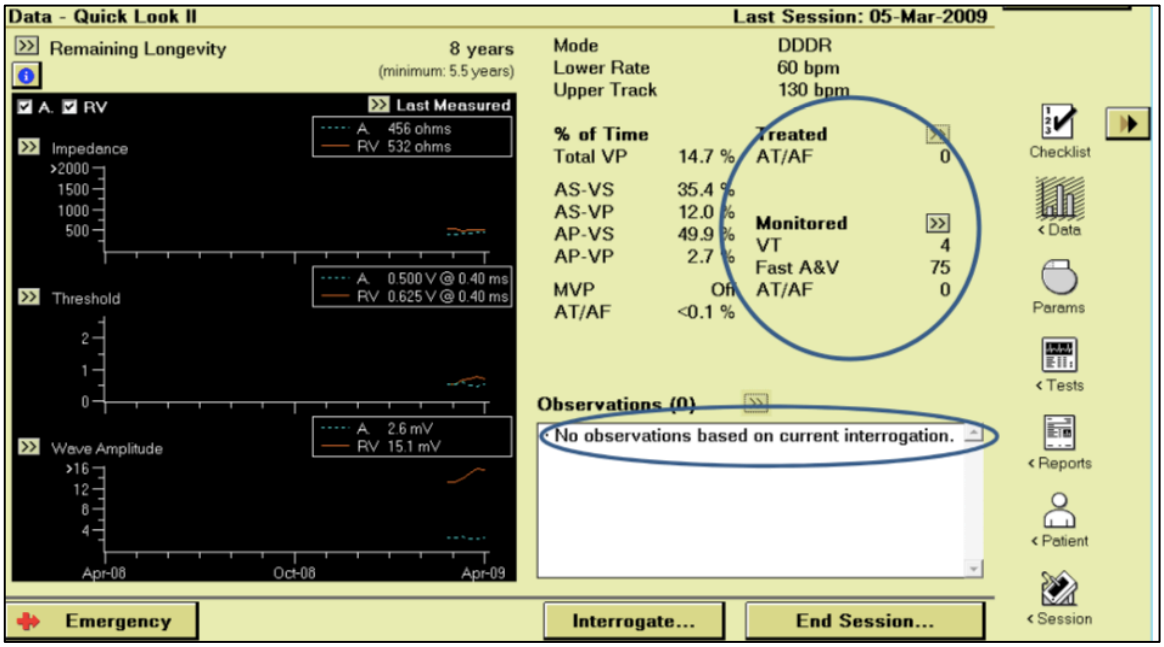
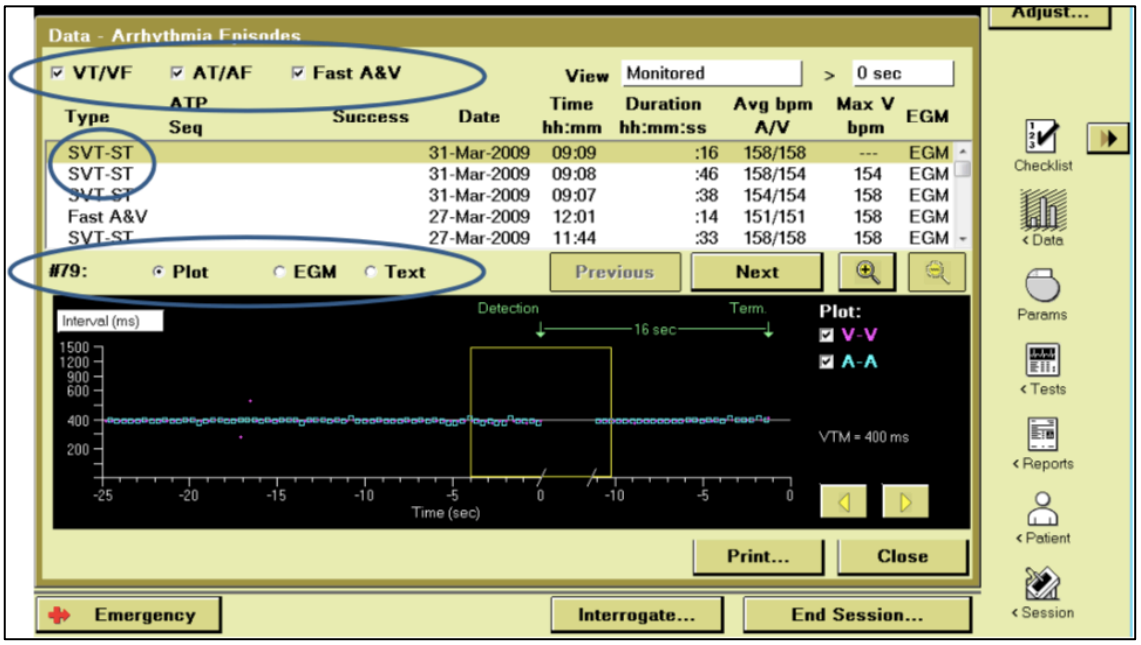


Figure 4.15: Screenshot of CIED programmer – diagnostic report 2



- Assess current parameters

Figure 4.16: Screenshot of CIED programmer – current parameters (circled)

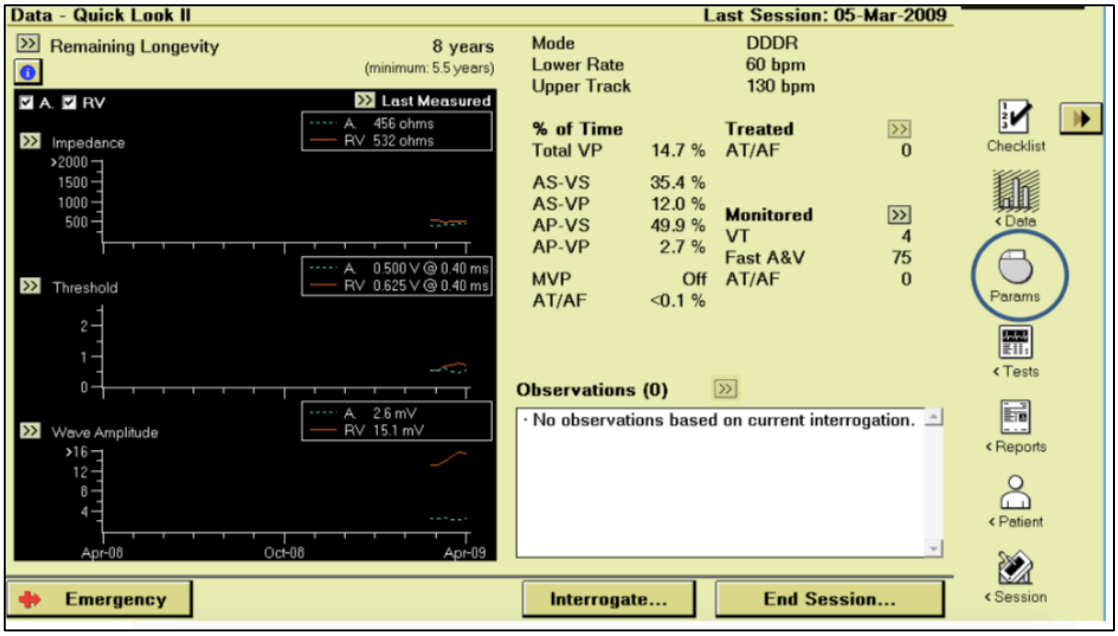
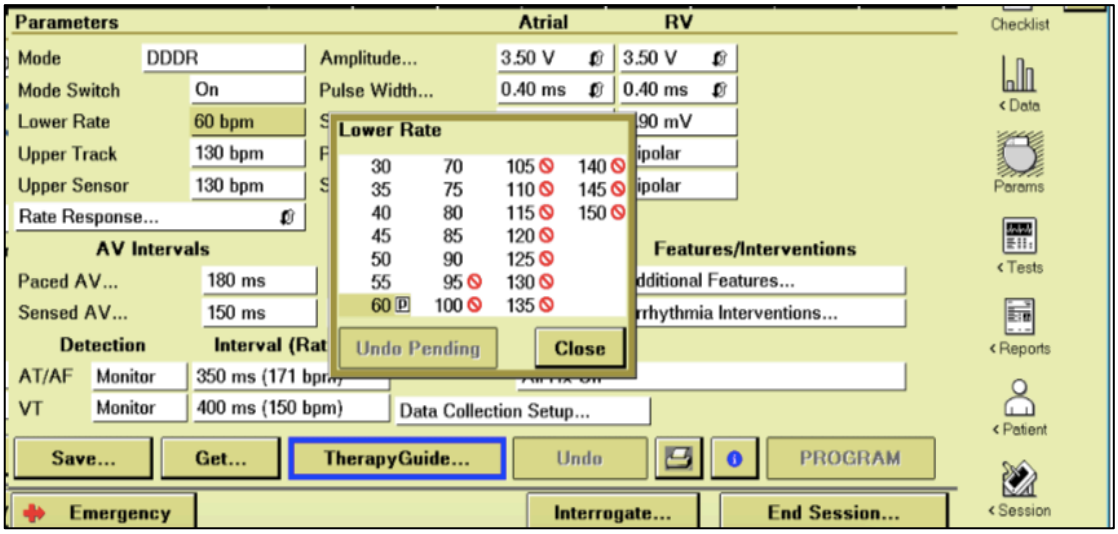
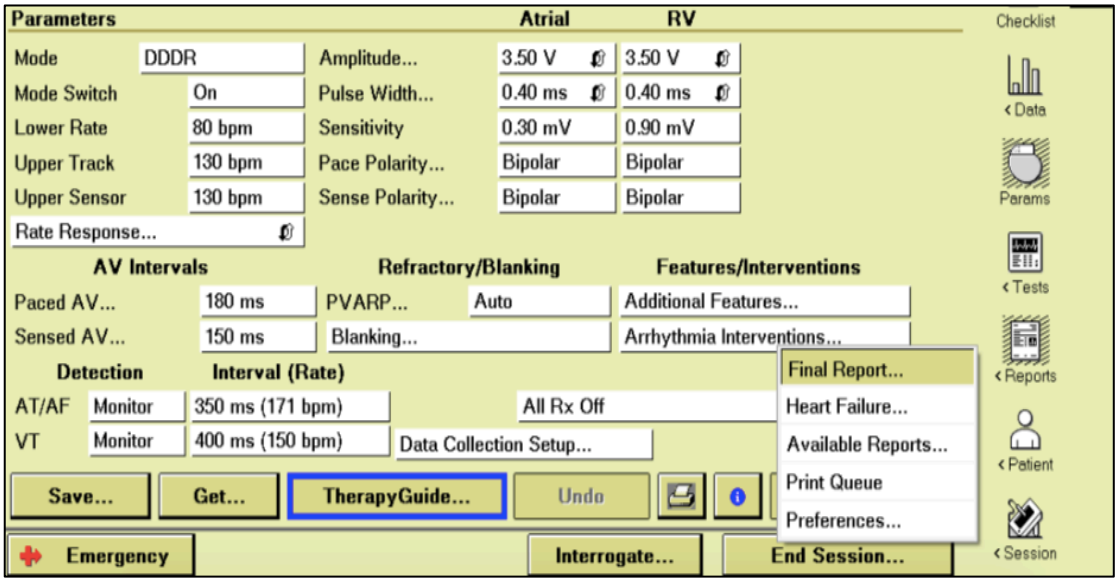


Figure 4.17: Screenshot of CIED programmer – current parameters – therapy guide



- Once interrogation was completed, a full service report was provided (which can either be downloaded onto USB or printed).

Figure 4.18: Screenshot of CIED programmer – Full service report - selection



4.5.2 Implementation of the method

Study 4

To investigate and evaluate the relationship between cumulative ionising radiation dose and the damage sustained to CIED leads

Introduction

Although ionising radiation may affect the function of the CIED, CIED leads are considered to be resistant to these effects (Lau, 2008). However, anecdotal evidence from clinical practice suggests that ionising radiation might not just have an impact on the CIED but may also affect the physical condition, construction and the movement and vibration of the CIED leads that monitor and activate the device. Also, no CIED manufacturers have issued any ionising radiation tolerance doses for CIED leads.

Lead malfunction is the most common cause of CIED therapy failure (Lau, 2008). Lead malfunction has been defined as not performing according to specifications or intentions (Lau, 2008). Even when all the electrical parameters are within normal limits, structural compromises in a CIED lead may still pose dangers to the patient through cardiac perforation, thrombogenesis, bacterial infection, interference with adjacent leads and difficulty in extraction (Lau, 2008).

Aim:

- To determine the effect of ionising radiation and or EMI on CIED leads

Research questions:

- What is the relationship between cumulative ionising radiation dose and damage sustained to CIED leads?
- Does exposure to ionising radiation affect the dielectric properties of CIED leads?
- Is there is a safe minimum ionising radiation tolerance dose to CIED leads?
- How will any damage to the CIED lead impact the patient clinically?

Hypothesis:

- As the level of ionising radiation dose increases, the greater the likelihood of CIED lead damage and therefore lead malfunction or failure.

Research design and method

Research design

The study was conducted under laboratory conditions and used a quantitative research strategy and adopted an experimental approach to data collection.

CIED lead testing

This study looked to determine effects of physical construction (as this differs between leads), physical condition and levels of degradation as a result of exposure to ionising radiation.

This study consisted of two parts:

1. **CIED lead testing –** exposure to ionising radiation
2. **CIED laboratory lead testing –** the measurement of the effect of ionising radiation on the dielectric properties of the poly(ether)urethane sheath that insulates the CIED leads.

CIED lead conditions

- Thirty-six CIED leads (four different lead types) from manufacturer X were investigated in this study.

Lead Testing

- A standard radiotherapy unit (Varian 650c linear accelerator with 120MLC, portal imaging, beam energy 6MeV and 10MeV set at a dose rate of 600MU/minute) was used to deliver the ionising radiation.
- The distance from the head of the linear accelerator to the surface of the phantom including the tissue equivalent bolus was 100cm and the ionising radiation field size was set at 10x10cm^2.
- In order to mimic clinical practice, the CIED lead sat in a 'groove' in a clear polymethylmethacrylate block phantom and tissue equivalent bolus material was placed on top of it, such that the lead was located at the maximum dose depth to provide full backscatter conditions (1.5cm for 6MeV photon beam and 2.5cm for 10MeV photon beam).

- The CIED lead being irradiated and interrogated was positioned precisely along the projected central axis (isocentre) of the primary radiation beam.

Environmental conditions:

- LINAC room temperature and room pressure recorded as part of the daily QA procedure prior to data collection to ensure LINAC output was within expected tolerance
- Linear accelerator beam energy – 6MeV and 10MeV*

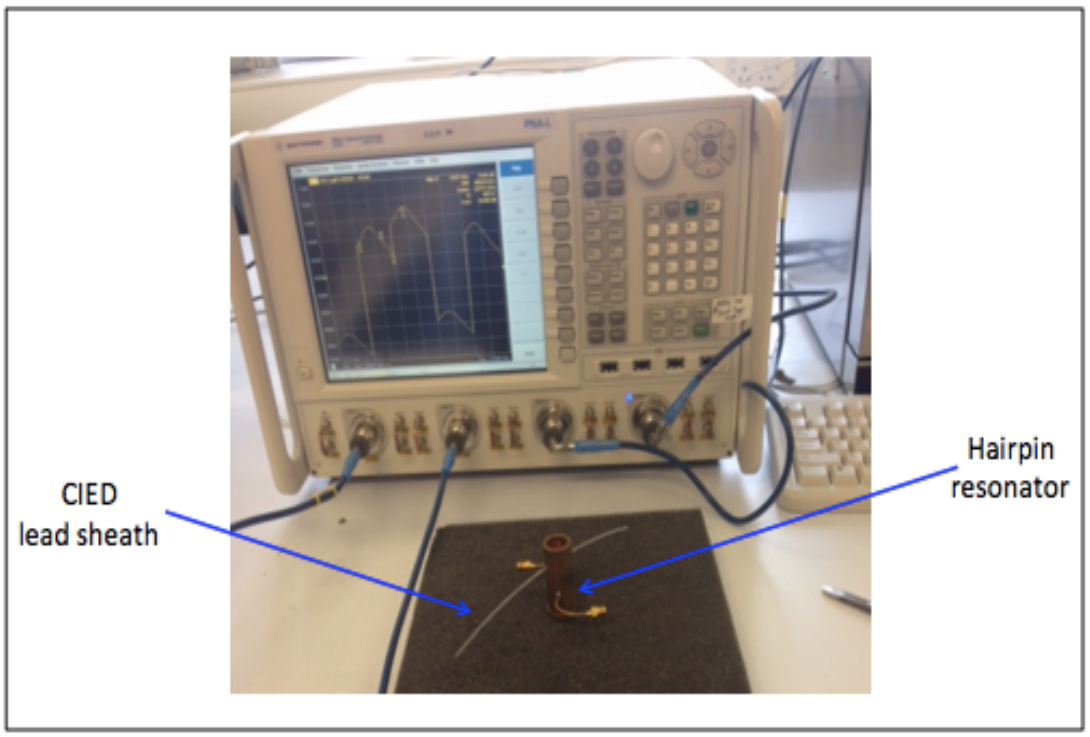
Testing protocol:

Research has shown that CIED leads are considered to be resistant to effects of ionising radiation and EMI (Hurkmans, 2005 and Zaremba 2015). Results from the preliminary study suggested that CIED leads can be effected starting at a cumulative ionising radiation dose of 30Gy. Therefore, phase 1 of the study tested CIED leads starting at 20Gy and further test increments of 10Gy per fraction to 120Gy. The leads were subjected to magnetic and electrical testing, which measured the dielectric properties of the polymer / sheath of the CIED lead. If the CIED leads showed any changes in physical construction, physical condition or showed evidence of degradation, phase two testing was undertaken. As the CIED leads have been previously irradiated in 10Gy increments, identification of the ionising radiation dose range that caused this change was recorded. Therefore, phase two testing used the same testing set-up and protocol but the leads were irradiated in 2Gy increments. The leads were then subjected to the same magnetic and electrical testing. Using this lower incremental fractionation allowed for accurate identification at which point any changes in the CIED lead occurred. The CIED leads were irradiated to a total cumulative ionising radiation dose at which point the CIED lead failed (120Gy). The testing protocol was repeated for both the 6MeV and 10MeV photon beams.

Table 4.2 : Testing protocol for CIED lead exposure to ionising radiation

LEAD	CIED Manufact.	Control	6MeV				10MeV			
Lead *Type 1*	**X**	L1 X1	L1 X2	L1 X3	L1 X4	L1 X5	L1 X6	L1 X7	L1 X8	L1 X9
Lead *Type 2*	**X**	L2 X1	L2 X2	L2 X3	L2 X4	L2 X5	L2 X6	L2 X7	L2 X8	L2 X9
Lead *Type 3*	**X**	L3 X1	L3 X2	L3 X3	L3 X4	L3 X5	L3 X6	L3 X7	L3 X8	L3 X9
Lead *Type 4*	**X**	L4 X1	L4 X2	L4 X3	L4 X4	L4 X5	L4 X6	L4 X7	L4 X8	L4 X9

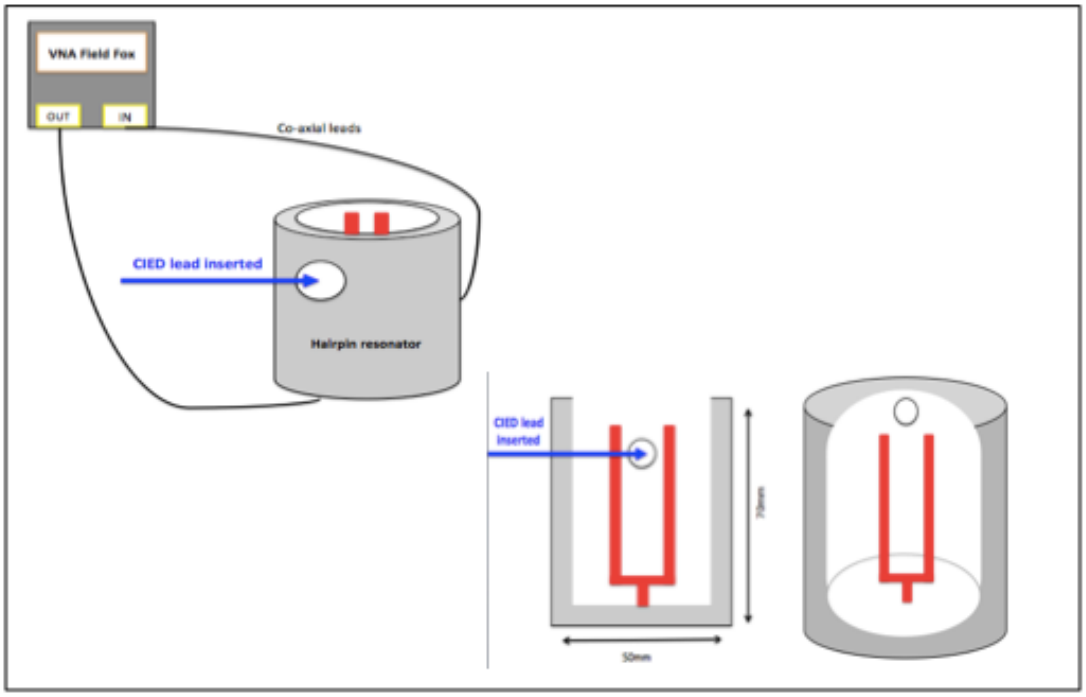
Figure 4.19: Photograph showing the CIED lead sheath interrogation equipment set-up



This research investigated the dielectric properties of the poly(ether)urethane sheath that insulates the CIED leads. The aim of the study was to determine the dielectric strength and identify if the physical condition of the polyurethane sheath has been altered and damaged due to the exposure to ionising radiation.

As part of this study, a novel microwave experiment was established to test this hypothesis. Measurements of the electrical conductivity of the polymer at microwave frequencies were taken. A microwave resonant cavity (hairpin resonator) was connected to a vector network analyser and the sections of CIED lead sheath were inserted into the cavity in order to 'perturb' or change the cavity characteristics. This technique is well established but has never before been used to characterise any polymer changes in CIED leads.

Figure 4.20: Schematic representation showing the CIED sheath lead testing set-up



4.5.3 Implementation of the method

Study 5

To investigate and evaluate the relationship between EMI and the damage sustained to CIEDs (pacemakers, ICDs and rate response activated CIEDs)

Aim:

- To determine the effect of EMI on CIEDs (pacemakers and ICDs)

Research questions:

- What is the relationship between EMI and damage sustained to CIEDs?
- How will any damage to the CIED impact the patient clinically?

Hypothesis:

- As exposure to EMI increases, the greater the likelihood of CIED damage and therefore CIED malfunction or failure.

Research design and method

Research design

The study was conducted under laboratory conditions and used a quantitative research strategy and adopted an experimental approach to data collection.

This study consisted of 3 parts:

1. **Electro-magnetic field measurements –** the measurement of electromagnetic fields in the radiotherapy treatment room (linear accelerator)
2. **Laboratory tests –** the measurement of the effect of non-ionising radiation electromagnetic fields on CIEDs in a laboratory setting

3. **CIED testing with ionising radiation –** the measurement of the effect of ionisng radiation electromagnetic fields on CIEDs in the radiotherapy treatment room (linear accelerator)

1. Electro-magnetic field measurements

The electromagnetic spectrum is organised by frequency; lower frequency radiation is on the left, and higher frequency radiation is on the right. The properties of electromagnetism change at different frequencies, and electric and magnetic fields behave differently along the spectrum. The interaction between electro-magnetic radiation and matter changes as the frequency changes. In order to determine the effect of EMI on CIEDs, firstly the levels of EMI emitted from the linear accelerator during ionising radiation exposure were measured and recorded.

A standard Varian 650c linear accelerator was used, with 120MLC, portal imaging, beam energy 6MeV and 10MeV set at a dose rate of 600MU/minute was used. In a linear accelerator electrons are accelerated by the action of radio-frequency electromagnetic waves. Relatively low energy electrons are injected into an accelerating structure and gain energy as they travel down the structure. In most electron linear accelerators, very high frequency waves (usually of wavelength of around 10cm equal to approximately 3 GHz) are used and these are made to propagate down the accelerating structure in the same direction as the electrons. The RF power at 3 GHz, used for electron acceleration, is well contained within the transmission and accelerating waveguides in the linear accelerators (Burke et al, 2099). In practice the RF power levels needed to perform electron acceleration are such that this action cannot be sustained continuously and almost all linacs operate in a pulsed repetitive mode, thereby emitting RF noise while producing pulsed radiation (Carlone *et al* 2008, 2007) due to the switching of large voltages. For example, discharging of the pulse-forming network in the modulator causes large

currents and voltages to be switched in several linac components (e.g., magnetron, thyratron, etc), which can lead to unwanted RF emissions. Burke et al (2009), In a study by Burke et al (2009), they investigated the RF emissions produced by three different clinical linear accelerators at both 6MeV and 15MeV operations. They concluded that the RF spectra produced, showed little dependence on beam energy. Results from study two of this research project shows that patients had exhibited cardiac reactions when receiving radiotherapy treatment at both 6MeV and 10MeV even when their CIED received a negligible dose of ionising radiation. Therefore, as part of this study RF noise was investigated at both beam energies, to determine if that linear accelerator caused different CIED reactions depending on the beam energy. The results from this provided radiofrequency (RF) measurements, which are measurements of ambient (surrounding) electromagnetic fields produced by the linear accelerator, which can penetrate through many materials and reflect off others.

The electromagnetic field measurements were performed and recorded using sensors, probes (antenna) and a FieldFox vector network analyser (VNA). The measurement system consisted of a field antenna and a frequency selective receiver or spectrum analyser, which monitored the frequency range of interest. The field antenna was placed in the radiotherapy treatment room, next to the treatment couch, near the couch midpoint. When the linear accelerator was switched ON, the VNA scanned the resulting RF emissions. The EMI signals were amplified and recorded using a signal analyser and the EMI frequency spectra was produced.

A VNA is a test system, precision measuring tool that tests the electrical performance of high frequency components, in the radio frequency (RF), microwave, and millimetre-wave frequency bands. The VNA is a stimulus response test system, composed of an RF source and multiple measurement receivers. This research determined the EMI frequency spectra within the RF range and was used to measure

the scattering parameters (S-parameters) of RF components. S-parameters describe the electrical behaviour of linear electrical networks when undergoing various steady state stimuli by electrical signals. Although applicable at any frequency, S-parameters are mostly used for networks operating at radio frequency (RF) and microwave frequencies where signal power and energy considerations are more easily quantified than currents and voltages. This research investigated within this range.

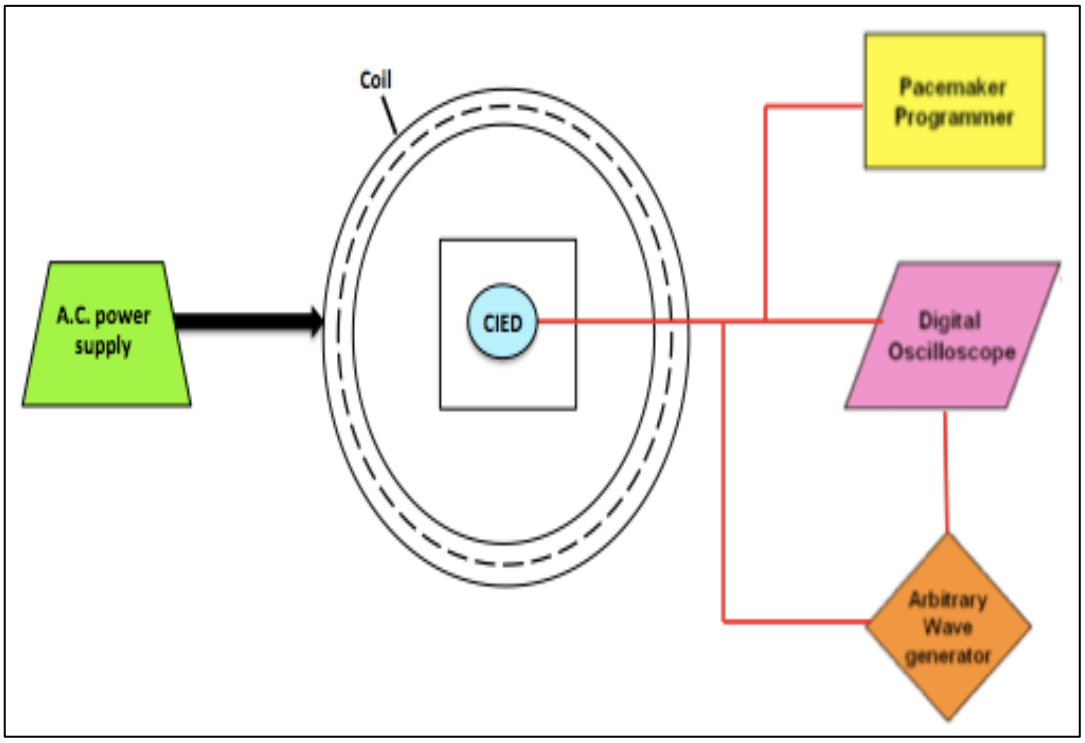
One of the most fundamental concepts of high-frequency network analysis involves incident, reflected and transmitted waves traveling along transmission lines. RF waves travelling along a transmission line can be thought of in a similar way to the way light waves travel through a medium. Consider what happens when incident light strikes a lens of different materials. If the lens is clear, most of the light passes through and only a small amount of light is reflected off the surface of the lens. On the other hand, if the lens has a mirrored surface, then most of the light will be reflected and little or none would be transmitted through the lens. This principle also applies to RF signals; except the electromagnetic energy is in the RF range and electrical devices replace the lenses and mirrors. Network analysis is concerned with the accurate measurement of the ratios of the reflected signal and the transmitted signal to the incident signal.

2. Laboratory tests

The influence of EMI on CIEDs was tested in the laboratory under experimental conditions. A coil was connected to an alternating current (AC) supply, which produced electro-magnetic fields in the frequency range of 10-10000Hz. The CIED was placed in the phantom and then inside the coil. The CIEDs were connected to a simulator and a CIED programmer to replicate the electrical behaviour of a paced heart. The output pulse was monitored using an oscilloscope and an ECG machine.

The CIED's operating parameters and signal were generated by the arbitrary wave generator and connected to the digital oscilloscope and synchronised the patients intrinsic heart beat with the function of the CIED. The operation of the CIED was monitored throughout exposure to the electromagnetic fields. The CIEDs were subjected to programming and functionality tests after each electromagnetic field exposure.

Figure 4.21: Schematic representation of the design principle and set-up for EMI testing



3. CIED testing with ionising radiation

CIED conditions

- Total of sixteen CIEDs from manufacturer X were investigated in this study:
  - Five new pacemakers

- Six new pacemakers with rate response activated (three with rate response sensor accelerometer detection and three with rate response sensor minute ventilation detection)
- Five new ICDs from manufacturer X were tested
- The control group consisted one pacemaker, one pacemaker with rate response sensor accelerometer detection, one pacemaker with rate response sensor minute ventilation detection and one ICD. These devices were not exposed to EMI
-

Table 4.3 : Testing protocol for CIED exposure to EMI

CIED type	CIED Manufact.	Control	6MeV		10MeV	
PM	**X**	PM X8	PM X9	PM X10	PM X11	PM X12
PM *1	**X**	PM X1RA	PM X2RA		PM X3RA	
PM *2	**X**	PM X1RMV	PM X2RMV		PM X3RMV	
ICD	**X**	ICD X6	ICD X7	ICD X8	ICD X9	ICD X10

***1 -** Rate response activated CIED. Sensor – Accelerometer (A) detection*

***2 -** Rate response activated CIED. Sensor – Minute (MV) detection*

Environmental conditions

- LINAC room temperature and room pressure recorded as part of the daily QA procedure prior to data collection to ensure LINAC output was within expected tolerance
- Linear accelerator beam energy – 6MeV and 10MeV*

A standard radiotherapy Varian linear accelerator unit was used in this study. When the linear accelerator was switched on it produced both ionising radiation and

electro-magnetic fields. In order to classify the damage sustained to the CIEDs as a result of exposure to these electro-magnetic fields only, the CIEDs (in the phantom) were not placed within or in close proximity to the radiotherapy treatment beam. Therefore, the calculated cumulative ionising radiation dose to the CIED was negligible and all effects exhibited by the CIED would be due to interference (EMI) with the electromagnetic fields generated by the linear accelerator.

CIED testing / irradiation

The CIEDs were connected to a simulator and a CIED programmer to replicate the electrical behaviour of a paced heart. The output pulse was monitored using an oscilloscope and an ECG machine and a stepped attenuator was used to give preset amplitude inhibition pulses. The CIED's operating parameters and signal was generated by the arbitrary wave generator and connected to the digital oscilloscope and synchronised the patients intrinsic heart beat with the function of the CIED.

Figure 4.22: Schematic representation of the design principle and set-up for EMI testing – between the radiotherapy treatment room and control room

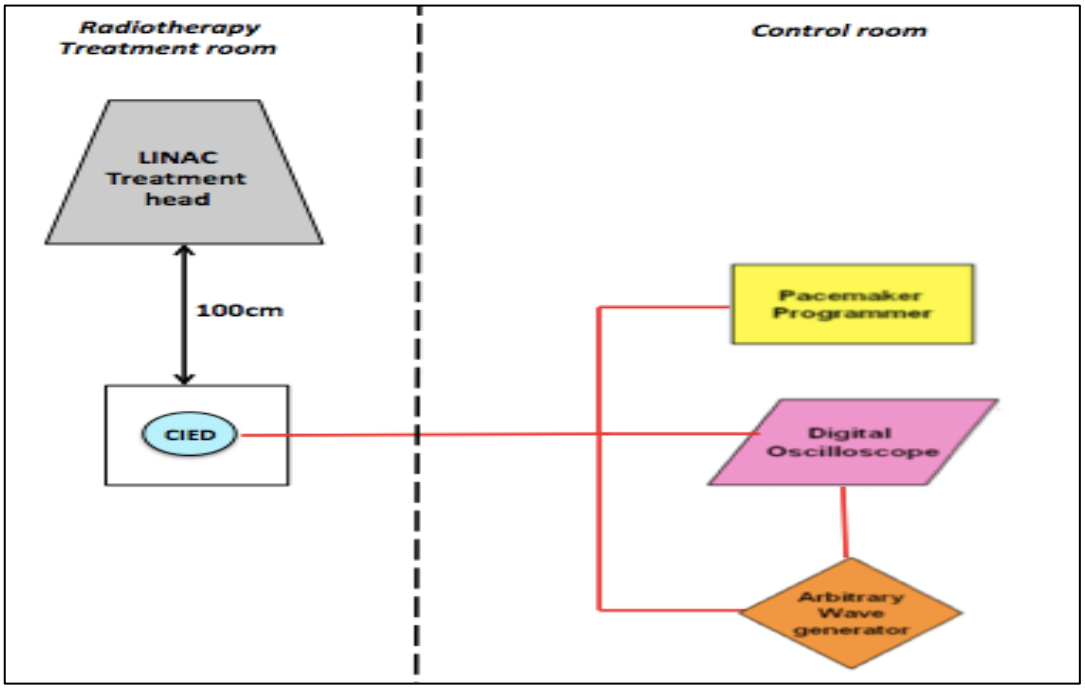
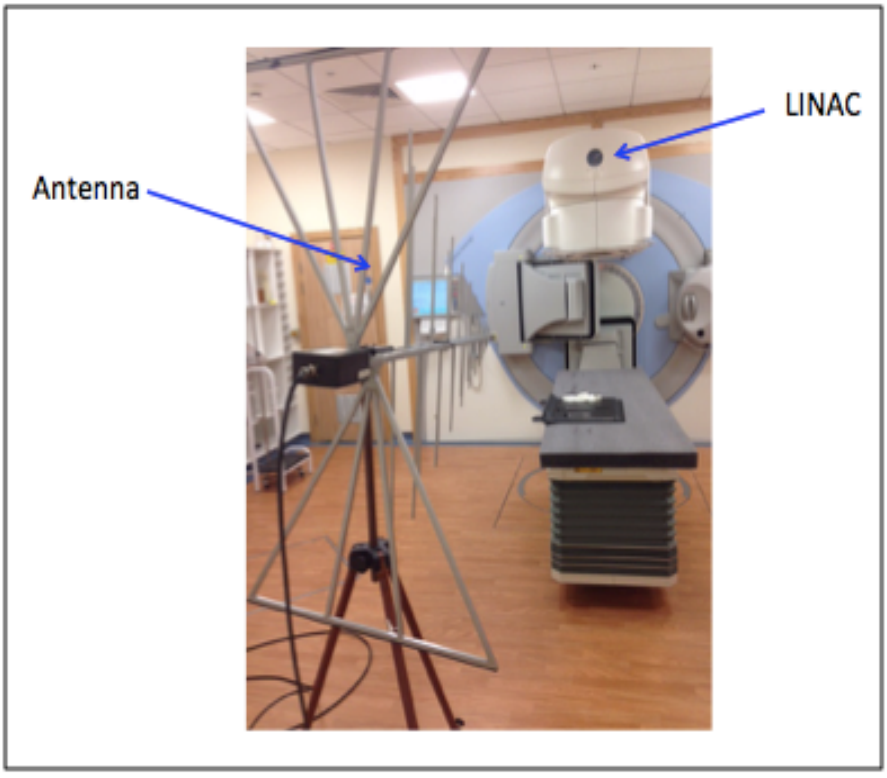


Figure 4.23: Photograph showing EMI testing equipment in the radiotherapy treatment room



In order to determine at which point the CIED exhibited malfunctions, the devices were exposed to levels of EMI as per daily radiotherapy treatment, six separate radiation beams per fraction:

- Pre-EMI beam On exposure (1 minute)
- Beam ON - switch ON point (Instant)
- During beam ON - when the LINAC is emitting ionising radiation (90 seconds)
- Beam OFF - switch OFF point (Instant)
- Post-EMI beam OFF exposure (1 minute)

Total CIED exposure to EMI occurred on a daily basis for ten fractions with a two-day break after five fractions to enable device recovery between fractions. The CIEDs were subjected to programming and functionality tests after each ionising radiation exposure. This testing protocol was repeated for both the 6MeV and 10MeV photon beams.

CIED interrogation

Before and after each EMI exposure, measurements were taken of the CIEDs pulse rate, pulse width and inhibition sensitivity. During exposure, the simulator provided programming and functionality data, which was then analysed to determine if the program memory has been corrupted. The devices inhibition will also checked to determine whether the devices were in 'interference mode' or 'safe' mode.

The CIED were subjected to the following programming and functionality tests after each ionising radiation exposure:

- Noise during the EMI exposure
- Spontaneous change in programmed device parameters without reset to backup mode

- Reset to backup mode or other error recoverable using the programmer
- Error not recoverable using the programmer
- Clinically significant reduction in battery capacity
- Inappropriate antitachycardia pacing or delivery of shock therapy in the ICDs (even though this feature of the ICDs were deactivated during irradiation)
- Loss of telemetry
- Pacing inhibition
- Inappropriate tracking
- CIEDs failure
- Runaway pacing with induction of potentially life-threatening ventricular arrhythmias

4.6 Research outcomes

Study 6

To provide evidence based guidelines for the safe management of cancer patients with CIEDs receiving radiotherapy treatment

Introduction

In 2013, as part of the PhD research project, the researcher conducted and published a national review of cardiac device policies in use in radiotherapy departments across the UK and reported that most policies do not reflect current best evidence (Lester el al, 2014). In 2014, The Royal College of Radiologists, the Society and College of Radiographers and the Institute of Physics and Engineering in Medicine formed a multidisciplinary working party comprising clinical oncology, cardiology, therapeutic radiography and medical physics expertise to develop guidelines for the management of cancer patients receiving radiotherapy with a CIED. Based on the researcher's previous research in this field, specific PhD

research and aims and publications, they were appointed to co-chair this working party. This paper was published for clinical use in UK radiotherapy departments (Sor.org, 2015). (See appendix F).

The PhD research project has investigated the effects of ionising radiation and EMI on CIEDs and leads. Results from this research will provide recommendations that will allow for the publication of up to date, evidence based guidelines for the safe management of patients with a CIED receiving radiotherapy treatment.

Aim:

- Review the evidence and literature to determine current 'gold standard' practice
- Provide recommendations for the management of cancer patients who have a CIED and are receiving radiotherapy.

Research design and method

Research design

The study adopted a systematic review as the research methodology. It reviewed the evidence and literature to determine current 'gold standard' practice and in conjunction with the findings of the PhD research project, provided recommendations for the management of cancer patients who have a CIED and are receiving radiotherapy.

This systematic review was conducted prospectively, using a pre-defined proforma and checklist that guided the data collection and synthesis process, it defined and logically structured all steps in the systematic review

Step 1 – Review question

The review questions were set to establish an objective methodology and search criteria, which guided the systematic review

Step 2 – Literature search

The literature review was divided into two stages. The first was a broad exploratory Ovid Medline search, designed to identify appropriate medical subject headings (MeSH). The keywords used at this stage were radiotherapy, pacemaker, defibrillator, ICD and cardiac device. Hand searching of journals, relevant books, and review articles was also carried out. The second stage of the process was the application of the generated MeSH terms and keywords in a comprehensive search of the following databases: MEDLINE, EMBASE, and Cancerlit. Subject headings were modified as required by individual databases. All published literature on the use of radiotherapy in patients with CIEDs was reviewed to define best practice and inform guideline development.

Step 3 – Critical appraisal

An in-depth appraisal of the selected studies was conducted by judging it against criteria identified at the first stage. All subsequent published literature on the use of radiotherapy in patients with CIEDs was reviewed using the Critical Appraisal Skills Programme (CASP - Critical Appraisal Skills Programme, 2018) in order to define best practice.

Step 4 – Data extraction

Data extraction is 'the process by which researchers obtain the necessary information about study findings from the included studies'. In this step, all relevant findings meeting the selection criteria to form the body of evidence regarding the research questions were extracted.

Step 5 – Data synthesis

The reviewed studies were summarised to form the outcome of the systematic review. The strength of the study findings was assessed, using agreed upon, specified assessment criteria and summarised the results in a systematic, evidence-based literature review document.

4.7 Chapter conclusion

This chapter outlines and explains the reasoning and approach by which the research was undertaken; it addresses the research questions stated and the development of the research methodology and method for each study. In discussing the preliminary study, the methods of data collection and data analysis procedures were detailed. It concludes with explaining how the results from the preliminary study informed the PhD research project. Finally, this chapter outlines the implementation of the PhD research project and details the research method and data collection procedures for all six studies. The results from these studies will be discussed in subsequent chapters.

Chapter Five

Test compliance, knowledge, understanding and perception

5.1 Introduction

As part of the PhD research project, it was considered fundamental to establish current UK practice regarding the management of patients with CIEDs undergoing radiotherapy treatment and compare this practice to current 'gold standard' evidence-based guidelines. This chapter details the findings of the national audit and reinforces the outcomes that show patients with CIEDs are being put at significant risk of harm when exposed to ionising radiation and EMI when receiving radiotherapy treatment.

A series of audits of clinical practice at a Welsh radiotherapy centre were carried out to determine the effects of ionising radiation and EMI on all patients with CIEDs receiving radiotherapy treatment. This chapter outlines radiotherapy induced device malfunction and discusses the results from this audit.

Earlier chapters have documented the developments and improvement in pacing CIED technology, one such advancement being *rate response activated* CIEDs, which are increasingly being implanted in patients for the management of their cardiac conditions. However, there is no research into the effect of ionising radiation and EMI on these particular devices, hence a second clinical audit was carried out to assess device malfunctions in these patients. This chapter details the observed clinical reactions in patients and discusses the need for research into the effect of ionising radiation and EMI on these contemporary CIEDs as part of the PhD research project.

5.2 Study 1

To establish current UK practice regarding the management of patients with CIEDs undergoing radiotherapy treatment and to compare this practice with current 'gold standard' evidence-based guidelines.

Results

In total, sixty-seven radiotherapy centres were identified in the UK and contacted. Overall, 47/67 (70%) centres responded to the request to provide their policy for inclusion in the audit. Forty-five centres provided their policy and two centres were currently re-writing their CIED policy and thus excluded from the results. Twenty centres did not respond to the request. The analysis was carried out on the forty-five polices submitted that are currently in use.

Table 5.1: Results - Roles and responsibilities of healthcare professionals

Roles and responsibilities	Number of radiotherapy department policies n= 45	%
Consultant oncologist:		
Identify patient's CIED status and highlight on radiotherapy referral form	39	87
Contact patient's cardiology department before starting radiotherapy treatment	41	91
Request cardiology assessment	34	76
Provide medical physics with information to calculate cumulative radiotherapy dose to CIED	36	80
Dose to the implantable internal pacemaker does not exceed 2 Gy	31	69
Dose to the ICD does not exceed 2 Gy	5	11
Consent – patient aware of potential adverse effects of radiotherapy on cardiac device	12	27
Consent – switch off ICD during radiotherapy	5	11
Planning radiographers:		
Annotated patient's CIED status	34	76
CIED included in scan if in/close to the radiotherapy treatment field	35	78
Medical physics informed of patient's CIED status	35	78
Contact consultant if CIED is within radiotherapy treatment field or estimated dose too high	29	64
Treatment radiographers:		
Appropriate monitoring procedure for patients with pacemakers	14	31
Appropriate monitoring procedure for patients with ICDs	12	27
Medical physics:		
Dose estimation calculated for CIEDs and leads	36	80

Overall, 39/45 (87%) policies require the clinical oncologist to state whether a CIED is present on the radiotherapy referral form; 41/45 (91%) policies require the clinical oncologist to contact the patient's cardiology department before starting radiotherapy; 34/45 (76%) policies require a cardiology assessment prior to commencement of radiotherapy treatment; 36/45 (80%) policies require the clinical oncologist to provide relevant information to medical physics to allow the calculation of the estimated cumulative dose to the CIED before starting radiotherapy; 12/45 (27%) policies require patients fitted with CIEDs to be informed of the risks to themselves and their device before starting radiotherapy; 5/45 (11%) policies state that patients fitted with ICDs should be informed about the possibility of ICD malfunction or failure during radiotherapy treatment and must give consent to deactivate the ICD during radiotherapy treatment.

Of note is that in only 29/45 (64%) policies is it mandatory for the planning radiographer to contact the treating consultant if the CIED is within a radiotherapy treatment field or if the estimated dose is too high. Less than a third of policies include appropriate monitoring procedures for treatment radiographers in patients with pacemakers or ICDs. There is no requirement for medical physics to calculate the estimated dose to CIEDs and leads in 9/45 (20%) policies.

Table 5.2: Results - Adherence to American Association of Physics in Medicine (AAPM) (Marbach et al, 1994) and Frizzell (2009) Guidelines

Adherence to American Association of Physics in Medicine (AAPM) and Frizzell Guidelines	Number of radiotherapy department policies (n=45)	%
Pacemakers - AAPM guidelines:		
2 Gy radiotherapy tolerance dose to device stated	31	69
Requirement to contact cardiology if radiotherapy dose to pacemaker exceeds 2 Gy	21 (of 31) *	68
No radiotherapy tolerance dose stated	14	31
Do not contact cardiology	14 (of 14) *	100
Cardiology follow-up made after radiotherapy completed	30	67
ICDs - Frizzell Report:		
0.5 Gy radiotherapy tolerance dose to device stated	5	11
Requirement to contact cardiology if radiotherapy dose to ICD exceeds 0.5 Gy	5 (of 5) *	100
1 Gy radiotherapy tolerance dose to device stated (exceeding 0.5 Gy tolerance dose)	9	20
Do not contact cardiology if radiotherapy dose to ICD exceeds 1 Gy	9 (of 9) *	100
2 Gy radiotherapy tolerance dose to device stated (exceeding 0.5 Gy tolerance dose)	14	31
Do not contact cardiology if radiotherapy dose to ICD exceeds 2 Gy	13 (of 14) *	93
No radiotherapy tolerance dose stated	17	38
Do not contact cardiology if no radiotherapy tolerance dose is stated	17 (of 17) *	100
Cardiology follow-up made after radiotherapy completed	30	67

* *represents different 'n'*

31/ 45 (69%) policies define the radiotherapy tolerance dose to the pacemaker recommended in the AAPM guidelines. Of these, 21/31 (68%) policies require the cardiology department to be contacted to discuss safe management of the patient. In total, 14/45 (31%) policies do not define a tolerance dose limit to the pacemaker and none of these radiotherapy centres contact the patient's cardiology department. Only 5/45 (11%) policies define the radiotherapy tolerance dose limit to the ICD as 0.5Gy and all five of these radiotherapy centres contact the cardiology department to discuss the management of the patient; 23/ 45 (51%) policies define a dose limit of >0.5Gy to the ICD and 17/45 (38%) policies do not define a dose limit. 39/40 (98%) policies that use an incorrect tolerance dose limit or do not define a dose limit do not mandate contacting the patient's cardiology department for advice. 30/45 (67%) policies require a follow-up appointment to be made with the patient's cardiology department after the completion of radiotherapy.

Table 5.3: Results – Monitoring requirements for patients with CIEDs receiving radiotherapy

Clinical practice - monitoring of patients with cardiac devices	Number of radiotherapy department policies (n=45)	%
Pacemakers - AAPM guidelines:		
Appropriate monitoring procedure	14	31
Appropriate staff used to monitor patients	14	31
Close observation of patient using cardiac monitor on first fraction of radiotherapy	14	31
Subsequent monitoring requirements assessed and annotated	14	31
ICDs - Frizzell report:		
Appropriate monitoring procedure	12	27
Appropriate staff used to monitor patients	12	27
12 lead continuous strip ECG before first fraction of radiotherapy	12	27
Deactivate ICD with magnet during radiotherapy	12	27
Continuous strip ECG monitoring for all subsequent treatments	12	27
Document any change in patient's status	12	27

Overall, 31/45 (69%) policies do not define monitoring procedures for patients with pacemakers in line with the AAPM guidelines (Marbach et al, 1994) and none mandate the use of appropriately trained staff to monitor patients. Similarly, 33/45 (73%) policies do not define monitoring procedures for patients with ICDs in line with the Frizzell report (2009) and none mandate the use of appropriately trained staff to monitor patients.

Discussion

The number of patients with CIEDs undergoing radiotherapy treatment is increasing (National Radiotherapy Advisory Group, 2007). The audit of UK radiotherapy departments' CIED policies highlighted substantial differences in the management of patients who have a CIED and are receiving radiotherapy treatment (Lester et al, 2014). Whilst most medical treatments pose little danger to the functioning of CIEDs, some such as radiotherapy have the potential to cause undesirable interactions. A further complication is the variability in behaviour of any given CIED when it is in, or in close proximity to, the radiotherapy treatment field (Solan et al, 2004). In addition

to issues of radiation and electromagnetic interference effects, published literature is inconsistent in its findings and recommendations on the management of radiotherapy tolerance doses to cancer patients with a CIED. An American report suggests that 12% of oncology centres have neither a formal risk management strategy nor a CIED policy, and that only 15% actually have a written policy (Solan et al, 2004). As it is not clear whether the situation is similar here in the UK, the lack of written national policy and deviation from evidence-based guidelines such as the AAPM was of major concern. Therefore, one of the aims of the audit was to determine current UK radiotherapy departmental practice and if necessary, reinforce the need for a national policy documenting the safe and efficient management of patients with CIEDs who undergo radiotherapy. This audit used the 1994 AAPM guidelines (Marbach et al, 1994) and recommendations of Frizzell (2009) as the benchmark to analyse UK radiotherapy centres' current CIED policies, as these guidelines had the most robust evidence-base to support them.

The aim of the audit was to determine how many UK radiotherapy centres have a CIED policy in routine use. All radiotherapy department managers were asked to provide their current CIED policy for analysis. The audit yielded a response rate of 70%; 45 respondents provided their policy while two centres stated that they were in the process of re-writing their policy. A third follow-up email was sent from the Society and College of Radiographers asking radiotherapy centres to forward their policy or to inform them if they did not have one. At that point, it wasn't known whether the remaining 20 radiotherapy centres who had not responded had a policy. The lack of an over-arching national policy on this therapy area is not specific to the UK. As Solan et 2004 shows the United States to have similar deficiencies.

The audit results highlight major differences between policies in the roles and responsibilities of healthcare professionals involved in the patient pathway and the management of patients with a CIED receiving radiotherapy. From the results of the audit, in 87% of radiotherapy centres, the treating Clinical Oncologist determines CIED status and highlights it on the radiotherapy referral form. This means that in 13% of the policies included in this review, it is left to radiographers to identify whether a CIED is present. Anecdotal evidence from this audit shows that in some cases, a CIED is not discovered until a patient attends for radiotherapy. One radiotherapy department highlighted an incident whereby a patient informed the treatment radiographer on the first day of radiotherapy that they had a pacemaker. Records show that the patient had not previously been asked if they had a CIED. Therefore, radiotherapy treatment could not commence that day. There was further delay, while the patient's cardiology department was contacted and all information regarding the patient and their CIED was obtained. This information revealed that patient had an ICD, which required the device to be switched off during radiotherapy treatment and close monitoring. This potentially dangerous scenario is less likely if the treating Clinical Oncologist determines early on in the treatment pathway that a CIED is present and informs the planning and treatment teams.

Worryingly, in only 29/45 (64%) policies is it mandatory for the treating consultant to be contacted if the CIED is within a radiotherapy treatment field or if the estimated dose is too high. In most cases, this communication would probably happen even in the absence of policy. However, given the potential harm to the patient, this should be explicit. There is clearly a need for policies in use to include monitoring procedures for treatment radiographers in patients with pacemakers or ICDs. These procedures are currently included in less than one-third of policies and it is vital that patients having treatment are monitored to minimise the chance of harm. There is no requirement for medical physics staff to calculate the estimated dose to CIEDs and

leads in 9/45 (20%) policies. Without this estimation being made before radiotherapy starts, patients may be exposed to doses of radiation that exceed the limits recommended by AAPM and Frizzell (Marbach et al, 1994 and Frizzell, 2009).

The AAPM report recommended that the cumulative radiotherapy dose to the pacemaker be limited to less than 2Gy (Marbach et al, 1994). In the audit, only 69% of radiotherapy centres limit the cumulative dose to the pacemaker to 2Gy and of these, only 68% communicate with the cardiology department if the dose exceeds 2Gy. It is concerning that 32% of policies defined no tolerance dose to the pacemaker. There is evidence that even low cumulative doses of radiotherapy may damage CIEDs and it is likely that patients are being put at risk of harm with the current CIED policies in use (Last, 1998). If the calculated dose to the pacemaker is greater than 10Gy, the Clinical Oncologist must immediately contact the referring cardiology department with a view to re-siting the pacemaker. This consultation should be completed as soon as possible, as further surgery for re-siting will cause a delay in the delivery of the patient's radiotherapy treatment. If the cumulative dose to the pacemaker is between 2-10Gy, the Clinical Oncologist would need to liaise with medical physics to discuss how to optimise the patient's radiotherapy plan and limit the dose to the pacemaker. At one radiotherapy department, during the radiotherapy planning process, it was noted that 3 patients would be receiving a total dose of greater than 2Gy to the pacemaker. The referring cardiology department was immediately contacted and the patients were reviewed and underwent a device check. The cardiology department then informed the Clinical Oncologist that the patient's radiotherapy treatment could commence, but close monitoring was deemed necessary. During radiotherapy treatment, Patient One displayed 'device malfunctions', due to a change in sensitivity and experienced symptoms typical of bradycardia (dizziness), which prompted a device, check midway through their treatment. Patient Two displayed 'device malfunctions', due to a change in capture

threshold during radiotherapy treatment. Both patients' cardiac devices required re-programming post-radiotherapy treatment. Patient Three received a mid-therapy check due to an increased total dose of 2.8Gy received by the device but no re-programming was necessary. In following the AAPM guidelines (Marbach et al, 1994), this radiotherapy department recognised the increased dose to the pacemaker and correctly followed their departmental guidelines. Had the policy not been adhered to, damage to the pacemaker could have occurred and had a detrimental effect on the patient.

Frizzell (2009) recommends a lower radiotherapy tolerance dose of 0.5Gy for ICDs and that they should be deactivated prior to radiotherapy by placing a magnet over the device to prevent inappropriate therapy or shock delivery as a result of accidental sensing of EMI interference (Frizzell, 2009). The audit shows that only 11% of radiotherapy centres limit the ICD dose to 0.5Gy. That means that in the majority of centres with a CIED policy, ICDs are potentially exposed to doses of radiotherapy that may affect function and cause serious harm to the patient. In addition, it is of major concern that only 14% of CIED policies differentiate between pacemakers and ICDs and subsequently apply the appropriate radiotherapy tolerance dose limits to both types of device. In these policies, ICDs are subject to the same radiotherapy tolerance dose limits and the same monitoring procedures as pacemakers. As a result, ICDs are almost certainly being subjected to radiotherapy doses beyond tolerance and ICD malfunction has potentially life-threatening consequences.

Patients consenting for any type of treatment need to be informed of potentially serious side effects related to that treatment. They should be made aware of potential damage that radiation can cause in both the short and long term and as a result they will be subject to close monitoring and further follow-up procedures. On receiving this information, patients are able to make an informed decision and give

consent as to whether they want to proceed. Nearly 75% of policies do not mandate discussion of potential damage to the CIED during and after radiotherapy in the treatment consent process. Given the lack of contemporary research in this area, it is not possible to quantify this risk of damage or harm at present, but consideration should be given to discussing potential complications in all patients with a CIED. It is likely that ICDs are susceptible to radiotherapy damage at lower doses than pacemakers, and ICD patients should be informed about the possibility of malfunction, failure or both of their ICD during radiotherapy treatment as the consequences may be life-threatening. ICD patients also need to be told in advance of radiotherapy that their device will be deactivated using a magnet during treatment.

The AAPM report and Frizzell recommend that all patients with CIEDs be monitored with a continuous ECG strip during their first radiotherapy treatment and reviewed for any evidence of pacing disruption (Marbach et al, 1994 and Frizzell, 2009). Particular attention should be given to any pacing discrepancies when the radiation beam is turned on and off. If the patient is classified as 'low risk' (dose to the cardiac device is <2Gy and the patient is non-pacemaker dependent) and there were no changes on the ECG monitoring, the patient would not require further monitoring during the remainder of their radiotherapy treatment. If the patient is classified as 'intermediate or high risk' (dose to the cardiac device is >2Gy and the patient is pacemaker dependent or has an ICD) they will require ECG monitoring throughout the course of their radiotherapy. One radiotherapy department in the audit stated that if there were limited monitoring resources for the patient on their first radiotherapy treatment, treatment could proceed but monitoring would be carried out on the patient's second treatment. Departmental policies should clearly state that monitoring of this classification of patient must be carried out for every treatment. ICD patients would also require daily monitoring due to their device being switched off during radiotherapy treatment. Monitoring staff should document any changes in

the patient's physical status and any changes in the ECG trace should be documented after every radiotherapy treatment. If at any point, any malfunction is suspected or detected the Clinical Oncologist and Cardiologist should be immediately informed. This monitoring should be carried out by fully trained and competent health professionals. If therapeutic radiographers are monitoring patients, they should receive specific training on the management and monitoring of such patients. All staff should be conversant with their departmental policies and protocols and be able to safely manage CIED related issues if and when they occur. The audit shows that only 32% of policies require the use of an appropriately trained health professional to carry out the monitoring. Therefore, a substantial number of patients with CIEDs are undergoing radiotherapy with no monitoring and in those that are monitored; the majority of staff involved may not have appropriate training to interpret ECG or clinical changes.

Last (1998) highlighted the importance of both short and long term follow-up monitoring for patients who have a CIED and have received radiotherapy treatment. Patients should have their CIED checked within two weeks of completion of their radiotherapy treatment. The results of the audit show that 67% of the policies require a follow-up appointment to be made with patient's cardiology department following completion of radiotherapy. A study in one Welsh radiotherapy centre and cardiology department evaluated the follow-up assessment of 26 patients with varying CIEDs who had received radiotherapy between July 2005 and March 2011 (68 months). The results showed that at the patient's first cardiology follow-up appointment, two patients' CIEDs experienced malfunctions. Patient One's CIED experienced a change in capture threshold and Patient Two's CIED showed changes in sensitivity threshold. These changes were deemed 'significant' as they required device re-programming and were classified as 'radiotherapy induced malfunctions'. There are a limited number of previous clinical studies with which comparisons can be made.

The largest of these prospectively analysed 37 pacemaker patients and 8 ICD patients who underwent radiotherapy, and found varying malfunctions that occurred after a median follow-up of 26 months (Ferrara et al, 2010). Two smaller studies with a combined total of 15 pacemakers also reported no detrimental effects from radiotherapy (Wadasadawala et al, 2011 and Kapa et al, 2008). Research suggests that devices exhibiting signs of a malfunction should be followed-up with increased frequency. This will allow for determination of a temporary malfunction that may occur due to a build-up of charge within the semiconductor, or more permanent circuitry damage. Should any additional changes be observed during the follow-up period then immediate device revision is likely to be necessary.

Conclusion

One of the aims of the PhD was to audit and establish current UK practice regarding the management of patients with implanted CIEDs undergoing radiotherapy and compare this practice to current 'gold standard' evidence-based guidelines. 30% of radiotherapy centres did not respond to the audit so it is not appropriate to draw definitive conclusions on UK practice, but important themes have emerged nevertheless. The outcomes and implications of this audit were sent for external peer review and subsequently published in *Clinical Oncology*, the international journal of the Royal College of Radiologists (Lester et al, 2014). It is clear that policies differ between radiotherapy centres and the implementation of these policies is variable. In addition, a significant proportion of policies do not adhere to current established tolerance doses for CIEDs. It can be concluded that as a consequence, it is very likely that patients are being put at significant risk of harm.

5.3 Study 2

To undertake an audit of clinical practice to determine any effects of ionising radiation and EMI on patients with CIEDs receiving radiotherapy treatment at a RCW.

Audit 1 :Clinical audit – all patients with a CIED receiving radiotherapy treatment

Results

In this clinical audit, 'radiotherapy induced device malfunction' was defined as any change to the device that required reprogramming (Tondato et al, 2009). Twenty-six patients with CIEDs presented for radiotherapy at a Welsh radiotherapy department. 59% of patients were male, 41% were female, and the mean age at commencing their RT treatment was seventy-six years of age.

Table 5.4: Results – Patient demographics

Demographics	Total	
Number of patients	22	
Number of RT treatments	22	
Gender	Male = 13	Female = 9
Mean age at RT start (years)	76	

Effect of ionising radiation and EMI on CIED function

In the audit, patients' radiotherapy treatment areas were classified into three anatomical radiotherapy treatment sites*;* 50% of these patients were receiving radiotherapy treatment to the thorax (chest), 32% to the pelvis and 18% to the head and neck region. CIEDs are implanted within the thoracic (chest) cavity, therefore the CIEDs of patients receiving radiotherapy to the thoracic region, will receive a higher dose of ionising radiation than other parts of the body.

Table 5.5: Results – Radiotherapy treatment information

Radiotherapy treatment site	Total (22 patients)
Head and neck	4
Pelvis	7
Thorax	11

From the total irradiated CIEDs, seventeen were pacemakers (sixteen dual-chamber, one single-chamber), four were ICDs and one was a CRT-D, which is a cardiac resynchronisation therapy (CRT) with defibrillator capability. Of the patients' CIEDs in the audit, nine were manufactured of by Medtronic, five by St. Jude Medical, three by Biotronik, two by Boston Scientific and one from Biotec, Sorin and Vitatron

From the twenty-two patients in this audit, three patients (14%) received a total cumulative dose of greater then the AAPM recommendations of 2Gy. These patients were treated and monitored according to the department's Cardiac Pacemaker and ICD Policy. All three patients received a mid-radiotherapy CIED check at the cardiology department. One of the three patients (Patient A) who was receiving radiotherapy to the left lung (thorax) had a radiotherapy induced device malfunction, which required a programming revision. Of the other two patients, their mid-radiotherapy CIED check found that no revisions were deemed necessary. Patient B was receiving radiotherapy to the left maxillary antrum (head and neck region), therefore their CIED was receiving a negligible dose of ionising radiation. However, during radiotherapy treatment the patient exhibited symptoms of bradycardia. Following departmental policy, the radiotherapy department arranged a mid-radiotherapy CIED cardiology check at the cardiology department and results showed that the CIED required a programming revision.

Table 5.6: Results – CIED information

CIED	Total (22 patients)
Dual chamber	16
Single chamber	1
ICD	4
CRT-D	1

Table 5.7: Results – CIED manufacturer

CIED manufacturer	Total (22 patients)
Medtronic	9
St. Jude Medical	5
Biotronik	3
Biotec	1
Guidant/Boston Scientific	2
Sorin	1
Vitatron	1

Table 5.8: Results – Patient information - effect of ionising radiation on their CIED

	Dose to Device (Gy)	Area of RT	Parameter changed?
Patient A	2.8Gy	Left lung	Ventricular Sensitivity – Reduced R-wave amplitude (15mV to 2.5mV)
Patient B	0Gy (>10cm away)	Left maxillary antrum	Ventricular capture threshold – Increased from 0.5V @ 0.4ms to 3.75V @ 0.4ms

Discussion

The aim of this retrospective clinical audit was to assess device malfunction in patients with a CIED that have been exposed ionising radiation and EMI and as part of their radiotherapy treatment. Previous studies have concluded that radiotherapy can potentially cause damage and malfunction to CIEDs, by direct ionising radiation and/or EMI (Hurkmans et al, 2012 and Zaremba et al, 2015).

From this audit, twenty-two patients with a CIED presented for radiotherapy treatment. The CIEDs of two patients (A and B) required a revision to the

programming at their mid-radiotherapy CIED check. These changes were classed as significant, as they required an immediate intervention in the form of device re-programming.

Patient A was having radiotherapy to the left lung for lung cancer; their CIED received a cumulative ionising radiation dose of 2.8Gy. At their mid-radiotherapy CIED check a change in sensitivity threshold (reduction in sensitivity) was observed and required a programming revision. As the CIED received a greater cumulative ionising dose than that of 2Gy recommended by AAPM, this malfunction could be a result of the higher dose of ionising radiation. Patient B was having radiotherapy to the left maxillary antrum and their CIED was receiving a negligible dose of ionising radiation as the CIED was further than 10cm from the radiotherapy treatment site. However, during the radiotherapy treatment they exhibited symptoms of bradycardia and a mid-radiotherapy CIED check was carried out. The CIED showed a change in capture threshold (increase in capture threshold) and required a programming revision. As the CIED was not exposed to direct ionising radiation, this malfunction could be a result of scatter radiation or EMI.

Patient A and B's CIEDs were manufactured by Medtronic. Medtronic states that radiotherapy can cause interference, memory errors, or permanent damage. They suggest that scattered neutron radiation is the primary mechanism for memory errors, such as device reset, although they provide no evidence for this. Medtronic state a tolerance of 5Gy for their pacemakers, and between 1-5Gy for ICDs (Medtronic, 2013). It is of note that both the CIEDs in this audit, requiring mid-radiotherapy programme revisions received a cumulative ionising radiation dose less than the 5Gy stated by the manufacturer.

In this audit, all patients were treated and monitored in accordance to departmental policy, based on the AAPM recommendations. An American report suggests that

12% of oncology centres have neither a formal risk management strategy nor a CIED policy, and that only 15% actually have a written policy (Solan et al, 2004). As it is not clear whether the situation is similar here in the UK, the lack of written national policy and deviation from evidence-based guidelines such as the AAPM is of major concern. This supported publication of the national audit, to determine current UK radiotherapy departmental practice regarding the management of patients with a CIED receiving radiotherapy treatment.

Conclusion

The aim of this retrospective clinical audit was to assess device malfunction in patients with CIEDs that have been exposed to ionising radiation and EMI as part of their radiotherapy treatment. The number of cancer patients with CIEDs receiving radiotherapy treatment is increasing. Radiotherapy can be delivered if direct irradiation of CIEDs is avoided, appropriate monitoring and the cumulative ionising radiation dose to the pacemaker is below 2Gy and the ICD is below 0.5Gy. The results of this audit highlighted the need for further research. A key aim of this PhD research project is to define the effect of radiotherapy on CIEDs, the effect on patients and to issue management guidelines.

Audit 2: Clinical audit – patients with a *rate response activated* CIEDs receiving radiotherapy treatment

Results

One hundred and thirty-two patients with CIEDs presented for radiotherapy treatment at a Welsh radiotherapy department. Fifty-three devices (40%) had the rate response setting switched to ON and sixteen devices (12%) had rate response setting switched to PASSIVE. Therefore, sixty-nine devices (52%) were susceptible to EMI effects during irradiation. Twenty-eight devices (21%) had the rate response

setting switched to OFF and for thirty-five devices (27%), the rate response setting was unknown.

Table 5.9: Results – Patient data set

CIED – Rate response setting	Patient Numbers (N = 132)
ON	53
PASSIVE	16
OFF	28
Unknown	35

Effect of EMI on rate response activated CIED function

This audit included patients from the cardiology department at one hospital only, therefore data collection proceeded with twenty-two patients, of which fourteen patients (64%) exhibited a clinical reaction during their radiotherapy treatment. From the twenty-two patients in the audit, no patients CIEDs' received a total cumulative ionising radiation dose of greater than the AAPM recommendations of 2Gy (Marbach et al, 1994).

Table 5.10: Results – Observed CIED mediated tachycardia (clinical reactions)

Patient	Radiotherapy treatment region	Clinical observation
1	Pelvis	Patient's heart rate accelerated to 145bpm on numerous occasions. Had CIED check half way through RT
2	Thorax	HR increased to 200+bpm halfway through RT for beam
3	Thorax	HR increased at end of RT beam exposure. Discussed with cardiac pacing clinic - not inclined to reset rate response if the patient can tolerate the increased HR. Fraction 2 - rate response switched off - no change in HR. Fraction 5 - HR increased on Beams1,3,4 - cardiology reinstated rate response. Fraction 6 - copper sheet applied over pacemaker - no effect. RT beam stopped every 8mu to allow HR to decrease to 80bpm before beaming on. Fraction 7 - limit to 25mu before beaming off Remaining fractions (total 15 fractions) continuous problems with increased HR on all fractions Patient was in extreme discomfort during RT – "could feel it pounding" / hot / nausea
4	Pelvis	Pacing throughout. HR rapidly increased from 62-73bpm. Delivered 170mu – HR rapid increase – beam on stopped until HR decreased to 62. Delivered remained of RT before HR reached 73bpm.
5	Thorax	Problems pacing throughout. Fraction 1 - HR increased to 110bpm. Fraction 2 - ventricular paced HR to 110bpm. Stop/start treatment to allow HR to decrease - cardiology department informed. Assessed by SHO -pain not related to heart
6	Thorax	HR affected - increased to 78bpm throughout RT beam on. Heart rate affected during numerous fractions of RT
7	Pelvis	HR increased to 135 (upper limit) on delivery of RT, dose delivered stopping every 55-60 MU to allow HR to return to lower limit. HR observed 65-135. Pacing clinic informed.
8	Pelvis	HR increased on delivery of RT
9	Pelvis	HR increased rapidly on delivery of RT
10	Pelvis	HR increased and erratic on RT
11	Thorax	ECG trace - Double sensing throughout treatment. Erratic and increased heart rate
12	Head and neck	Patients heart rate increased to 98bpm
13	Pelvis	Fraction 2 - HR increased during CBCT (102bpm) Mixture of pacing and non pacing rhythms . Fraction 3 -irregular pacing associated with ectopic episode , HR not stable.. Fraction 5 - HR 140bpm. Fraction 11 = peaked 110bpm during CBCT. Fractions 16-20 - not pacing at all
14	Pelvis	Irregular pacing throughout RT

In the audit, the patients of who exhibited CIED mediated tachycardia reactions, were classified into three anatomical radiotherapy treatment sites; 57% of these patients were receiving radiotherapy treatment to the pelvis, 36% to thorax (chest), and 7% to the head and neck region.

A clinical observation of CIED mediated tachycardia, where the patient's baseline heart rate increased to over 100 beats per minute during the delivery of the radiotherapy treatment was detected in eighteen radiotherapy courses (fourteen patients). These patients received their radiotherapy treatment using different radiotherapy treatment modalities, including linear accelerators (manufacturers Elekta and Varian) and Xstrahl (superficial radiotherapy treatment unit).

In twelve of the fourteen patients that were observed with CIED mediated tachycardia; their CIEDs were from same manufacturer. All CIEDs were implanted between 2004 and 2014 (average lifetime of device seven years). No CIED mediated tachycardia was observed in patients implanted with CIEDs from the remaining manufacturers.

Of the fourteen patients were observed with CIED mediated tachycardia. Ten patients had DDDR (both chambers capable of being paced and sensed) and four patients were VVIR (ventricular pacing and sensing). There should be no difference in clinical response of DDR vs VVIR as the CIEDs should react the same. The ratio is consistent with current implant rates at 70/30 in favour of DDDR. VVIR is only for patients in atrial fibrillation and currently there is a reduction in their clinical use.

No trend in treatment modality, cumulative ionising radiation dose to the CIED or leads, radiotherapy treatment site or CIED mode (DDDR/ VVIR) indicate which patients are at risk of CIED mediated tachycardia. All clinical observations are based

on acute reactions observed by cardiac monitoring trained radiographers during the patients' radiotherapy treatment. No long-term effects have been reported or documented by the cardiology department on review of the patients and their CIEDs at the post radiotherapy device follow-up appointment.

Discussion

The findings of the national audit (Lester et al, 2014), in study 1 identified an inadequate understanding and compliance with existing guidelines. Together with the advances in CIED technology, there are now a wide variety of complex multi-programmable CIEDs and programmable pacing modes used in the treatment of cardiovascular disease. This underlines the need for this research. As documented in chapter three, rate response activated CIEDs can be affected by EMI from the radiotherapy treatment machine, but the reaction is highly specific to the make, model, design and CIED manufacturer. For example, a CIED that uses a minute-ventilation sensor for rate response can be caused to operate at the upper limit and trigger rapid pacing by activating the sensor due to EMI interference. Rate response activated CIEDs may also erroneously interpret the signals generated by the radiotherapy treatment machine (linac) and this can lead to the CIED increasing the patient's heart rate.

The aim of this clinical audit was to assess CIED mediated tachycardia in patients with a rate response activated CIED that have been exposed to ionising radiation and EMI as part of their radiotherapy treatment at a Welsh radiotherapy department. A CIED mediated tachycardia, could be due to:

1. A rate response setting that is too sensitive
2. Tracking of atrial noise (an effect of EMI)
3. Inappropriate CIED manipulation with rate response switched on
4. Tracking of an atrial tachyarrhythmia related to upper rate setting

A pre-requisite of the PhD research project was an understanding of the functions of CIEDs, how device malfunction is presented on an ECG trace and the clinical symptoms exhibited as a result of CIED damage. During the PhD research, it was identified that an increasing number of patients are presenting for radiotherapy treatment with rate response activated CIEDs and a proportion of these patients displayed CIED mediated tachycardia. Further investigation was needed to establish if guidelines existed for the safe management of these patients. On conducting a literature review, there was no research in this area. Therefore, working with the cardiologist to review the evidence from this audit, device specific (rate-response activated) testing was devised as part of the PhD study methodology.

The interrogated data for those patients who exhibited heart rate changes and CIED mediated tachycardia during their radiotherapy treatment was reviewed. Due to the sampling frequency for data collection of the programmed CIED, it is not possible to view the rate trends at the exact point of observed reaction during their radiotherapy. There are no prolonged high-rate episodes documented. Some of the patients were in atrial fibrillation with no pacing observed. Consequently there is quite a beat-to-beat variation in the R-R (rest rate) cycle length. This will give rise to a variance on the heart rate monitor despite the patient being at rest. No programming changes or electrical reset have been brought about from the radiotherapy treatment. Rate increases due to sensor activation are recognised by the CIED manufacturers and they recommend deactivation of the sensor during therapy if changes are observed. As the different CIED manufacturers use different activity sensors, the response can vary between the manufacturers.

One of the CIED manufacturers (St. Jude Medical, 2013) recognise in their own literature that 'linear accelerators produce strong electromagnetic fields as well as ionising radiation, which can also affect device operation.'

They list potential effects of exposure to radiation as follows:

- Permanent damage
- Temporary loss of sensing
- Temporary loss of device inhibition
- Temporary loss of capture
- Temporary increased sensor rate
- Temporary rate changes
- Device reset or reversion to back up VVI pacing

Consequently, St. Jude Medical (2013) state that 'for rate-adaptive devices, if the sensor is ON, exposure to radiation may cause the device to pace at rates up to the programmed maximum sensor rate. Therefore, to prevent such transient rate increases the sensor can be programmed to PASSIVE or OFF before administering the radiotherapy treatment.

Conclusion

Radiotherapy departments' CIED policies and guidelines need to include the management of patients with rate response activated CIEDs. Cardiology knowledge and understanding of radiotherapy induced CIEDs reactions, and subsequent management is dependent on feedback from radiotherapy departments and healthcare professionals employed to monitor patients during radiotherapy. However, not all radiotherapy departments liaise with the cardiology department prior to radiotherapy, and/or monitor patients with CIEDs receiving radiotherapy. Therefore there is a risk of patients with rate response activated CIEDs experiencing unmanaged tachycardia during their radiotherapy treatment.

This research found that there is no overarching documented guidance governing the management of patients with rate response activated CIEDs receiving radiotherapy treatment. St Jude Medical (2013) recommend that rate response activated CIEDs be switched off during radiotherapy treatment, however this is not always possible, especially in the case of emergency treatments. Therefore, awareness is required for radiotherapy and cardiology departments of the potential issues and their subsequent management.

The results of the clinical audit show that a significant number of patients exhibited CIED mediated tachycardia while receiving radiotherapy treatment at a Welsh radiotherapy department. This department's CIED policy was following current 'gold-standard' recommendations, thereby identifying adverse clinical reactions, monitoring these and liaising with the cardiology department. Recently, there has been a marked increase in the number of patients with rate response activated CIEDs receiving radiotherapy treatment and the current guidelines do not include recommendations for the management of patients with rate response activated CIEDs. Therefore, this research will investigate the effect of ionising radiation and EMI as part of the device specific testing of the PhD study methodology. Results from this will lead to the development of national guidelines and radiotherapy tolerance doses to rate response activated CIEDs.

5.4 Chapter conclusion

The results from the national audit concluded that CIED policies vary between radiotherapy departments and the implementation of these policies is inconsistent. In addition, a significant proportion of policies do not adhere to current established tolerance doses for CIEDs. It can be concluded that as a consequence, it is very likely that patients are being put at significant risk of harm.

These results and those from both clinical audits, reinforce the need for further research in this area and to publish up-to-date clinical guidelines for the management of patients with CIEDs receiving radiotherapy treatment.

Chapter Six

Scientific Research

6.1 Introduction

The previous chapter discussed the findings of the initial studies 1 and 2, which looked at the knowledge and perceptions of healthcare staff within UK radiotherapy centres toward the management of cancer patients having implanted cardiac devices and the implications of them receiving radiotherapy. This was followed up by a series of audits within one RCW to investigate the possible effects of radiation and EMI to support anecdotal evidence that these occur. The ongoing scientific empirical investigations resulted and this chapter will discuss the outcomes from these under the following study headings:

- ***Study 3 -*** To investigate and evaluate the relationship between cumulative ionising radiation dose and the damage sustained to CIEDs (pacemakers and ICDs).
- ***Study 4 -*** To investigate and evaluate the relationship between cumulative ionising radiation dose and the damage sustained to CIED leads.
- ***Study 5 -*** To investigate and evaluate the relationship between EMI and the damage sustained to CIEDs (pacemakers, ICDs and rate response activated CIEDs).

This chapter will present the findings, analyse the study's results and discuss the mechanisms that cause CIED malfunctions and / or failure. In reporting CIED malfunctions and failure the effect of radiotherapy treatment and the clinical impact to the patient will be discussed. Recommendations regarding radiotherapy tolerance doses to all CIEDs will be made.

6.2 Study 3

6.2.1 Introduction

The aim of this study was to investigate and evaluate the relationship between cumulative ionising radiation dose and the damage sustained to CIEDs (pacemakers and ICDs). This section will present the findings of study three, analyse the results and discuss the mechanisms that cause malfunctions and / or failure in CIEDs when exposed to ionising radiation. In discussing specific CIED malfunctions and failure, the effect of radiotherapy and the clinical impact to the patient will be discussed. This study outcome concludes by recommending safe radiotherapy tolerance doses to all CIEDs.

6.2.2 Data analysis – Effect on ionising radiation on CIEDs (pacemakers)

Table 6.1: Results – First malfunction observed resulting in pacemaker failure - Classified by type of device malfunction

Pacemaker	Pacemaker failure	RT Dose (Gy)
1 - Pacing pulse		
6MeV		
PM X3	No output and amplitude deviations (atrial channel). Point of failure = Device failure	120Gy
3 – Sensing		
10MeV		
PM Y7	Unable to sense Point of failure = Device failure	52Gy
4 – Telemetry		
6MeV		
PM Z3	No output / permanent loss of telemetry. Point of failure = Device failure	23Gy
10MeV		
PM X5	No communication Point of failure = Device failure	28Gy

22% of pacemakers (4 pacemakers; PM X3, PM Y7, PM Z3 and PM X5) irradiated at both 6MeV and 10MeV, exhibited POF in the range of 23Gy to 120Gy.

At 6MeV, POF was first observed in PM Z3 at 23Gy due to no output resulting in permanent loss of telemetry and second POF was observed in PM X3 at 120Gy (test to destruction ionising radiation dose) due to no output and amplitude deviations in the atrial channel resulting in pacing pulse failure. At 10MeV, POF was observed in PM X5 at 28Gy due to no communication resulting in permanent loss of telemetry and second POF was observed in PM Y7 at 52Gy due to the pacemaker being unable to sense resulting in sensing failure.

Table 6.2: Results – First malfunction observed in pacemakers during exposure to ionising radiation – Classified by type of device malfunction (Malfunctions are only indicated when seen at each respective energy)

Pacemaker	Pacemaker malfunction	RT Dose (Gy)
1 – Pacing pulse		
6MeV		
PM X4	Output discrepancies	70Gy
PM X3	No output. Point of failure = Device failure	120Gy
2 – Pacing frequency		
6MeV		
PM Y3	Inhibition during irradiation longer than 5s	44Gy
10MeV		
PM X6	Deviation in pacing frequency	2.5Gy
3 – Sensing		
6MeV		
PM X2	Under sensing	3Gy
PM Y4	Sensing discrepancies	10.5Gy
10MeV		
PM Y5	Programming error	4.5Gy
PM Y6	Programming error	7Gy
PM Y7	Unable to sense Point of failure = Device failure	52Gy
PM Z5	Sensing error	41Gy
4 – Telemetry		
6MeV		
PM Z2	Communication error	20.5Gy
PM Z3	No output. Point of failure = Device failure	23Gy
10MeV		
PM X5	No communication Point of failure = Device failure	28Gy
PM X7	Communication error	17Gy
PM Z6	Communication error	21Gy
PM Z7	Communication error	8.5Gy
5 – Battery		
6MeV		
PM Z4	Battery problems	12Gy
6 – Lead impedance changes		
6MeV		
PM Y2	Increased lead impedance	80Gy

- ***1, Pacing pulse malfunctions***

At 6MeV, 22% of the pacemakers (2 pacemakers: PM X4 and PM X3) both from CIED manufacturer X exhibited CIED pacing pulse malfunctions as the first malfunction. In PM X4 output discrepancies were observed at a cumulative ionising radiation dose of 70Gy. In PMX3, no output was recorded, resulting in POF observed at point of destruction 120Gy.

- ***2, Pacing frequency malfunctions***

At 6MeV, 11% of pacemakers (1 pacemaker: PM Y3) from CIED manufacturer Y exhibited pacing frequency malfunctions as the first malfunction. Inhibition during irradiation longer than 5s was observed at a cumulative ionising radiation dose of 44Gy. At 10MeV, 11% of pacemakers (1 pacemaker, PM X6) from CIED manufacturer X exhibited a deviation in pacing frequency as the first malfunction at 2.5Gy.

- ***3, Sensing malfunctions***

At 6MeV, 22% of pacemakers (2 pacemakers: PM X2 and PM Y4) from CIED manufacturers X and Y exhibited sensing malfunctions as the first malfunction. In PM X2, under sensing was observed at a cumulative ionising radiation dose of 3Gy and sensing discrepancies was observed at 10.5Gy in PM Y4. At 10 MeV, 44% of pacemakers (4 pacemakers: PM Y5, PM Y6, PM Y7 and PM Z5) from CIED manufacturers Y and Z exhibited sensing malfunctions as the first malfunction. From manufacturer Y, PM Y5 and PM Y6 exhibited programming errors as the first malfunction at a total cumulative ionising radiation dose of 4.5Gy and 7Gy respectively and PM Y7 reached a POF at 52Gy, as the device was unable to sense. PM Z5 from manufacturer Z exhibited a sensing error as the first malfunction at a total cumulative ionising radiation dose of 41Gy.

- ***4, Telemetry malfunctions***

At 6MeV, 22% of pacemakers (2 pacemakers: PM Z2 and PM Z3) both from CIED manufacturer Z exhibited telemetry malfunctions as the first malfunction. In PM Z2, a communication error was observed at a cumulative ionising radiation dose of 20.5Gy. In PM Z3, no output was recorded resulting in POF at 23Gy. At 10MeV, 44% of pacemakers (4 pacemakers: PM X5, PM X7, PM Z6 and PM Z7) from CIED manufacturers X and Z exhibited telemetry malfunctions in the form of communication errors as the first malfunction. The first communication error was displayed at 8.5Gy in PM Z7, in PM X7 at 17Gy followed by PM Z6 at 21Gy. PM X5 reached a POF at 28Gy, as the device was no longer able to communicate.

- ***5, Battery malfunctions***

At 6MeV, 11% of pacemakers (1 pacemaker: PM Z4) from CIED manufacturer Z exhibited battery malfunctions as the first malfunction. Battery problems / warning alert was observed at a cumulative ionising radiation dose of 12Gy.

- ***6, Lead impedance changes***

At 6MeV, 11% of pacemakers (1 pacemaker: PM Y2) from CIED manufacturer Y exhibited lead impedance changes as the first malfunction. Increased lead impedance was observed at a cumulative ionising radiation dose of 80Gy.

Table 6.3: Results – Pacemaker malfunctions observed during exposure to ionising radiation – Classified by type of device malfunction

(Malfunctions are only indicated when seen at each respective energy)

Pacemaker	Pacemaker malfunction	RT Dose (Gy)
2 – Pacing frequency		
6MeV		
PM X4	Inhibition during irradiation longer than 5s	94Gy ➔
PM Y3	Inhibition during irradiation longer than 5s	44Gy ➔
PM Z2	Inhibition during irradiation longer than 5s	20.5Gy ➔
3 – Sensing		
6MeV		
PM X2	Under sensing	3Gy ➔ 5Gy ➔
PM X4	Communication error	90Gy ➔
PM Y4	Sensing discrepancies	10.5Gy ➔
10MeV		
PM X7	Under sensing Sensing inhibition during irradiation	30Gy ➔ 56Gy ➔
PM Y5	Under sensing Sensing inhibition during irradiation	5Gy ➔ 50Gy ➔
PM Y6	Sensing inhibition during irradiation	18Gy➔
PM Z5	Sensing inhibition during irradiation	41Gy➔
PM Z6	Sensing inhibition during irradiation	21Gy➔
4 – Telemetry		
6MeV		
PM Z2	Communication error	90Gy ➔
10MeV		
PM Z6	Communication error	90Gy ➔
PM Z7	Communication error (battery problems)	29Gy ➔
6 – Lead impedance changes		
6MeV		
PM Y2	Continued increase in lead impedance	82Gy ➔

- ***2, Pacing frequency malfunctions***

At 6MeV, 38% (3 pacemakers: PM X4, PM Y3 and PM Z2) exhibited inhibition during irradiation longer than 5s resulting in pacing frequency malfunctions. Inhibition during irradiation longer than 5s was observed at a cumulative ionising radiation dose starting at 20.5Gy in pacemakers from manufacturer Z, next at a cumulative ionising radiation dose starting at 44Gy in pacemakers from manufacturer Y and finally at a cumulative ionising radiation dose starting at 94Gy in pacemakers from manufacturer X.

- ***3, Sensing malfunctions***

At 6MeV, 38% (3 pacemakers: PM X2, PM X4 and PM Y4) exhibited sensing malfunctions. PM X2, exhibited under sensing at a cumulative ionising radiation dose starting at 3Gy and sensing inhibition during irradiation starting at a cumulative ionising radiation dose of 5Gy. PM X4, exhibited communication errors at a cumulative ionising radiation dose starting at 90Gy and PM Y4 exhibited sensing discrepancies at a cumulative ionising radiation dose starting at 10.5Gy. At 10MeV, 63% (5 pacemakers: PM X7, PM Y5, PM Y6, PM Z5 and PM Z6) exhibited sensing malfunctions. The first sensing malfunction during ionising radiation exposure was exhibited by PM Y5 starting a total cumulative ionising radiation dose of 5Gy. This device then exhibited further sensing malfunctions, as it displayed sensing inhibition during irradiation at a total cumulative ionising radiation dose of 50Gy. The same sequence of sensing malfunctions was also observed in PM Y7 from manufacturer Y, but at higher ionising radiation doses. This device exhibited under sensing firstly at 30Gy and then sensing inhibition during irradiation at 56Gy. All 3 remaining pacemakers (PM Y6, PM Z5 and PM Z6) displayed sensing inhibition during irradiation. Firstly PM Y6 starting at a total cumulative ionising radiation dose of 18Gy, then PM Z6 and PM Y5 starting at a cumulative ionising radiation doses of

21Gy and 50Gy respectively. Therefore 100% of the pacemakers exhibited sensing inhibition during irradiation exposure.

- ***4, Telemetry malfunctions***

At 6MeV, 13% of pacemakers (1 pacemaker: PM Z2) exhibited telemetry problems in the form of no communication. This clinical malfunction was observed at a cumulative ionising radiation dose starting at 90Gy. At 10MeV, 22% of pacemakers (2 pacemakers: PM Z6 and PM Z7) both from manufacturer Z exhibited telemetry problems in the form of communication errors. This observed clinical malfunction (further defined as battery problems) was observed firstly in PM Z7 starting at a cumulative ionising radiation dose of 29Gy and then in PM Z6 starting at a cumulative ionising radiation dose of 90Gy. Of note, PM Z6 first exhibited sensing malfunctions (sensing inhibition during irradiation) starting at a cumulative ionising radiation dose of 21Gy.

- **5, Battery malfunctions**

No effects were seen due to battery failure.

- ***6, Lead impedance changes malfunctions***

At 6MeV, 13% of pacemakers (1 pacemaker: PM Y2) exhibited a continued increase in lead impedance. This clinical malfunction was observed at a cumulative ionising radiation dose starting at 82Gy.

Table 6.4: Results – Point of device failure (POF) observed in pacemakers – Classified by type of device malfunction

(Malfunctions are only indicated when seen at each respective energy)

Pacemaker	Pacemaker failure	RT Dose (Gy)
1 - Pacing pulse		
6MeV		
PM X2	No output and amplitude deviations (atrial channel)	120Gy
PM X3	No output and amplitude deviations (atrial channel)	120Gy
PM Y4	No output and amplitude deviations (atrial channel)	120Gy
10MeV		
PM X6	No output	90Gy
3 - Sensing		
6MeV		
PM Y4	Unable to sense	120Gy
10MeV		
PM Y5	Unable to sense	70Gy
PM Y6	Unable to sense	90Gy
PM Y7	Unable to sense	52Gy
PM Z5	Unable to sense	120Gy
4 – Telemetry		
6MeV		
PM X4	No communication	120Gy
PM Y2	No output	120Gy
PM Y3	No output	120Gy
PM Z2	No communication	120Gy
PM Z3	No communication	23Gy
PM Z4	No communication	13.5Gy
10MeV		
PM X5	No communication	28Gy
PM X7	No communication	100Gy
PM Z6	No communication	90Gy

5 - Battery		
6MeV		
PM Y4	Elective replacement indicator (ERI)	120Gy
10MeV		
PM Y5	Elective replacement indication (ERI)	70Gy
PM Z7	Elective replacement indication (ERI)	120Gy

Point of failure - Total cumulative ionising radiation dose

At 6MeV, the POF at 120Gy was observed in 78% of the pacemakers (7 pacemakers: PM X4, PM Y2, PM Y3, PM Z2, PM X2, PM X3 and PM Y4). 57% (4 pacemakers: PM X4, PM Y2, PM Y3 and PM Z2) exhibited no communication resulting in telemetry POF. 29% (2 pacemakers: PM X2 and PM X3) exhibited no output and amplitude deviations in the atrial channel resulting in pacing pulse POF. 14% (1 pacemaker: PM Y4) exhibited no output and amplitude deviations in the atrial channel and was unable to sense and the battery elective replacement indicator warning was observed resulting in both sensing and battery POF. The telemetry POF resulting from no communication in the remaining 22% of the pacemakers (2 pacemakers: PM Z3 and PM Z4) was observed at 23Gy and 13.5Gy respectively both from manufacturer Z. At 10MeV, the POF at 120Gy was observed in 22% (2 pacemakers: PM Z5 and PM Z7) of the pacemakers. 11% (1 pacemaker: PM Z5) was unable to sense resulting in sensing failure and 11% (1 pacemaker: PM Z7) displayed battery elective replacement indicator (ERI) resulting in battery failure.

At 10MeV, 40% of pacemakers (4 pacemakers: PM Y5, PM Y6, PM Y7 and PM Z5) from CIED manufacturers' Y and Z exhibited POF due to being unable to sense resulting in sensing failure. 75% of the pacemakers were from manufacturer Y. PM Y7 exhibited the first sensing POF at a cumulative ionising radiation dose of 52Gy, followed by PM Y5 at 70Gy and then PM Y6 at 90Gy. PM Z5 from manufacturer Z reached a sensing POF at the test to destruction cumulative ionising radiation dose

of 120Gy. 30% of pacemakers (3 pacemakers: PM X5, PM X7 and PM Z6) from CIED manufacturers X and Z exhibited telemetry malfunctions. PM X5 was the first device to display no communication resulting in telemetry POF at 28Gy. The same observation was seen in PM Z6 and PM X7 but at the higher cumulative ionising radiation doses of 90Gy and 100Gy respectively. 20% of pacemakers (2 pacemakers: PM Y5 and PM Z7) from CIED manufacturer Y and Z exhibited elective replacement indicator warning resulting in battery POF. PM Y5 was the first device to exhibit this POF at total cumulative ionising radiation dose of 70Gy and then it was observed in PM Z7 at the test to destruction cumulative ionising radiation dose of 120Gy. 10% of pacemakers (1 pacemaker: PM X6) from CIED manufacturer X exhibited no output resulting in POF at a cumulative ionising radiation dose of 90Gy.

Table 6.5: Results – POF in pacemakers – Test to destruction ionising radiation dose (120Gy) – Classified by CIED manufacturer

(Malfunctions are only indicated when seen at each respective energy)

Pacemaker	Pacemaker failure	RT Dose (Gy)
Manufacturer X		
6MeV		
PM X2	**Pacing pulse** No output and amplitude deviations (atrial channel)	120Gy
PM X3	**Pacing pulse** No output and amplitude deviations (atrial channel)	120Gy
PM X4	**Telemetry** No communication	120Gy
Manufacturer Y		
6MeV		
PM Y2	**Pacing pulse** No output	120Gy
PM Y3	**Pacing pulse** No output	120Gy
PM Y4	**Sensing** Unable to sense **Battery** Elective replacement indicator	120Gy
Manufacturer Z		
6MeV		
PM Z2	**Telemetry** No communication	120Gy
10MeV		
PM Z5	**Sensing** Unable to sense	120Gy
PM Z7	**Battery** Elective replacement indication (ERI)	120Gy

At 6MeV, 22% of pacemakers (2 pacemakers: PM X2 and PM X3) both from CIED manufacturer X exhibited CIED pacing pulse malfunctions at a cumulative ionising radiation dose of resulting in POF observed at point of destruction 120Gy. 11% of pacemakers (1 pacemaker: PM Y4) from CIED manufacturer Y was unable to sense and the battery elective replacement indicator warning was observed resulting in both sensing and battery POF. 17% (1 pacemaker: PM X4) exhibited no communication, therefore 100% of the pacemakers from manufacturer X reached POF at 120Gy. 33% of pacemakers (2 pacemakers, PM Y2 and PM Y3) from

manufacturer Y exhibited no output, therefore 100% of these pacemakers also reached POF at 120Gy.

At 10MeV, the POF at the test to destruction ionising radiation dose of 120Gy was observed in 22% of pacemakers (PM Z5 and PM Z7). 100% of the pacemakers POF was observed at 120Gy were from manufacturer Z. 50% were unable to sense, which resulted in sensing POF and 50% received an elective replacement indicator warning (ERI), which resulted in battery POF.

Table 6.6: Results – POF in pacemakers – Below 120Gy – Classified by CIED manufacturer

(Malfunctions are only indicated when seen at each respective energy)

Pacemaker	Pacemaker failure	RT Dose (Gy)
	Manufacturer X	
10MeV		
PM X5	**Telemetry** No communication	28Gy
PM X6	**Pacing pulse** No output	90Gy
PM X7	**Telemetry** No communication	100Gy
	Manufacturer Y	
10MeV		
PM Y5	**Sensing** Unable to sense **Battery** Elective replacement indicator (ERI)	70Gy 70Gy
PM Y6	**Sensing** Unable to sense	90Gy
PM Y7	**Sensing** Unable to sense	52Gy
	Manufacturer Z	
6MeV		
PM Z3	**Telemetry** No communication	23Gy
PM Z4	**Telemetry** No communication	13.5Gy
10MeV		
PM Z6	**Telemetry** No communication	90Gy

At 6MeV, from manufacturer Z, 67%, 2 pacemakers (PM Z3 and PM Z4) exhibited no communication resulting in telemetry POF at ionising radiation dose of 23Gy and 13.5Gy respectively.

At 10MeV, in the remaining 78% (7 pacemakers) the POF ranged from 28Gy to 100Gy. All 3 of the pacemakers from CIED manufacturer X, failed at a cumulative ionising radiation dose below test to destruction (120Gy). PM X5 was the first pacemaker to exhibit POF as communication was lost resulting in telemetry POF, which occurred at 28Gy. PM X7 also displayed telemetry POF, as no communication was observed but this occurred at a high cumulative ionising radiation dose of 100Gy. PM X6 was the only pacemaker to display pacing pulse POF as a result of no output and this occurred at 90Gy.

100% of the pacemakers from CIED manufacturer Y exhibited POF due being unable to sense resulting in sensing POF. PM Y7 reached POF at 52Gy, PM Y5 at 70Gy and PM Y6 at 90Gy. Of note at POF PM Y5, also exhibited battery failure of the same dose. Therefore, at 70Gy this device displayed two distinct forms of failure.

PM Z6 was the only pacemaker from CIED manufacturer Z to reach POF below 120Gy; it displayed no communication resulting in telemetry POF at 100Gy.

6.2.3 Data analysis – Effect on ionising radiation on CIEDs (ICDs)

Table 6.7: Results – First malfunction observed resulting in ICD failure – Classified by type of device ICD malfunction

(Malfunctions are only indicated when seen at each respective energy)

ICD	ICD malfunction	RT Dose (Gy)
1 – Pacing Pulse		
6MeV		
ICD Y3	Output error	0.5Gy
3 – Sensing		
6MeV		
ICD X2	Sensing threshold too low	60Gy
ICD X4	No sensing = Device failure	120Gy
ICD Y2	Inhibition during sensing	4Gy
ICD Y3	Over sensing	0.5Gy
ICD Z2	Sensing threshold too high	1.5Gy
10MeV		
ICD Y4	Sensing threshold too low	5Gy
4 – Telemetry		
6MeV		
ICD Y3	Communication discrepancies	0.5Gy
10MeV		
ICD Y5	Communication discrepancies	12.5Gy
5 – Battery		
10MeV		
ICD X4	Battery charge time increase = Device failure	120Gy
ICD Y5	Battery error	12.5Gy
7 – Shock		
6MeV		
ICD X3	Shock energy too low	45Gy
10MeV		
ICD X5	Shock energy too low	10Gy
ICD Z3	Shock energy too low	8.5Gy

100% of all ICDs (10 ICDs) exhibited device malfunctions when exposed to 6MeV and 10MeV ionising radiation.

At 6MeV, the first ICD malfunctions were observed in ICD Y3. This device exhibited sensing, pacing pulse and telemetry malfunctions at a cumulative ionising radiation dose of 0.5Gy. Of note, this is the radiation tolerance dose to ICDs for patients receiving radiotherapy treatment.

60% of ICDs (3 ICDs; ICD Y2, ICD Y3 and ICD Z2) exhibited their first malfunction at a cumulative ionising radiation dose below 4Gy at 6MeV. 100% of these devices, showed sensing malfunctions as the first malfunction. 40% of ICDs (2 ICDs; ICD X2 and ICD X3) both from manufacturer X, exhibited their first malfunction at a cumulative ionising radiation dose above 45Gy. ICD X3 exhibited shock malfunctions as the first malfunction at 45Gy and ICD X2 exhibited sensing malfunctions as the first malfunction at 60Gy.

At 10MeV, the first ICD malfunctions were observed in ICD Y4, this device exhibited a sensing threshold too low resulting in sensing malfunctions at a cumulative ionising radiation dose of 5Gy. 80% of ICDs (4 ICDs; ICD X5, ICD Y4, ICD Y5 and ICD Z3) exhibited their first malfunction at a cumulative ionising radiation dose below 12.5Gy. ICD X5 and ICD Z3 displayed shock energy too low resulting in shock malfunctions at 10Gy and 8.5Gy respectively. ICD Y5 displayed a battery error resulting in battery malfunctions and communications discrepancies resulting in telemetry malfunctions at a cumulative ionising radiation dose of 12.5Gy. ICD X4 displayed its first malfunction and POF failure as the battery charge time increased resulting in battery failure, at the test to destruction ionising radiation dose of 120Gy,

ICD malfunctions:

- ***1, Pacing pulse malfunctions***

At 6MeV, 20% of ICDs (1 ICD: ICD Y3) exhibited an output error resulting in pacing pulse malfunctions at 0.5Gy as one of the first malfunctions in this particular ICD.

- ***3, Sensing malfunctions***

At 6MeV, 80% of ICDs (4 ICDs: ICD X2, ICD Y2, ICD Y3 and ICD Z2) from all 3 CIED manufacturers (X, Y and Z) exhibited sensing malfunctions as the first malfunction. In 3 ICDs (ICD Y3, ICD Z2 and ICD Y2) these malfunctions occur at a low ionising radiation dose, below 4Gy (ICD Y3 at 0.5Gy, ICD Z2 at 1.5Gy and ICD Y2). Therefore 100% of ICDs from CIED manufacturer Y exhibited sensing malfunctions as the first malfunction at low ionising radiation dose (below 4Gy). Both these devices displayed inhibition during sensing and ICD Y3 (0.5Gy) also displayed over sensing. ICD X2 displayed a sensing threshold too low resulting in sensing malfunctions as the malfunction but at a higher ionising radiation dose of 60Gy.

At 10MeV, 17% of ICDs (1 ICD: ICD Y4) exhibited a sensing threshold too low, resulting in sensing malfunctions as the first malfunction at 5Gy.

- ***4, Telemetry malfunctions***

At 6MeV, 20% of ICDs (1 ICD: ICD Y3) exhibited communication discrepancies resulting in telemetry malfunctions at 0.5Gy as one of the first malfunctions in this particular ICD. At 10MeV, 17% of ICDs (1 ICD: ICD Y5) exhibited communication discrepancies, resulting in telemetry malfunctions as the first malfunction at 12.5Gy.

- ***Battery malfunctions***

At 10MeV, 33% of ICDs (2 ICDs: ICD X4 and ICD Y5) from all CIED manufacturers (X and Y) exhibited battery malfunctions as the first malfunction. ICD Y5 exhibited a battery error at 12.5Gy and ICD X4 reached POF due to battery failure at test to destruction ionising radiation dose of 120Gy.

- ***7, Shock malfunctions***

At 6MeV, 20% of ICDs (1 ICD: ICD X3) exhibited shock energy too low resulting in shock malfunctions at 45Gy. This device tolerated the largest dose of ionising radiation before exhibiting the first device malfunction. At 10MeV, 33% of ICDs (2 ICDs; ICD X5 and ICD Z3) exhibited shock energy too low resulting in shock malfunctions at 8.5G and 10Gy respectively.

Table 6.8: Results – ICD malfunctions observed during exposure to ionising radiation – Classified by type of device malfunction

(Malfunctions are only indicated when seen at each respective energy)

ICD	ICD malfunction	RT Dose (Gy)
3 – Sensing		
6MeV		
ICD X2	Ventricular tachycardia (VT) – Cause inappropriate delivery of shock therapy	70Gy ➔
ICD X3	Inhibition during sensing	46Gy ➔
ICD Y2	Under sensing	5Gy ➔
ICD Z2	Ventricular tachycardia (VT) – Cause inappropriate delivery of shock therapy	1.5Gy ➔
10MeV		
ICD Y4	Inhibition during sensing	5Gy ➔
ICD Y5	Inhibition during sensing	12.5Gy ➔
ICD Z3	Ventricular tachycardia (VT) – Cause inappropriate delivery of shock therapy	9Gy ➔
4 – Telemetry		
10MeV		
ICD X5	Communication discrepancies	20Gy ➔
ICD Y4	Communication discrepancies	6Gy ➔
ICD Y5	Communication discrepancies	14Gy ➔
7 – Shock		
6MeV		
ICD Y2	Shock energy too low	5Gy ➔
8 – Battery		
6MeV		
ICD Y2	Battery warning	40Gy ➔

- ***3, Sensing malfunctions***

At 6MeV, 80% of ICDs (4 ICDs; ICD X2, ICD X3, ICD Y2 and ICD Z2) exhibited sensing malfunctions when exposed to ionising radiation. ICD Y2 was the only device that exhibited under sensing resulting in sensing failure during irradiation and this occurred at 5Gy.

100% of ICDs from CIED manufacturer X exhibited sensing malfunctions during irradiation at a higher ionising radiation dose. ICD X3 exhibited inhibition during sensing starting at 46Gy and ICD X2 exhibited ventricular tachycardia (VT) causing inappropriate delivery of shock therapy starting at 70Gy resulting in sensing malfunctions. In comparison ICD Z2 also exhibited ventricular tachycardia (VT) causing inappropriate delivery of shock therapy but at a much lower cumulative ionising radiation of 1.5Gy.

At 10MeV, 50% of ICDs (3 ICDs; ICD Y4, ICD Y5 and ICD Z3) exhibited sensing malfunctions when exposed to ionising radiation. 100% of the ICDs from manufacturer Y exhibited inhibition during sensing malfunctions during irradiation. ICD Y4 was the first ICD to display this at a cumulative ionising radiation dose starting at 5Gy and ICD Y5 displayed this malfunction starting at 12.5Gy. ICD Z3 exhibited ventricular tachycardia (VT) which can cause inappropriate delivery of shock therapy if the ICD is activated starting at a cumulative ionising radiation dose of 9Gy.

- ***4, Telemetry malfunctions***

At 10MeV, 50% of ICDs (3 ICDs; ICD X5, ICD Y4 and ICD Y5) exhibited telemetry malfunctions when exposed to ionising radiation. 100% of the ICDs from manufacturer Y exhibited communication discrepancies resulting in telemetry malfunctions during irradiation. ICD Y4 was the first ICD to display this at a

cumulative ionising radiation dose starting at 4Gy and ICD Y5 displayed this malfunction starting at 14Gy. ICD X5 from manufacturer X exhibited communication discrepancies resulting in telemetry malfunctions starting at a cumulative ionising radiation dose of 9Gy.

- ***7, Shock malfunctions***

At 6MeV, ICD Y2 had exhibited sensing malfunctions during irradiation at 5Gy; also at this ionising radiation dose the device exhibited a shock energy too low resulting in shock malfunction.

- ***8, Battery malfunctions***

At 6MeV, ICD Y2 exhibited sensing and shock malfunctions during irradiation at 5Gy. At 40Gy this device displayed a battery warning resulting in a battery malfunction.

Table 6.9: Results – Point of device failure (POF) observed in ICDs – Classified by type of device (ICD) malfunction

(Malfunctions are only indicated when seen at each respective energy)

ICD	ICD failure	RT Dose (Gy)
1 – Pacing pulse		
6MeV		
ICD X2	Device failure No output	100Gy
ICD X3	Device failure No output	70Gy
ICD Y3	Device failure No output	1Gy
ICD Z2	Device failure No output	3.5Gy
10MeV		
ICD Y4	Device failure No output	15Gy
ICD Y5	Device failure No output No signal	120Gy
ICD Z3	Device failure No signal	10Gy
3 – Sensing		
10MeV		
ICD X4	Device failure No sensing	120Gy
7 – Shock		
6MeV		
ICD X3	Device failure No shock	70Gy
ICD Y2	Device failure No shock	90Gy
ICD Z2	Device failure No shock	3.5Gy
10MeV		
ICD X5	Device failure No shock	80Gy

Point of failure - Total cumulative ionising radiation dose:

At 6MeV, 100% (5 ICDs) reached POF before the test to destruction ionising radiation dose of 120Gy. 60% of the ICDs (3 ICDs: ICD X2, ICD X3 and ICD Y2) reached a POF in the range of 70-100Gy. 100% of the ICDs from CIED

manufacturer X (ICD X2 and ICD X3) reached POF because of no output resulting in pacing pulse failure. ICD X2 exhibited this at 100Gy and ICD X3 exhibited pacing pulse POF at 70Gy due to both no output and no shock. ICD Y2 exhibited POF at 90Gy due to no shock resulting in pacing pulse failure and no shock resulting sensing failure.

40% of the ICDs (2 ICDs: ICD Y3 and ICD Z2) reached a POF in the range of 1-3.5Gy. ICD Y3 reached POF at 1Gy and exhibited no output resulting in pacing pulse failure. ICD Z2 also displayed no output resulting in pacing pulse failure at POF 3.5Gy. At this ionising radiation dose, ICD Z2 also displayed no shock resulting in shock failure.

ICD Y3 was the first ICD to reach POF at a cumulative ionising radiation dose of 1Gy. Followed by ICD Z2, which reached POF at a cumulative ionising radiation dose of 3.5Gy. Both ICDs from manufacturer X, reached POF at higher cumulative ionising radiation doses of 100Gy and 70Gy respectively.

4 ICDs (ICD X2, ICD X3, ICD Y3 and ICD Z2) failed due to no output resulting in pacing pulse failure. ICD Y3 was the first ICD to reach POF at a cumulative ionising radiation dose of 1Gy. Followed by ICD Z2 which reached POF at a cumulative ionising radiation dose of 3.5Gy. Both ICDs from manufacturer X, reached POF at higher cumulative ionising radiation doses of 100Gy and 70Gy respectively.

3 ICDs (ICD X3: ICD Y3, and ICD Z2) failed due to no shock resulting in shock failure. ICD Z2 exhibited both pacing pulse failure and shock failure at a cumulative ionising radiation dose of 3.5Gy. ICD X3 and ICD Y2 reached POF at higher cumulative ionising radiation doses of 70Gy and 90Gy respectively. ICD Y2 was the only ICD to exhibit a sensing defect resulting in sensing POF at 90Gy.

At 10MeV, 40% (2 ICDs: ICD X4 and ICD Y5) reached POF at test to destruction ionising radiation dose of 120Gy. ICD X4 was unable to sense resulting in pacing pulse failure at 120Gy and ICD Y5 had no output and no signal resulting in sensing failure at 120Gy.

60% (3 ICDs; ICD Y4, ICD X5 and ICD Z3) reached POF in the range of 10-80Gy. ICD Y4 and ICD Z3 were the first devices to exhibited failure, as no output and no signal resulted in pacing pulse failure at a cumulative ionising radiation dose of 15Gy and 10Gy respectively. ICD exhibited no shock resulting in shock failure at a POF of 80Gy.

Table 6.10: Results – POF observed in ICDs – Classified by CIED manufacturer (Malfunctions are only indicated when seen at each respective energy)

6MeV		
ICD	**ICD failure**	**RT Dose (Gy)**
Manufacturer X		
6MeV		
ICD X2	**Pacing pulse** No output	100Gy
ICD X3	**Pacing pulse** No output **Shock** No shock	70Gy 70Gy
10MeV		
ICD X4	**Sensing** No sensing	120Gy
ICD X5	**Shock** No shock	80Gy
Manufacturer Y		
6MeV		
ICD Y2	**Sensing** Sensing defect **Shock** No shock	 90Gy 90Gy
ICDY3	**Pacing pulse** No output	1Gy
10MeV		
ICD Y4	**Pacing pulse** No output	15Gy
ICD Y5	**Pacing pulse** No output No signal	120Gy
Manufacturer Z		
6MeV		
ICD Z2	**Pacing pulse** No output No shock	3.5Gy
10MeV		
ICD Z3	**Pacing pulse** No signal **Shock** No shock	10Gy 10Gy

100% of the ICDs from CIED manufacturer X (ICD X2 and ICD X3) reached POF because of no output resulting in pacing pulse failure at 6MeV. ICD X2 exhibited this at 100Gy and ICD X3 exhibited pacing pulse POF at 70Gy due to both no output and no shock. ICD Y2 exhibited POF at 90Gy due to no shock resulting in pacing pulse failure and no shock resulting sensing failure.

At 6MeV, ICDs from CIED manufacturer Y (ICD Y2 and ICD Y3) reached POF because due to sensing, shock and pacing pulse failure. ICD Y2 exhibited both sensing and shock failure at 90Gy. ICD Y3 exhibited POF at a much lower ionising radiation dose of 1Gy due to no output resulting in pacing pulse failure.100% of the ICDs from CIED manufacturer Z (ICD Z2) reached POF because of no output and no shock resulting in pacing pulse failure at 3.5Gy

From manufacturer X, ICD X4 reached POF because of no sensing at test to destruction ionising radiation dose of 120Gy and ICD X5 reached POF because of no shock resulting in shock failure at 80Gy at 10MeV.

At 6MeV, 100% of ICDs from CIED manufacturer Y (ICD Y4 and ICD Y5) reached POF because due to pacing pulse failure. ICD Y4 exhibited no output at 15Gy, in comparison to ICD Y5 that exhibited POF at a much higher ionising radiation dose of 120Gy due to no output and no signal resulting in pacing pulse failure. ICD Z3 from manufacturer Z failed at a low cumulative ionising radiation dose of 10Gy due to no signal resulting in pacing pulse failure and no shock resulting in shock failure.

6.2.4 Effect of ionising radiation on CIEDs

The CIED malfunctions and failures from this study are discussed under the following headings:

1. Pacing pulse malfunctions and failure
2. Sensing malfunctions and failure
3. Telemetry malfunctions and failure
4. Battery malfunctions and failure
5. Shock malfunctions and failure

Pacing pulse malfunctions and failure:

Over the past three decades, one of the technological advances in CIEDs is software-based developments to minimise pacing energy and threshold (pace the cardiac chamber of interest with the lowest feasible energy) but with good safety margins. The pacing threshold is the lowest electrical pulse, delivered outside the natural refractory periods, that consistently elicits the propagation of a depolarising wave-front. The pulse energy of the CIED has to be programmed and set to high to stimulate the heart. Usually, the pulse energy is programmed at an approximately 50% higher value than the lower threshold value to stimulate the heart of an individual patient. The patient will therefore probably not notice an energy drop of 25%, however, it might indicate that the pacemaker has been damaged during exposure to ionising radiation. A failure of output is suspected if the heart rate is below the programmed lower rate of the CIED. This malfunction would be observed on an ECG trace, as no pacing spike would be present despite an indication to pace. This may be due to battery failure, lead fracture, break in lead insulation, oversensing (inhibiting pacer output), poor lead connection and 'cross-talk' (ie a phenomenon seen when atrial output is sensed by a ventricular lead in a dual-chamber pacer) (Atlee and Bernstein, 2001).

In this study, three pacemakers and seven ICDs exhibited pacing pulse device failure. Two of the three pacemakers exhibited no output and amplitude deviations in the atrial channel resulting in pacing pulse failure both at 120Gy. One pacemaker exhibited no output and amplitude deviations in the atrial channel resulting in pacing pulse failure at 90Gy. Out of the seven ICDs that exhibited pacing pulse failure, five ICDs displayed no output at 1Gy to 100Gy, one ICD displayed no signal at 10Gy and one ICD displayed both no output and no signal at 120Gy all resulting in device failure. Pacing threshold changes may vary over time because of a spontaneous threshold rise after CIED implantation, micro dislodgment of a CIED lead, myocardial

ischemia and exposure to radiation or magnetic waves (Curtis et al, 1991). These variations in pacing threshold may narrow the safety margin of pacing stimulation, therefore raising potential safety issues regarding the functioning of the CIED and the clinical effect on the patient. The CIEDs in this study exhibited pacing pulse failure, as they would not stimulate a patient's heart to elicit propagation of a depolarising wavefront and therefore not pace the cardiac chamber appropriately. As a result patients' lives would be put at risk.

A study by Souliman and Christie in 1994 irradiated three pacemakers with daily fractions of 2.8Gy. They reported that all three pacemakers lost atrial chamber output at 16.8Gy to 28Gy and this was followed by a loss of ventricular chamber pacing at 36.4Gy to 64.4Gy. All devices exhibited some form of permanent pacing pulse malfunctions, for example as the pulse interval of the ventricular channel increased, at the same time atrial channel failure was observed. Transient or permanent loss of the ability to inhibit output and reduction in pulse rate occurred in all the pacemakers before complete loss of output resulting in device failure. The authors reported that pacemakers frequently exhibit the loss of atrial pacing and a reduction in the pulse rate when their batteries are depleted. Study three of this research, also observed this effect as one pacemaker exhibited pacing pulse failure at 90Gy and was unable to sense and the battery elective replacement indicator warning was alerted resulting in sensing and battery failure at the same ionising radiation dose.

The results from Study 3 show that pacing pulse failure in pacemakers occurred at higher ionising radiation doses (90Gy and test to destruction ionising radiation dose of 120Gy) than in the Souliman and Christie (1994) study. However, ICDs were not included in their research. As more patients are presenting for radiotherapy treatment with ICDs, which are more susceptible to the effect of ionising radiation

(Frizzell, 2009) they were included in study three of this research. Results showed that they exhibited pacing pulse failure in the range of 1Gy to 100Gy, with three ICDs displaying pacing pulse device failure at 10Gy and below. Therefore, the results show that they are more sensitive to ionising radiation than pacemakers, exhibiting device failure at 1Gy. However, due to the range of ionising radiation doses that caused ICDs pacing pulse failure it was not possible to identify the exact point at pacing pulse failure occurred.

A study by Hurkmans et al in 2005 irradiated nineteen new pacemakers and eleven new ICDs. Results showed that at 120Gy, three pacemakers exhibited amplitude deviations, two pacemakers displayed amplitude changes at both the atrial and ventricular channel and one pacemaker displayed amplitude deviation at the atrial channel only. A complete loss of signal was observed in seven pacemakers resulting in device failure at 80Gy to 130Gy. One ICD exhibited an amplitude increase during exposure to ionising radiation at 80Gy and this device subsequently displayed device failure. Seven ICDs exhibited complete loss of signal resulting in no output at 0.5Gy to 120Gy.

Results from Study 3 of this research support the findings of Hurkmans et al (2005) in respect to the higher ionising radiation doses that the pacemakers were found to withstand and pacing pulse failure in ICDs was exhibited at both low and high ionising radiation doses. In study three, pacing pulse failure occurred in pacemakers at 90Gy to 120Gy and in ICDs at 1Gy to 100Gy. Hurkmans et al found pacing pulse failure in pacemakers at 80Gy to 130Gy and in ICDs at 0.5Gy to 120Gy. Importantly, the cumulative ionising radiation tolerance dose to ICDs recommended by Frizzell (2009) is 0.5Gy. Therefore, both studies reinforce that ICDs are more susceptible to ionising radiation than pacemakers and that ICDs should be deactivated during radiotherapy treatment to prevent inappropriate anti-tachycardia shock therapy.

Sensing malfunctions and failure:

Sensing, or sensitivity defines the ability of a CIED to correctly detect and sense an intrinsic electrical signal and spontaneous cardiac events. The devices are equipped with entrance filters to allow the specific sensing of P waves in the atrium and R waves in the ventricle, based on the analysis of characteristics of these incoming electrical signals. The programmed sensitivity settings indicate the minimum intra-cardiac signal that will be sensed (seen) by the CIED to initiate the CIED response (inhibited or triggered). The correct programming of the sensing level should allow the detection of all spontaneous cardiac events occurring in the chamber containing the lead and should reject events of other origins, such as crosstalk from another chamber, myopotentials, or radiation and electromagnetic interference.

In this study, five pacemakers and one ICD were unable to sense resulting in sensing device failure. Of these five pacemakers; sensing device failure was observed at 52Gy, 70Gy, 90Gy and two pacemakers at 120Gy and sensing device failure was observed in one ICD at 120Gy. However, during exposure to ionising radiation, CIEDs in this study exhibited sensing malfunctions, such as sensing discrepancies, undersensing, oversensing and sensing threshold changes even when the cause for device failure was not a result of sensing failure. For example one pacemaker exhibited undersensing during irradiation but device failure occurred as a result of pacing pulse failure. In a study by Rodriguez et al(1991) he found that the first failures in pacemakers were sensitivity related. The study by Hurkmans et al, in 2005 reported that two ICDs were unable to sense any signal after an ionising radiation dose of 120Gy resulting in sensing device failure. Also, sensing interference detection was observed for all ICDs during exposure to ionising radiation, which was often caused by inhibition of the atrial channel, ventricular channel, or both. Therefore, all studies show that sensing device failure occurs in both pacemakers and ICDs. In addition, results from this PhD study and the study by

Hurkmans et al, show that sensing malfunctions occur during exposure to ionising radiation, irrespective of the specific cause of the device failure.

This study identified three pacemakers and one ICD exhibiting undersensing malfunctions during exposure to ionising radiation. Undersensing occurs when the CIED fails to detect spontaneous myocardial depolarisation, which results in asynchronous pacing. Atrial or ventricular pacing spikes arise regardless of P waves or QRS complex. The CIEDs incorrectly miss intrinsic depolarisation and pace despite intrinsic activity. On an ECG trace, the appearance of too many pacing spikes would be observed. The main causes of undersensing are CIED programming problems (incorrect sensing threshold) and this may be due to poor lead positioning, lead dislodgment, lead or CIED failure, low battery states, or myocardial infarction (Haghjoo, 2011). A patient experiencing undersensing would clinically present with heart palpitation and on the ECG trace skipped beats would be observed. These both indicate that the CIED is not working appropriately. To treat undersensing in patients, the CIED programmed settings would need to be adjusted to increase the CIEDs sensitivity, so that they could detect intrinsic electrical signals.

Also, in this study one ICD exhibited oversensing malfunctions during exposure to ionising radiation. Oversensing occurs when the CIED senses electrical signals that it should not normally encounter, which results in inappropriate inhibition of the pacing stimulus. In addition to the native cardiac depolarisation signals (P or R waves), any electrical signal with sufficient amplitude and frequent occurrence can be sensed and can inhibit the CIED when pacing is required. The CIED incorrectly senses electrical activity and is inhibited from correctly pacing. Oversensing can be caused by the device programmed incorrectly, battery failure, lead failure or physiological signals like T waves or by myopotential and non-physiological signals like electromagnetic interference (Haghjoo, 2011). In CIEDs exhibiting oversensing,

the device has become too sensitive. Therefore, the device senses the wrong signals and causes it to reset and increase the amount of time before the next discharge. A patient experiencing oversensing would clinically present with fatigue, bradycardia, hypotension and / or syncope and on the ECG trace the paced beats occur later than they should. These both indicate that the CIED is not working appropriately. To treat oversensing in patients, the CIED programmed settings would need to be adjusted to decrease the CIEDs sensitivity, so that the CIED could only detect intrinsic electrical signals that they are required to. The CIED settings should also be programmed to increase the minimum heart rate that the CIED senses.

Sensing threshold is the voltage of the minimum signal that consistently activates the pulse generator function. Sensing thresholds in most pacemakers are programmed to a constant value. Ventricular sensing channels in pacemakers typically operate at sensing thresholds of 2.5 to 3.5mV, which is about ten times less sensitive than those in ICDs (Kaszala and Ellenbogen, 2010). In this study, three ICDs exhibited sensing threshold malfunctions during exposure to ionising radiation at 1.5Gy, 9Gy and 70Gy. Therefore, the first sensing threshold malfunction occurred at a low ionising radiation dose of 1.5Gy but another ICD exhibited the same malfunction but at a higher ionising radiation dose of 70Gy. Also, in three ICDs ventricular tachycardia detection occurred. If these ICDs were implanted in patients and anti-tachycardia therapy was switched on, it would cause inappropriate shock therapy. In the study by Hurkmans et al, it was reported that in several ICDs the lower ventricular sensing threshold was 50–65% lower than programmed, with this usually occurring at the point of device failure. Results also showed that in four ICDs ventricular tachycardia or ventricular fibrillation occurred which would result in the inappropriate delivery of a shock. Both these studies show that ionising radiation changes the CIED sensing thresholds, which would cause CIEDs to either

undersense or oversense. For patients with ICDs, changes in sensing thresholds can lead to the incorrect detection of ventricular tachycardia or ventricular fibrillation, resulting in the delivery of inappropriate shock therapy.

Telemetry malfunctions and failure:

CIEDs are now multi-chamber systems with extensive programmability. In order to monitor and evaluate these CIEDs, manufacturers have incorporated diagnostic tools in the devices; these tools are essential to determine what the CIED is doing and why it is doing it. Complementing the interrogation of programmed data is the provision of measured data, including data obtained from the CIED detailing information on lead function, battery function, demand and asynchronous pacing rates. Telemetry is the ability to non-invasively change the functional and diagnostic parameters of the pacing system by coded commands transmitted to the CIED from the programmer. The CIEDs uses bidirectional telemetry, as the communication is two way, which means the CIED and the programmer can communicate with each other. Information and data can be transferred from the CIED to the programmer for evaluation and any programming changes relayed back to the CIED.

In this PhD study, nine pacemakers exhibited telemetry failure, as seven devices were unable to communicate and two devices had no output resulting in telemetry device failure. Six pacemakers exhibited telemetry failure at of 90Gy to 120Gy and three pacemakers failed at 13.5Gy to 28Gy. Hurkmans et al (2005) study reported that one pacemaker reached its point of failure due to loss of output, at a cumulative ionising radiation dose of 100Gy. At that time, no telemetry problems were observed but one-week later telemetry was lost. One other pacemaker showed problematic telemetry at 10Gy and lost total telemetry capability at 20Gy. The third pacemaker lost telemetry at 130Gy. Both the studies show that telemetry device failure can occur over a range of ionising radiation doses. If the devices are unable to

communicate the patients are being put at risk because there is no feedback mechanism to determine the status of the CIED and to show if it is programmed and working correctly.

Battery malfunctions and failure

The power source for CIEDs is a solid chemical battery; the most commonly used battery chemistry is lithium-iodine (LiI) (Kalahasty and Ellenbogen, 2010). CIEDs use half of their battery power for cardiac stimulation and the other half for monitoring and data logging. CIED batteries should last between five and fifteen years (average six to seven years), depending on how active the CIED is. The primary functions of a CIED battery is to store enough energy to stimulate the heart by generating 5V of power and to provide power to the sensors and timing devices. The battery must retain its power over many years, with a minimum time frame of four years and have a predictable life cycle providing an alert as to when the battery needs replacement. The battery must be able to function when hermetically sealed.

In this study, three pacemakers exhibited battery failure, as all the devices displayed the elective replacement indicator (ERI). Two pacemakers exhibited battery failure at 120Gy and one pacemaker exhibited battery failure at 70Gy. Prior to irradiation, all CIEDs were interrogated; results showed that all three of the pacemaker's batteries were full or nearly full. Therefore, exposure to ionising radiation, caused depletion of the batteries to an extent whereby the elective replacement indicator alert was observed. Battery drainage, could result in the CIED not working appropriately. In a study by Hurkmans et al, five pacemakers showed an elective replacement indicator and the authors recommended that the pacemaker should be replaced within a few weeks, to avoid the loss of therapy due to an empty battery. These studies show that ionising radiation does have an effect on battery life and this occurs at higher ionising radiation doses.

Shock malfunctions and failure:

ICDs provide continuous monitoring and treatment for cardiac arrhythmias. The ICD is a complex device and it is able to detect and distinguish between atrial and ventricular rhythms. The ICD can detect if the heart is beating in a regular rhythm (sinus rhythm), if the heart rhythm is irregular (atrial fibrillation) or if the heart rhythm is too fast (ventricular tachycardia or ventricular fibrillation). The ICD also has a pacemaker function, to regulate the rhythm should the heart beat too slowly.

If the ICD detects an abnormally fast heart rhythm it will monitor for a few seconds to see if it stops. If it does stop, the ICD will record that an episode of non-sustained arrhythmia has occurred. If the arrhythmia does continue, the ICD will initially try to treat by pacing out the arrhythmia by delivering a number of pre-set paced beats (anti-tachycardia pacing). During this therapy, some patients may experience a fluttering sensation in their chest. If anti-tachycardia pacing does not stop the arrhythmia, the ICD will deliver shock therapy and the patient will feel a firm thump in their chest.

In this study four ICDs exhibited shock failure, as all the devices were unable to shock. One ICD exhibited no shock at the low ionising radiation dose of 3.5Gy and three ICDs exhibited no shock at the higher ionising radiation doses of 70Gy, 80Gy and 90Gy. In a study by Hurkmans et al (2012) six ICDs were unable to deliver a shock. Four devices were unable to deliver a shock at very low ionising radiation doses; one ICD exhibited no shock at 0.5Gy, two ICDs at 1.5Gy and one ICD at 2.5Gy. The authors commented that after they failed to deliver a shock, the amplitude dropped and the ICDs showed a complete loss of function. Two ICDs exhibited no shock at the higher ionising radiation doses of 80Gy and 120Gy. The main life-saving therapy delivered by ICDs is shock therapy. Results from these

studies show that at even low ionising radiation doses, ICDs exhibited failure, as they are unable to shock and this could have serious implications for the patient.

6.2.5 Study 3 Conclusion

In this study, pacemakers exhibited a range of temporary and permanent malfunctions starting at cumulative ionising radiation dose of 3Gy. The AAPM report recommended that the maximum dose to a pacemaker should be limited to less than 2Gy (Marbach et al, 1994). A study by Mouton et al supported the AAPM recommendations (Mouton et al, 2002) as results showed that one pacemaker exhibited clinically significant disturbances at a cumulative ionising radiation dose of only 0.15Gy, two pacemakers exhibited defects at 1Gy and nine pacemakers failed at 2Gy (Mouton et al, 2002). Hurkmans et al (2005). reported that the most common damage observed was loss of device output at higher ionising radiation doses (Hurkmans et al, 2005). In contrast, in the Mouton study (2002) only one pacemaker malfunctioned below 50Gy, suggesting modern pacemakers may be relatively radioresisitant. Results from Study 3 of the research project agree with Mouton et al's (2002) findings as three pacemakers failed at or below 52Gy and one pacemaker failed at 120Gy. Therefore, results from this and previous studies conclude that the AAPM recommendations are still valid.

In 2009 Frizzell published a more contemporary review of CIEDs and radiotherapy, concluding that the AAPM recommendations were no longer comprehensive as ICDs were not discussed (Frizzell, 2009). ICDs are more sophisticated and have the ability to automatically defibrillate the heart by monitoring the patient's heart rate and deliver the appropriate electrical therapy. Frizzell (2009) recommended a lower radiotherapy tolerance dose of 0.5Gy for ICDs. This tolerance dose is partly based on work by Hurkmans et al (2012), where it was found that the ionising radiation dose at the first ICD malfunction was as low as 0.5Gy. Results from Study 3 of this

research project also observed the first ICD malfunction at a cumulative ionising radiation dose of 0.5Gy. Therefore, results from this and previous studies conclude that the Frizzell (2009) recommendations are still valid. Using results from this study, chapter seven will make recommendations regarding all aspects of the patient management for patients with CIEDs receiving radiotherapy treatment is discussed leading to the publication of UK guidelines.

6.3 Study 4:

6.3.1 Introduction

CIED leads are insulated flexible wires that conduct electrical signals from the generator to the heart muscle and relay information concerning the heart's intrinsic electrical activity back to the CIED pulse generator. The results from Study 3 showed that ionising radiation might affect the function of the CIED but that CIED leads are considered to be resistant to these effects. No CIED manufactures have issued any ionising radiation tolerance doses to CIED leads.

The aim of this study was to investigate and evaluate the relationship between cumulative ionising radiation dose and / or EMI and the damage sustained to CIED leads. This section will present the findings of Study 4, analyse the study's results and discuss malfunctions and or failure in CIED leads when exposed to ionising radiation. In discussing observed CIED malfunctions and failure, the effect of radiotherapy on the CIED leads and the clinical impact to the patient will be discussed. It concludes by stating the precautions that need to be considered when CIED leads are in the radiotherapy treatment field.

6.3.2 CIED leads

In this study, the effect of ionising radiation and EMI on the CIED lead sheath was investigated following anecdotal evidence and clinical audits of practice. The sheath is made from poly(ether)urethane, which is a synthetic, segmented polymer with very high tensile strength and resistance to mechanical abrasion. Due to its physical properties, it can be used as a thin layer of insulation to cover the CIED lead conductors. Polyurethane has excellent lubricity (the measure of the reduction in friction and or wear by a lubricant) and handling characteristics, with a low frictional coefficient, which can facilitate implantation of two or three lead systems by decreasing the physical interactions between the leads. Pacing lead insulation is a critical and vulnerable component but it can also be the cause of lead failure. For example, polyurethane leads are stiff and not fully biostable and may be subject to in vivo polymer degradation that can cause insulation and late lead failure. All insulating materials fail at some level of applied voltage. This study investigated the dielectric strength of the CIED lead sheaths; that is the voltage a material can withstand before breakdown occurs.

In the study, four different leads from CIED manufacturer X were used. Lead type one were bipolar pacemaker leads and composed of two individually coated conductor wires co-radially wound together to form a single conductor coil. The lead included a silicone rubber or polyurethane outer insulation layer. Pacing and sensing occurs between the distal pole and the ring electrode and fixing to the myocardium is achieved by silicone rubber tines. Lead type two was also bipolar pacemaker leads and consisted of a multi-strand conductor coil-within-a-coil design that provides a conductive pathway and acts as a drive mechanism for extending and retracting the fixation helix. The conductors are each sheathed in a thin-walled tube of silicone rubber insulation. This lead has a proprietary coating that makes the silicone lead surface feel more lubricious. The coating reduces both the static and

dynamic coefficients of friction, making the lead feel like polyurethane. Lead type three was bipolar pacemaker leads and consisted of a coaxial design that includes single-filar inner and outer coils designed for MRI conditional use. The conductors are separated by both a silicone rubber and polytetrafluroethylene (PTFE) lining. Both the inner and outer coil are covered in ethylene tetrafluroethylene (ETFE) for extra insulation protection. The whole lead body is encompassed in a polyurethane outer insulation. The extendable and retractable helix fixation design anchors the distal tip electrode to the endocardial surface with support of trabecular structures. Lead type four, was bipolar ICD leads and consist of two coaxial coils, each of which is made up of several parallel wires. The coils make up the conduction paths to the tip and ring electrodes. They are insulated from each other and from the environment using silicone rubber. Pacing and sensing occurs between the distal pole and the ring electrode.

6.3.3 Results - Effect of ionising radiation on CIED leads

The results from Study 3 showed that ionising radiation affected the function of CIEDs. However, CIED leads are considered to be resistant to these effects. In this study the effect of ionising radiation and EMI on the insulation sheath of the CIED lead was investigated.

Laboratory testing - Insulation sheath of CIED leads

Individual sections of the CIED leads sheath were irradiated using a Varian linear accelerator at doses of 0.5Gy, 1Gy, 2Gy, 5Gy, 10Gy, 60Gy and 120Gy. The basic premise of this experiment was to determine if de-polymerisation occurred in the sheath material layer of the CIED lead as a result of exposure to ionising radiation and / or EMI. Essentially, high-energy photons produced by the linear accelerator

interacted with the polymer material of the CIED lead. This can cause long chain polymer bonds to break resulting in possible embrittlement of the polymer.

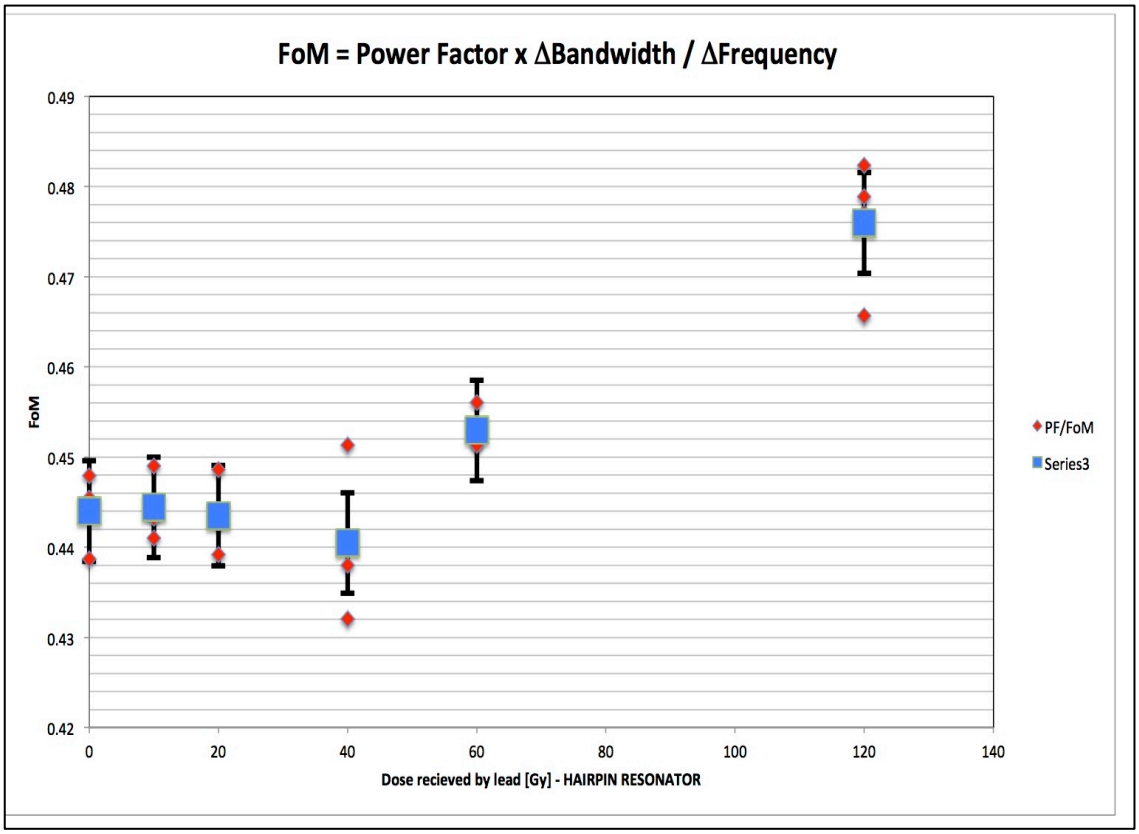
Initial results showed that this technique has the potential to provide the necessary insight into polymer degradation of CIED leads following exposure to ionising radiation and EMI. The graph below shows the change in the so-called figure of merit (FoM) as a function of ionising radiation dose received. The figure of merit is defined as a numerical expression taken as representing the performance or efficiency of a given device, material, or procedure.

The FoM combines all three parameters above in the form:

FoM = Insertion Loss x Change in bandwidth / Change in resonant frequency

This non-optimised experimental configuration highlighted that for ionising radiation doses at 40-120Gy, there is an observable change in FoM as the dose increased (see figure 6.1). Suggesting that, with further experimentation, a reliable means of quantifying CIED lead sheath damage could be feasible.

Figure 6.1: Graph of results to show FoM - ionising radiation dose delivered to insulation sheath of CIED leads)



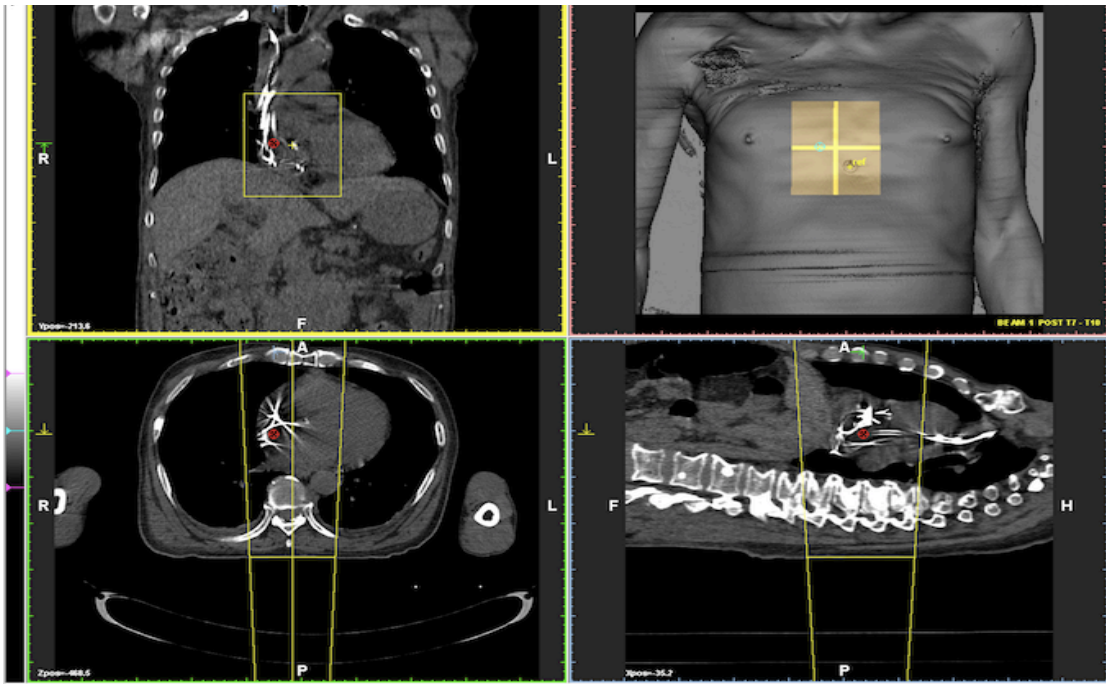
6.3.4 Clinical effect of ionising radiation and EMI on CIED leads

There is little research into the effects of ionising radiation and EMI on CIED leads. However, two reports have been published documenting the effect of ionising radiation on CIED leads. A case study published by John and Kaye in 2004 reported an ICD malfunction after a patient's radiotherapy treatment for left breast cancer. While the ICD had been shielded, the CIED leads received a full dose with partial exposure of the ICD. During the post radiotherapy cardiology follow-up appointment, the patient's CIED battery was found to have depleted. CIED interrogation showed the shock impedance of the ICD had increased, which resulted in shock coil failure, possibly due to structural damage to the CIED leads when exposed to ionising radiation. Therefore, the patient required surgical intervention and implantation of a new CIED and CIED leads. In 2011, Dasgupta et al published a case report,

detailing the radiotherapy treatment to the right cardiac atrium and ventricle of a patient with a pacemaker. The cumulative ionising radiation dose to the CIED leads was 5Gy. They were monitored throughout their radiotherapy treatment and a single episode of ventricular under sensing with pacing stimuli during T-waves was successfully addressed by the reprogramming of the CIED. Therefore, the authors suggested that ionising radiation had an effect on CIED leads.

Clinical observations were made of a patient with a pacemaker receiving radiotherapy treatment in a RCW. This patient exhibited a marked clinical cardiac reaction during their radiotherapy treatment. The patient was receiving thoracic radiotherapy of 20Gy in five fractions. The pacemaker was 6cm away from the radiotherapy treatment site, therefore receiving a negligible dose of ionising radiation. However, the CIED leads were directly in the radiotherapy treatment field. Medical physics calculated that the cumulative ionising radiation dose to the CIED leads was 14Gy. Shortly after radiotherapy treatment commenced the patient exhibited a rapid heart rate, experienced chest pain, felt light headed, dizzy and nauseous and appeared flushed and was sweating. Liaising with the consultant oncologist and consultant cardiologist, the patient was reviewed and the CIED was checked. It was found that the CIED showed no malfunctions or failure and they concluded that the reaction was due to the direct irradiation of the CIED leads. All three cases indicate that ionising radiation and or EMI have an effect on CIED leads as manifested in these patients' clinical reaction or CIED function.

Figure 6.2: CT images of a patient radiotherapy treatment planning scan



However, two reports from Munshi et al (2008) and Kirova et al (2012) documented that they had found no effects on CIED function or adverse effect to the patient when the CIED leads were exposed to ionising radiation and EMI. In 2008, Munshi et al published a case report for a breast cancer patient where the CIED leads were in the radiotherapy treatment field. They documented that there was no malfunction to the patient's CIED but concluded that the dose to the CIED and CIED leads should be kept as low as possible. In 2012, Kirova et al published a case report for a patient receiving radiotherapy to the thoracic spine. The cumulative ionising radiation dose to the CIED leads was 5Gy. They observed no change in CIED function during and after radiotherapy treatment and concluded that all patients with CIEDs should be monitored during their radiotherapy treatment. Both cases state that ionising radiation has no effect on CIED leads or a clinical effect on patients but they also recommend that all patients with CIEDs are monitored during their radiotherapy treatment.

6.3.5 Study 4 Conclusion

There is limited published evidence to inform ionising radiation dose constraints to CIED leads and also no consensus in the results reported from case studies regarding clinical reactions of patients with CIED when the CIED leads were exposed to ionising radiation. Therefore, when treating patients with CIEDs with radiotherapy, every effort should be made to keep the CIED leads out of the radiotherapy treatment field. If this is not possible, then the ionising radiation dose to the CIED leads should be kept as low as possible.

6.4 Study 5

6.4.1 Introduction

The aim of this study was to investigate and evaluate the relationship between EMI and the damage sustained to CIEDs. This section will present the findings of Study 5, analyse the results and discuss the mechanisms that cause malfunctions and or failure in CIEDs when exposed to EMI. In discussing specific CIED malfunctions and failure, the effect of EMI and the clinical impact to the patient will be discussed. The section concludes by recommending the monitoring requirements for all patients with CIEDs presenting for radiotherapy treatment.

6.4.2 Effect of EMI on CIEDs

Table 6.11: Results – Effect of EMI on pacemakers

DEVICE Pacemakers	6MeV		At what point CIED malfunction observed
	Fraction	CIED malfunctions observed	
PM X9	**1 – 3**	**3 – Sensing** Over sensing of EMI by the atrial channel – trigger ventricular pacing near upper tracking rate limit	During EMI exposure
	4	**1 – Pacing pulse** Noise reversion mode triggered	During EMI exposure
	5 – 6	No CIED malfunction observed or recorded	
	7 – 9	**1 – Pacing pulse** Noise reversion mode triggered	During EMI exposure
	10	**1 – Pacing pulse** Noise reversion mode triggered Reset to backup mode	During EMI exposure
PM X10	1 – 7	No CIED malfunction observed or recorded	
	8 – 10	**2 – Pacing frequency** Inappropriate pacing inhibition – Every beam	Beam ON During EMI exposure
10MeV			
PM X11	1 – 10	**2 – Pacing frequency** Inappropriate pacing inhibition – Every beam Pacing error – 'dropped beats'	Beam ON During EMI exposure
PM X12	1 – 9	**1 – Pacing pulse** Noise reversion mode triggered	During EMI exposure
	10	**1 – Pacing pulse** Noise reversion mode triggered Unable to detect cardiac activity = pacing error	During EMI exposure

All CIEDs used in this study were from CIED manufacturer X. At 6MeV and 10MeV, 100% of pacemakers exhibited malfunctions related to EMI exposure. PM X9 exhibited sensing malfunctions during EMI exposure on the first to fourth fraction. The device was over sensing EMI by the atrial channel, which would trigger ventricular pacing near the upper tracking rate limit. Also, on the fourth fraction, during EMI exposure the device triggered noise reversion mode resulting in a pacing pulse malfunction. During the fifth and sixth fraction, no CIED malfunction was observed or recorded. On the seventh, eight and ninth fractions once again during EMI exposure the device triggered noise reversion mode resulting in a pacing pulse malfunction. On the final fraction, at the point of beam ON the device triggered noise reversion mode again then during exposure to EMI, the pacemaker reset to backup mode.

No CIED malfunctions were observed or recorded for PM X10 for the first seven fractions. In fraction eight to ten, at the point of beam ON and during EMI exposure during every beam the pacemaker exhibited inappropriate pacing inhibition resulting in pacing frequency malfunctions.

In PM X11, for all ten fractions at the point of beam ON and during EMI exposure during every beam the pacemaker exhibited inappropriate pacing inhibition and the 'dropped beat' pacing error resulting in pacing frequency malfunctions.

In PM X12, during EMI exposure on the first to ninth fractions the device triggered noise reversion mode resulting in a pacing pulse malfunction. In the final fraction noise reversion mode was triggered but the device was also unable to detect cardiac activity resulting in a pacing error.

Table 6.12: Results – Effect of EMI on ICDs

DEVICE Pacemakers	6MeV		At what point CIED malfunction observed
	Fraction	CIED malfunctions observed	
ICD X7	1 – 9	**2 – Pacing frequency** Pacing error – 'Dropped beats'	Beam ON
	10	**5 – Battery** Decrease in battery capacity	Post beam OFF
ICD X8	1 – 6	**1 – Pacing pulse** Noise reversion mode triggered	During EMI exposure
	7	**3 – Sensing** Ventricular fibrillation (VF) – Cause inappropriate delivery of shock therapy	During EMI exposure
	8 – 10	**1 – Pacing pulse** Noise reversion mode triggered	During EMI exposure
10MeV			
ICD X9	1 – 5	No CIED malfunction observed or recorded-	
	6 – 10	**7 – Shock** Deactivation of shock therapy by reversion to OFF mode	During EMI exposure
ICD X10	1 – 3	No CIED malfunction observed or recorded-	
	4 – 6	**2 – Pacing frequency** Pacing error – Transient inhibition	Beam ON
	7 – 10	**2 – Pacing frequency** Pacing error – 'Dropped beats' Pacing error – Transient inhibition	Beam ON

At 6MeV and 10MeV, 100% of ICDs exhibited malfunctions related to EMI exposure. At 6MeV, during fractions one to eight, ICD X7 exhibited pacing frequency malfunctions at the point of beam ON. The device exhibited the 'dropped beat' pacing errors. For fractions nine and ten, post beam OFF the device showed a decrease in battery capacity resulting in battery malfunctions.

ICD X8 for the first eight fractions noise reversion mode was triggered during EMI exposure resulting in pacing pulse malfunctions. On the seventh fraction, during EMI exposure the device was over sensing EMI by the atrial channel, which would trigger ventricular pacing near the upper tracking rate limit. For fraction eight to ten during EMI exposure the ICD again triggered noise reversion mode resulting in pacing pulse malfunctions.

At 10MeV, ICD X9 exhibited no CIED malfunctions for the first five fractions. During EMI exposure on fraction six to ten, the device showed that the ICD shock therapy had been deactivated by reversion to OFF mode. ICD X10 exhibited no CIED malfunctions for the first three fractions. On the first to sixth fraction at the point of beam ON, the device exhibited transient inhibition resulting in a pacing error causing pacing frequency malfunctions. On the remaining three fractions at the point of beam ON, the device exhibited both transient inhibition and dropped beats resulting in pacing errors causing pacing frequency malfunctions.

Table 6.13: Results – Effect of EMI on rate response activated CIEDs

Rate response activated CIEDS	6MeV		At what point CIED malfunction observed
	Fraction	CIED malfunctions observed	
PM X3RA*1	1 – 10	No CIED malfunction observed or recorded	
PM X3RMV*2	1 – 10	**2 – Pacing frequency** Accelerated pacing – to maximum sensor driven rate	During EMI exposure
10MeV			
PM X2RA*1	1 – 10	No CIED malfunction observed or recorded	
PM X2RMV*2	1 – 10	**2 – Pacing frequency** Accelerated pacing – to maximum sensor driven rate	During EMI exposure

At 6MeV and 10MeV, both rate response activated devices that utilise accelerometer sensors (PM X3 RA*1 and PM X2 RA*1) exhibited no CIED malfunctions when exposed to EMI. In comparison both rate response activated devices that utilise minute ventilation sensors (PM X3 RMV*2 and PM X2 RMV*2) exhibited pacing frequency malfunctions during EMI exposure. The devices exhibited accelerated pacing up to maximum sensor driven rate.

6.4.3 Electro-magnetic interference (EMI)

In the electro-magnetic field measurement section of this study, the aim was to determine the levels of EMI emitted from the linear accelerator during ionising radiation exposure. The background electro-magnetic fields were captured using a EMC antenna connected to the field fox in 'spectrum analyser' mode. This provided a trace of power versus frequency. As radiotherapy treatment rooms are extremely well shielded from external sources of electro-magnetic radiation, the system was sensitive enough to detect external sources, for example radio broadcasts (BBC in 97-99MHz) and radiofrequency (RF) signals related to the hospital pager network. However, despite this level of sensitivity, no discernable power was observed that could be correlated with the linear accelerator system. This experiment was repeated and on all occasions, the antenna and field fox did not identify levels of EMI emitted from the linear accelerator system. This could simply be due to the transient nature of EMI or the resultant power is too great to be detected by the antenna. Furthermore, the sweep parameters and bandwidth used with the field fox could be too fast or too narrow respectively. Further investigation is required to determine the factors effecting detection of EMI in the radiotherapy treatment room.

6.4.4 Device responses to EMI

The most frequent responses to EMI are inappropriate inhibition or triggering of pacemaker stimuli, reversion to asynchronous pacing, and spurious ICD tachyarrhythmia detection. Reprogramming of operating parameters and permanent damage to the device circuitry or the electrode to tissue interface are much less frequent (Pinski and Trohman, 2002).

Pacing Inhibition

In this study, two pacemakers and two ICDs exhibited device malfunctions that caused pacing inhibition. One pacemaker exhibited inappropriate pacing inhibition on every radiotherapy treatment delivery beam for the last two fractions of exposure to EMI and the other pacemaker exhibited inappropriate pacing inhibition on all ten fractions of EMI exposure. This occurred on every beam and also, throughout EMI exposure pacing errors occurred in the form of dropped beats. In both pacemakers, pacing inhibition was observed when the radiotherapy treatment machine / radiation beam was switched ON and also during EMI exposure.

For nine fractions of EMI exposure, one ICD exhibited pacing inhibition and dropped beats were observed when the radiotherapy treatment machine / radiation beam was switched ON. Subsequently, on the final fraction post EMI exposure the device displayed a decrease in battery capacity. The other ICD exhibited no device malfunction for the first three fractions of EMI exposure but then on fractions four to six, pacing errors were observed and on the remaining three fractions dropped beats and transient inhibition was observed when the radiotherapy treatment machine / radiation beam was switched ON.

Triggering of rapid or premature pacing

One pacemaker and one ICD exhibited sensing malfunctions causing the devices to pace rapidly. For the first four fractions that the pacemaker was exposed to EMI, during exposure oversensing of EMI by the atrial channel occurred which subsequently triggered ventricular pacing near the upper tracking rate limit. In the ICD on the seventh fraction of EMI exposure, during exposure the device sensed rapid pacing resulting in ventricular fibrillation. If the device were implanted in a patient, this would cause the ICD to inappropriately deliver shock therapy.

Noise reversion mode

Two pacemakers and two ICDs exhibited pacing pulse malfunctions resulting in the devices triggering noise reversion mode. One pacemaker had displayed oversensing for the first three fractions of EMI exposure and noise reversion mode was triggered on the fourth fraction during EMI exposure. Then on the final (tenth) fraction during EMI exposure the device reset to back-up mode. The other pacemaker triggered noise reversion mode on the first fraction of EMI exposure and during EMI exposure on the final fraction the pacemaker was unable to detect cardiac activity resulting in device failure. One ICD triggered noise reversion mode during EMI exposure for the first six fractions of EMI exposure, on the seventh fraction ventricular fibrillation was sensed and during EMI exposure on the remaining fraction noise reversion mode was triggered again. The other ICD exhibited noise reversion mode during EMI exposure on the sixth to tenth fraction of exposure and this caused the deactivation of ICD shock therapy by the reversion switching shock to OFF mode.

Hudson et al (2010) used the study by Souliman et al in 1994 to report that EMI had no impact on pacemaker malfunction. A further study by Hurkmans et al (2012) stated that EMI effects are mainly temporary or reversible and they concluded that EMI did not seem to be of clinical relevance. In 2015, Zaremba et al, stated that the effects of EMI are usually transient and EMI typically does not pose any threat to the function of CIEDs, as in his study no events of symptomatic inhibition or rapid pacing was observed during radiotherapy treatment. However, in this PhD study pacing inhibition, triggering of rapid pacing and activation of noise reversion mode was observed in a number of pacemakers and ICDs.

6.4.5 Rate response activated CIEDs

In this study both rate response activated devices that utilised minute ventilation sensors exhibited pacing frequency malfunctions during EMI exposure. The devices exhibited accelerated pacing up to the maximum sensor driven rate. The results from CIED exposure to EMI showed that both CIEDs reacted as outlined in the Boston Scientific caution.

The results from audit two (in study two), showed that CIED mediated tachycardia, was observed in all patients with rate response activated minute ventilation CIEDs undergoing radiotherapy treatment at a Welsh radiotherapy department. CIED mediated tachycardia occurred when the patient's baseline heart rate increased to over 100 beats per minute during the delivery of the radiotherapy treatment. Once again, the results from this audit support the caution from Boston Scientific. However, they recommend that the CIED MeV sensor should be deactivated when exposed to equipment that can cause an effect. This audit showed the clinical reactions that all patients exhibited. In one case the patient exhibited a marked cardiac physiological reaction during radiotherapy treatment as they felt "like they were having a heart attack on the bed". In liaising with the patient's cardiology department, the CIED MeV sensor was deactivated. However the patient could not tolerate the cardiac clinical consequences of this and the MeV sensor had to be reactivated. Radiotherapy treatment continued but treatment delivery time was increased. The radiation beam was switched ON and the patients heart rate increased to the upper tracking limit, at that point the radiation beam was switched OFF. This allowed that patient's heart rate to return to normal. This process was repeated until the prescribed ionising radiation treatment dose was administered.

6.4.6 Study 5 Conclusion

CIEDs (pacemakers, ICDs and rate response activated devices) exhibited a range of effects when exposed to EMI produced by the linear accelerator. When investigating these effects, the devices were not in, or in close proximity to, the radiotherapy treatment beam, therefore they received a negligible dose of ionising radiation. These reactions were a direct consequence of exposure to EMI only.

Results from Study 1, showed that a number of radiotherapy departments do not monitor CIED patients if the patient's CIED is not receiving an ionising dose of radiation. However, results from this study show that EMI is produced during irradiation and is present in the radiotherapy treatment room. Thus EMI can have an effect on CIEDs. Therefore, it is recommended that all patients with a CIED and receiving radiotherapy treatment should be monitored during their treatment.

Chapter Seven

Research outcomes

7.1 Introduction

Chapter five presented the data obtained from the UK Survey of radiotherapy practice in patients with CIEDs receiving radiotherapy treatment and the result of audits of clinical practice. Chapter six presented the scientific studies investigating the effect of ionising radiation and EMI on the CIEDs and CIED leads. Detailed consideration was also given to looking at possible justification and explanation for the findings obtained and relating these to previous studies. Results from study one showed that most UK radiotherapy departments' CIED policies do not reflect current best evidence. There is also a substantial difference in CIED policies regarding the management and monitoring of patients with a CIED receiving radiotherapy treatment**.** In addition, the majority of policies do not adhere to current established ionising radiation tolerance doses for CIEDs and it concluded that as a consequence, it is very likely that patients are being put at significant risk of harm (Lester et al, 2014).

The results from studies three, four and five show that CIEDs and CIED leads are sensitive to the effects of ionising radiation and / or EMI. Therefore, these results have provided a basis for the recommendations for the safe management of patients with a CIED receiving radiotherapy treatment. This chapter outlines how these recommendations were taken forward as supporting evidence (study six) to a national panel set up between the three professional bodies responsible for radiotherapy practice within the UK (Society and College of Radiographers, Royal College of Radiologists and Institute of Physics and Engineering in Medicine). This panel, of which the researcher was co-chair, subsequently published up to date,

evidence based clinical guidelines for the use of radiotherapy in patients with inserted cardiac devices (Sor.org, 2015) (see appendix H and I).

7.2 Summary of recommendations

- CIEDs should not be placed directly in the radiotherapy treatment beam
- The photon beam energy should be <10MeV
- The cumulative ionising radiation dose received by a pacemaker should not exceed 2Gy
- The cumulative ionising radiation dose received by an ICD should not exceed 0.5Gy
- The cumulative ionising radiation dose received by CIED leads should be kept as low as possible
- Patients with rate-response adaptive CIEDs should be reviewed in conjunction with the Cardiology Department and consideration given to temporary deactivation of the sensor whilst receiving radiotherapy treatment
- The dose contribution from on-treatment verification imaging should be taken into account when calculating cumulative radiotherapy dose to the CIED
- The patient's cardiologist should be informed in advance of any planned radiotherapy treatment for advice on monitoring during radiotherapy and subsequent follow-up
- Patients with CIEDs should be fully informed of the potential short and long-term risks of radiotherapy treatment. This should be included in patient information available from the cardiology department in addition to the radiotherapy patient information
- All patients with a CIED should be monitored during their radiotherapy treatment

- Appropriately trained staff should be involved in CIED monitoring during radiotherapy treatment

7.3 Before radiotherapy

All patients should be screened for the presence of a CIED as part of their radiotherapy planning process. When identified, CIED information should be annotated as stated on the patients' CIED identification card. Staff should be aware that some cardiologists place the CIED on the patients' right side if they are left-handed. Anecdotal evidence from earlier in the PhD showed that in some cases, a CIED is not discovered until a patient attends for radiotherapy treatment (Lester et al, 2014). This results in treatment being delayed or proceeding without appropriate safety measures in place. Planned radiotherapy treatment details should be recorded as per standard practice. The cardiology department should be informed as soon as possible to facilitate patient review before radiotherapy treatment to establish CIED functionality and to detect any possible change in pacing-dependency of the patient. If an examination of technical CIED function has not been conducted within the previous three months, it is recommended that it should be carried out prior to the patient commencing radiotherapy treatment. The cardiologist should also recommend appropriate CIED monitoring during and after radiotherapy treatment.

7.4 Radiotherapy planning

If the CIED is near or in the radiotherapy treatment field or volume, it should be included in the planning CT scan. This allows accurate estimation of the cumulative ionising radiation dose received by the CIED. The CIED should not be in the planning target volume (PTV) in order to minimise radiation dose to the device. Radiotherapy beam energy no greater than 10MeV should be used to avoid neutron contamination (Hurkmans et al, 2012; Gauter-Fleckenstein et al, 2015 and Gelblum

et al, 2009). The medical physics/radiotherapy planning team should be informed of the presence of a CIED and every effort should be made in the planning process to limit the cumulative ionising radiation dose to the CIED.

7.5 Ionising radiation tolerance doses to CIEDs and CIED leads

It is not possible to predict the exact behaviour of any given CIED when it is in, or in close proximity to, the radiotherapy treatment field (Gauter-Fleckenstein et al, 2015). Results from this research show that the risk of CIED malfunction increases as cumulative ionising radiation dose to the CIED increases and that EMI can cause device malfunctions, even when the CIED is receiving a negligible dose of radiation. In addition, the risk to the patient is greater if the patient is pacing-dependent, including patients whose pacemaker is pacing all the time (and who are at risk of asystole if the pacemaker malfunctions). Patients with a resynchronising pacemaker may be at risk of increased heart failure symptoms in an event of device malfunction.

Pacemakers:

In this research, pacemakers exhibited a range of temporary and permanent malfunctions starting at a cumulative ionising radiation dose of 3Gy. The AAPM report recommended that the maximum dose to a pacemaker should be limited to less than 2Gy (Marbach et al, 1994). Mouton et al supported the AAPM recommendations (Mouton et al, 2002) where their results showed that pacemakers exhibited defects at 1Gy and subsequently failed at 2Gy (Mouton et al, 2002). Therefore, results from this work and previous studies conclude that the AAPM recommendations are still valid.

ICDs:

Frizzell (2009) recommended a lower radiotherapy tolerance dose of 0.5Gy for ICDs. This tolerance dose is partly based on work by Hurkmans et al (2012), where it was

found that the ionising radiation dose at the first ICD malfunction was as low as 0.5Gy. Results from Study 3 of this research project also observed the first ICD malfunction at a cumulative ionising radiation dose of 0.5Gy. Therefore, results from this research and previous studies conclude that the Frizzell (2009) recommendations are still valid.

CIED leads:

It is recommended that every effort should be made to keep the CIED leads out of the radiotherapy treatment field. If this is not possible, then the ionising radiation dose to the CIED leads should be kept as low as possible. There is no definitive ionising radiation tolerance dose to the CIED leads with current knowledge and future work should be carried out to determine if there is any guidance limit.

7.6 Electromagnetic interference

Results from this research show that the EMI emitted from the LINAC when switched ON, can affect CIEDs. There is no clear, identifiable point at which EMI was observed to affect CIEDs. This research has also shown that rate response activated CIEDs are more susceptible to EMI and could lead to the patient exhibiting symptoms of CIED induced tachycardia during the radiotherapy treatment. Therefore, it is recommended that the cardiology department should review patients with rate response activated CIEDs before a planned course of radiotherapy treatment begins and consideration is given to deactivating the rate response sensor.

7.7 Risk group

In 2015, Gauter-Fleckenstein et al. proposed a risk categorisation that incorporates the CIED risk group based on their pacing dependency and estimated cumulative ionising radiation dose to the CIED (Gauter-Fleckenstein et al, 2015).

Table 7.1 Gauter-Fleckenstein et al (2015) risk catergorisation group

	Risk categorisation determined by dependence and cumulative radiotherapy dose to pacemaker		
	<2Gy	**2 – 10Gy**	**>10Gy**
Pacing independent	Low risk	Medium risk	High risk
Pacing dependent	Medium risk	High risk	High risk

Table 7.2 Gauter-Fleckenstein et al (2015) risk catergorisation group definition

Risk Group	
Low risk patients	Pacemaker independent, and the device is anticipated to receive a cumulative radiotherapy dose of less than 2Gy
Medium risk patients	Pacemaker dependent, and the device is anticipated to receive a cumulative radiotherapy dose of less than 2Gy
	Pacemaker independent and the device is anticipated to receive a cumulative radiotherapy dose of between 2Gy and 10Gy
High risk patients	Pacemaker dependent, and the device is anticipated to receive a cumulative radiotherapy dose of between 2Gy and 10Gy
	All patients (pacemaker dependent and independent) and the device is anticipated to receive a cumulative radiotherapy dose of more than 10Gy
	Patients with an ICD in situ should be regarded as high risk. The estimated cumulative radiotherapy dose to the ICD should not exceed 0.5Gy

EMI can affect CIEDs, at any point during the patient's radiotherapy treatment regardless of whether the device is in or in close proximity to the radiotherapy treatment field. Therefore, there is no distinct risk classification and all patients should be regarded as high risk and monitored accordingly (see below).

7.8 Consent

Patients consenting for any type of treatment need to be informed of potentially serious side effects related to that treatment. During the consent process the clinical oncologist (or consenting healthcare practitioner) should discuss the potential

damage to the CIED and the potential complications during and after radiotherapy treatment. Patients should be told they will be subject to close monitoring during radiotherapy treatment and further follow-up on completion of their treatment.

7.9 During radiotherapy

- All patients with CIEDs should be monitored with a continuous ECG strip during their radiotherapy treatments. This strip should then be reviewed for any evidence of pacing disruption when radiotherapy treatment is being administered. Particular attention should be given to any pacing discrepancies when the ionising radiation beam is switched ON and OFF

- All patients should be observed during radiotherapy treatment by audio-visual monitoring. Monitoring staff should document any changes in the patient's physical status, and any changes in the ECG trace should be documented and reviewed after every radiotherapy treatment

- The minimum level of training received by monitoring staff should include Immediate Life Support (ILS) and appropriate resuscitation equipment should be available at all times. If therapeutic radiographers are monitoring patients, they should receive specific training on the management and monitoring of these patients. If at any point CIED malfunction is suspected or detected, the clinical oncologist and cardiologist should be immediately informed

- Patients who have an ICD will require their device to be deactivated each day of their radiotherapy treatment, by placing a magnet over the device to prevent inappropriate therapy or shock delivery as a result of accidental sensing of ionising radiation interference. When deactivating ICDs, there

should be the ability to externally pace the patient if appropriate. Defibrillation devices available should be able to deliver external pacing and staff with Advanced Life Support (ALS) training or an ability to deliver external pacing should be available.

Table 7.3 Roles and responsibilities of staff involved in the management of CIED patients receiving radiotherapy

Clinical oncologist
Identify patient's CIED status and highlight on radiotherapy referral form
Contact patient's cardiology department before commencing their radiotherapy treatment
Request cardiology assessment / CIED device check
Provide medical physics with information to calculate cumulative radiotherapy dose to CIED
Check the dose to the pacemaker does not exceed 2Gy
Check the dose to the ICD does not exceed 0.5Gy
Consent – patient aware of potential adverse effects of radiotherapy on CIED
Consent – patient aware that ICD will be switched off during radiotherapy
Planning radiographers
Annotate patient's CIED status
CIED included in CT planning scan if in/close to the radiotherapy treatment field
Medical physics informed of patient's CIED status
No direct placement of CIED in radiotherapy beam
Limitation of radiotherapy beam energy to 10Mv
Contact consultant clinical oncologist if the CIED is within the radiotherapy treatment field or the estimated cumulative dose is too high
Appropriately trained radiographers
Assess patient prior to commencing their radiotherapy treatment
Highlight patient's monitoring requirements
Monitor the patient during their radiotherapy treatment
If the patient has an ICD, deactivate the device during each fraction of radiotherapy treatment
Arrange follow-up appointment with the patient's cardiology department
Treatment radiographers
Do not commence patient's radiotherapy treatment without ensuring correct procedure has been followed
Do not commence patient's radiotherapy treatment without the presence of the appropriately trained staff to monitor the patient
Read and be conversant in CIED department policy
Medical physics
Calculate estimated cumulative radiotherapy dose to the CIED and leads prior to the patient commencing radiotherapy treatment. Previous radiotherapy courses received must be taken into consideration

Table 7.4 Summary of management of CIED patients receiving radiotherapy

<table>
<tr><th colspan="2">Before radiotherapy</th></tr>
<tr><td colspan="2">Consultant clinical oncologist highlights CIED status</td></tr>
<tr><td colspan="2">CIED information annotated as stated on the patient device identification card:
• Type of device: eg bradycardia pacemaker, resynchronising pacemaker, ICD, or combined pacemaker/ICD, resynchronising pacemaker/ICD
• Manufacturer
• Make
• Model
• Date of implantation
• Implantation site
• Patient dependence on CIED</td></tr>
<tr><td colspan="2">Radiotherapy treatment details recorded:
• Radiotherapy treatment site
• Radiotherapy prescription
• Radiotherapy treatment technique</td></tr>
<tr><td colspan="2">Clinical oncologist should liaise with patient's cardiology department regarding:
• Monitoring requirements
• Requirement for device reprogramming or deactivation
• Follow-up and review appointments</td></tr>
<tr><td colspan="2">CIED to be included in CT planning scan if close to anticipated radiotherapy treatment field</td></tr>
<tr><td colspan="2">Medical physics calculate estimated cumulative radiotherapy dose to the CIED</td></tr>
<tr><td colspan="2">Patients allocated a risk categorisation</td></tr>
<tr><td colspan="2">Patients with CIEDs should be fully informed on the potential short and long term risks of radiotherapy and consent appropriately</td></tr>
<tr><th colspan="2">During radiotherapy</th></tr>
<tr><td rowspan="3">High risk patients (all CIEDs)</td><td>Potential CIED relocation</td></tr>
<tr><td>Audio-visual and ECG monitoring by appropriately trained staff for every fraction of radiotherapy treatment</td></tr>
<tr><td>Weekly CIED check by patient's cardiology department</td></tr>
<tr><td rowspan="4">ICD patients</td><td>Day one of radiotherapy – 12 lead ECG should be performed by an appropriately trained staff member as a baseline</td></tr>
<tr><td>Appropriately trained staff member must deactivate the ICD during radiotherapy treatment by placing the specialist magnet over the ICD</td></tr>
<tr><td>Audio-visual and ECG monitoring by appropriately trained staff for every fraction of radiotherapy treatment</td></tr>
<tr><td>Weekly ICD check by patient's cardiology department</td></tr>
<tr><th colspan="2">After radiotherapy</th></tr>
<tr><td colspan="2">CIED device check up, two weeks after radiotherapy treatment by cardiology department</td></tr>
<tr><td colspan="2">Cardiology follow-up one, three and six months after radiotherapy treatment or as advised by cardiology department</td></tr>
</table>

7.10 On-treatment verification imaging

For all CIEDs, the potential ionising radiation dose received from on-treatment verification imaging should also be taken into account. This is especially important with ICDs, which have a much lower recommended maximum cumulative radiotherapy dose of 0.5Gy.

There are no published guidelines that make recommendations on the potential contribution of imaging techniques to the cumulative ionising radiation dose to the CIED. Murphy et al (2004) stated that the dose from a kilovoltage cone beam CT scan is likely to be in the region of 10-80mGy. In 2008, Kan et al (2008) reported mean skin doses of 6.4cGy per kilovoltage cone beam CT chest scan. Even using the lower limit of 10mGy from Murphy et al, it is possible that daily cone beam CT in a twenty fraction radical lung treatment may contribute as much as 0.2Gy. Using the Kan et al skin dose estimates, it is possible the CIED may receive significantly more than 0.2Gy. An estimation of the dose contribution from the image verification method used should be made, and this should be taken into consideration when allocating CIED patients to a risk catergorisation group.

7.11 After radiotherapy

The importance of both short and long term follow-up monitoring for patients who have a CIED and have received radiotherapy was highlighted in a paper by Last (Last, 1998). Patients should have their CIED checked within two weeks of completion of their radiotherapy treatment and then one, three and six months after radiotherapy treatment. Devices exhibiting signs of malfunction should be followed-up with increased frequency. This will allow discrimination to be made between a temporary CIED device malfunction that may occur owing to a build-up of charge within the semiconductor, and more permanent circuitry damage (results from study three). Should any additional changes be observed during the follow-up period then immediate device revision is likely to be necessary.

7.12 Chapter conclusion

The overall aim of study six of this research was to provide evidence to support the publication of guidelines for the management of patients with CIEDs receiving

radiotherapy treatment. This chapter outlined the process by which the national guidelines were produced and discussed how the results of this research together with previous studies and literature led to the development of the first UK guidelines in the field.

Chapter Eight

Final remarks

8.1 Introduction

The purpose of this final chapter is to summarise the key findings of the research, relate these findings to the implications for theory and practice and finally offer recommendations for future work.

With an ageing population, and an increase in the incidence of both cardiovascular morbidity and cancer, the number of patients with CIEDs presenting for radiotherapy treatment will likely increase (Kalache and Keller, 2002; Brooks et al, 2005 and Boon et al, 2006). Although most medical treatments pose little danger to the functioning of CIEDs, radiotherapy has the potential to alter CIED function. CIEDs may be affected in two ways: direct damage via ionising radiation and electromagnetic interference (EMI), both of which may cause temporary or permanent CIED malfunction (Last, 1998), with consequences for the patient that range from mild inconvenience e.g. needing to be disconnected from their cardiac monitor during radiotherapy, through to possible severe effects causing catastrophic failure of the device, which could lead to implications for their heart condition.

The focus of this research project was to investigate the effects of radiotherapy treatment on cancer patients with CIEDs. This research identified how CIEDs are adversely affected by ionising radiation and / or EMI and how these effects can be minimised. It also looked to provide safe radiotherapy tolerance doses to CIEDs and provide data to support the issuing of national guidelines for the safe management of patients with CIEDs undergoing radiotherapy treatment. This study is important

because previous data in this field originated from small-scale patient studies or in-vitro experiments. Carrying out both clinical audits and laboratory based testing, this research provides new data regarding the effect of ionising radiation and / or EMI on CIEDs and also importantly upon the CIED leads, an area not previously studied.

8.2 Implications for theory and practice

i. One of the initial aims of the PhD research project was to audit and establish current UK practice regarding the management of patients with CIEDs undergoing radiotherapy and to compare this practice to current 'gold standard' evidence-based guidelines. Results from this study showed that 30% of radiotherapy centres did not respond to the audit so it is not appropriate to draw definitive conclusions on widescale UK practice, but important themes emerged nevertheless. It is clear that policies differ between radiotherapy centres and the implementation of these policies is variable. In addition, a substantial proportion of policies do not adhere to established ionising radiation tolerance doses for CIEDs. Therefore, it can be concluded that as a consequence, it is very likely that patients are being put at significant risk of harm.

ii. In order to determine the effects of ionising radiation and EMI on patients with CIEDs receiving radiotherapy treatment at a RCW, two clinical audits were conducted. The aim of the first audit was to assess device malfunction in patients with a CIED that have been exposed to ionising radiation and EMI as part of their radiotherapy treatment. From this audit, twenty-two patients with a CIED presented for radiotherapy treatment and two of the twenty-two patients required a revision to the programming of their CIED. The results from the second clinical audit showed that an increasing number of patients with rate response activated CIEDs had presented for radiotherapy treatment and a

large number of these patients exhibited a physiological response due to CIED mediated tachycardia during their treatment. The results of these audits identified that patients with CIEDs exhibited clinical reactions when receiving radiotherapy treatment. These clinical reactions could be a consequence of CIED malfunction or failure due to exposure to ionising radiation and EMI. Therefore, these audits reinforced the need for further research in this area.

iii. The empirical scientific arm of this research project focused on the effect of ionising radiation and EMI on CIEDs and CIED leads. Results showed that CIEDs exhibited a range of temporary and permanent malfunctions. Pacemakers exhibited a range of malfunctions starting at a cumulative ionising radiation dose of 3Gy. The 1994 AAPM report (which was utilised as the basis for previous guidelines) recommended that the maximum dose to a pacemaker should be limited to less than 2Gy (Marbach et al, 1994). Results from this study agreed with the radiotherapy dose to pacemakers of 2Gy and concluded that the AAPM recommendations are still valid. Results also showed that ICDs exhibited device malfunctions starting at a cumulative ionising radiation dose of 0.5Gy. In 2009, Frizzell (2009) published a review of CIEDs and radiotherapy and concluded that the AAPM recommendations were no longer comprehensive as ICDs were not discussed and recommended a lower radiotherapy tolerance dose of 0.5Gy to ICDs. Results from this PhD study also observed that the first ICD malfunction occurred at a cumulative ionising radiation dose of 0.5Gy, thereby concluding that the Frizzell recommendations are also still valid.

iv. There is limited published evidence to inform ionising radiation dose level constraints to CIED leads and also no consensus in the results reported from

other case studies regarding the clinical reactions of patients with CIED when the CIED leads were themselves exposed to ionising radiation. Results from this research indicated that when treating patients who have a CIED with radiotherapy, every effort should be made to keep the CIED leads out of the radiotherapy treatment field. If this is not possible, then the ionising radiation dose to the CIED leads should be kept as low as possible.

v. All CIEDs (pacemakers, ICDs and rate response activated devices) exhibited an effect when exposed to EMI produced by the linear accelerator. When investigating these effects, the devices were not in, or in close proximity to, the radiotherapy treatment beam, thereby receiving a negligible dose of ionising radiation. These CIED malfunctions or failures were thus deemed to be a direct consequence of exposure to EMI only. It is therefore recommended that all patients with a CIED who are receiving radiotherapy treatment should be monitored during their treatment as a result of the presence of EMI in the radiotherapy treatment room having an effect on the CIED.

vi. The over-arching aim of this research project was to publish up-to-date evidence based guidelines for the management of cancer patients with CIEDs receiving radiotherapy treatment. Results from study one showed that CIED policies differ between radiotherapy centres in the UK and a significant number of policies do not adhere to current established tolerance doses for CIEDs. In the departments where there is a CIED policy, the majority do not reflect best evidence (Lester et al, 2014). There is limited published research on the effect of radiotherapy on CIEDs, but the results from studies three to five of this research show that radiotherapy, even at low doses, can cause device malfunctions and / or failure with potentially life-threatening consequences. Based on these results and given the risk to patients, study six stated that all

radiotherapy centres should have policies in place to support the safe delivery of radiotherapy treatment to patients with CIEDs. Publication of these guidelines will have a direct impact on UK radiotherapy departments treatment policies and protocols and subsequently patient management and care (Sor.org, 2015).

8.3 Final words

8.3.1 Limitations of the study

If this research were to be repeated, different makes and models of CIEDs and CIED leads from all CIED manufacturers should be used. This would allow for a comprehensive understanding of how ionising radiation and / or EMI affect all CIEDs and CIED leads implanted in patients.

This research showed that EMI had an effect on the function of CIEDs, in particular rate response-activated devices. However, the level of EMI emitted from the linear accelerator during irradiation was unable to be identified using the Keysight Field Fox spectrum analyser. This could be due to the transient nature of EMI or the resultant power frequency being outside the range of the antenna used. Furthermore, the sweep parameters and bandwidth used with the Field Fox could be too fast or too narrow respectively. Therefore, further research is needed to establish equipment design and test protocol.

When investigating the effect of ionising radiation and / or EMI on CIED leads, a novel microwave experiment was used to provide measurements of the electrical conductivity of the CIED lead sheath polymer at microwave frequencies. Initial results showed that this technique has the potential to provide the necessary insight

into polymer degradation of CIED leads following exposure to ionising radiation and EMI.

8.3.2. Recommendations for future work

From this research the following recommendations for future work have emerged:

- This research was conducted on one manufacturer's radiotherapy treatment linac (Varian). As per research testing protocol, the ionising radiation dose delivered to the CIED will remain the same regardless of the linac manufacturer. Therefore, this future study should determine if different manufacturers linear accelerators emit different levels of EMI and the resultant effects on CIEDs.

- This research adopted an experimental approach to data collection (static bench tests). Future work should use the same testing methodology but the testing protocol should be amended to include different radiotherapy treatment techniques in current clinical use.

- As the level of EMI emitted from the linear accelerator could not be established, further investigation is required to determine if there are other means of identifying and quantifying the levels of EMI within the radiotherapy treatment room.

- When investigating the effect of ionising radiation and / or EMI on CIED leads, the design set up and proof of principle testing functioned appropriately and provided data. Results showed that the equipment and testing protocol

could be used as a reliable means of quantifying CIED lead sheath damage. However, further experimentation is needed to develop this testing protocol.

- All CIED manufacturers should be involved in research to allow for the quantification of the exact ionising radiation tolerance doses and / or EMI levels to CIEDs and CIED leads. This would enable cross-industry baseline limits to be established.

- This research was conducted using photon beam energy. Proton treatment is increasingly being used as a treatment modality in clinical practice. Therefore, in future research, the testing methodology and protocol will be replicated using proton beam energies.

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Appendix A

Appendix A – Table 1

Studies examining the effects of radiotherapy on pacemakers *in vitro* (since 1994)

Year	Author	n	Beam type	Beam energy (MV)	Maximum CIED dose (Gy)	Main results
1994	Souliman	18	Photons	8	70	• Complete failure at 16.8-70Gy in 11 PMs • No effect from EMI alone
1999	Mouton	42	Photons (n=19) Co-60 (n=23)	LINAC = 4 Co-60 source = 1.17-1.33	140	• No malfunction at therapeutic doses (n=15) • Frequency modifications (n=9) starting at 2Gy • Deprogramming and modification in battery characteristics (n=11) starting at 4Gy • Destruction of PM (n=7) at 44-77Gy
2002	Mouton	96	Photons	18	200	• Amplitude change >10% in 38 PMs at 2-130Gy • Silence >10s in 35 PMs at 0.15-74Gy • Permanent silence in 12 PMs at 0.5-170Gy
2005	Hurkmans	19	Photons	6	120; 130 (n=2)	• 5 PMs = no malfunction • 7 PMs = no output at 80-130Gy • 5 PMs = ERI at 120-130Gy • 2 PMs = no communication at 20-130Gy • 8 PMs = inhibition during direction irradiations
2014	Zaremba	10	Photons	6 / 18	*150*	*6MV group:* • 1 episode of malfunction at 150Gy *18MV group:* • 14 episodes of malfunctions starting at 30Gy

Appendix A – Table 2

Studies examining the effects of radiotherapy on ICDs *in vitro* (since 1994)

Year	Author	n	Beam type	Beam energy (MV)	Maximum CIED dose (Gy)	Main results
2002	Hoecht	5	NA	NA	Scatter = >50	• No effects from EMI • Scatter radiation = 1 fallback • Direct exposure = malfunctions at >50Gy, unspecified
2005	Hurkmans	11	Photons	6	120	• Sensing failure in all ICDs – which would have resulted in shock delivery in 4ICDs • Failure of all devices at 0.5-120Gy • Complete loss of function at 0.5-1.5Gy in 4 ICDs
2008	Kapa	20	Photons	6	4	• No malfunctions
2013	Hashii	10	Photons	10 / 18	Scatter	• More soft errors during irradiation with 18MV photons compared with 10MV photons • No hard errors or permanent malfunctions
2014	Mollerus	8	Photons	6	131.11	• 4 contemporary devices remained functional after 131.11Gy despite minor memory faults in 3 of them • 4 older devices failed to deliver shock therapy after 41.11Gy and had changes in lead impedance
2014	Zaremba	2	Photons	6 / 18	150	*6MV group:* • No malfunctions *18MV group:* • No malfunctions, except the loss of patient data after 44Gy

Appendix A – Table 3

Studies examining the effects of radiotherapy on pacemakers *in vivo* (since 1994) - 1

Year	Author	n	Tumour	Beam type	Beam energy (MV)	Tumour dose (Gy)	CIED dose (Gy)	Outcome	Clinical consequence
2000	Tsekos	1	RT lower arm & axilla	NA	NA	50.4	50.4	Decrease in magnet rate; returning to normal 4 months later	Replacement of the device
2001	Nibhanupudy	1	LT breast & SCF	Photons	6	50.4	1.82	No malfunctions	-
2006	Ampil	3	Lung	Photons	NA	20-60	NA	No malfunctions	-
2006	Mitra	1	RT lung & mediastinum	Photons	NA	40	1.66	No malfunctions	-
2008	Kapa	8	Head and neck; thorax	Photons	6	30-69.96	NA	No malfunctions	-
2009	Zweng	1	Oesophagus	Photons	NA	30	0.11	Runaway PM; Change from DDD to AAI with a fixed rate of 185bpm;Corruption Of the software	Circulatory collapse; replacement of the device
2010	Ferrara	37	Various	Photons; electrons	6 / 18	8-79.2	>2 (n=5) <2 (n=32)	No malfunctions	-
2011	Croshaw	3	Breast	Photons	6	38.5	0.23-0.73	No malfunctions	-
2011	Dasgupta	1	Heart	Photons	6	37.5	0.37	Transient ventricular undersensing	Devices successfully reprogrammed
2011	Soejima	60	Various	NA	NA	20-74	20.69 in 1 patient otherwise not exceed 4.78	1 CRT-P was found Initialised at 46Gy and 56Gy (treated with 74Gy) 15MV photons	Device successfully reprogrammed
2011	Wadasadawala	8	Head and neck; breast; lung	Co-60 (n=3) Photons (n=5)	Photons 6MV (n=3) 15MV (n=2)	45-70	0.14-60	No malfunctions	-
2012	Kesek	2	Lung	Photons	6	80	48	No malfunctions	-

Appendix A – Table 3

Studies examining the effects of radiotherapy on pacemakers *in vivo* (since 1994) - 2

Year	Author	n	Tumour	Beam type	Beam energy (MV)	Tumour dose (Gy)	CIED dose (Gy)	Outcome	Clinical consequence
2012	Kirova	1	Thoracic spine	Photons	20	30	0.3 (leads irradiated directly)	No malfunctions	-
2012	Makkaer	50	Various	Photons; electrons	Photons: 6 (n=26); 16 (n=24). Both with or without electrons	NA	0.844 +/- 0.997	No malfunctions	-
2014	Ampil	2	Head & neck	Photons	6	NA	NA	No malfunctions	-
2014	Gossman	67	Various	Photons	Various	NA	<2 in 85% >2 in 15% Not Exceed 6.5Gy	Failure at 0.3Gy (n=1) Increase in sensor rare during RT (n=1) Irregular heartbeat leading to reprogramming (n=1) Twinging in the chest wall resulting in respiratory arrest (n=1)	Not specific in more detail
2015	Zaremba	487	Various	MV photons, kV photons, electrons	9	Various	NA	Reset or deprogramming (n=9); increase in atrial pacing threshold from 1.25 to 2.75V (n=1) out of 394 PMs	Devices successfully reprogrammed. No device replacements.

Appendix A – Table 4

Studies examining the effects of radiotherapy on ICDs *in vivo* (since 1994) - 1

Year	Author	n	Tumour	Beam type	Beam energy (MV)	Tumour dose (Gy)	CIED dose (Gy)	Outcome	Clinical consequence
2002	Hoecht	4	NA	NA	NA	NA	NA	2 ICDs of the same model in the same patient fell into the fall back mode at <0.5Gy to the ICD (RT to pelvis)	The device was replaced due to the first episode
2004	John	1	LT breast	NA	NA	50	Leads: 50 Partial exposure to generator	Shock coil failure due to structural damage during RT was suspected (shock impedance >125ohms)	A new system was implanted
2004	Thomas	1	RT lung	Photons	18	56	NA (outside the field)	Electrical reset	Unspecified (asymptomatic)
2007	Nemec	1	LT lung	NA	NA	59.4	NA (outside the field)	Rapid pacing triggering polymorphic VT during the 3rd fraction of 1.8Gy	Collapse requiring resuscitation. Device removal afterwards
2007	Sepe	1	Larynx	Photons	6	60	2.5	No malfunctions	-
2008	Kapa	5	Various	Photons	6	18-56	NA (outside the field)	No malfunctions	-
2008	Lau	1	Prostate	Photons	23	74	0.004	Resets during 2nd and 9th fractions of 2Gy	RT completed without other events. Normal ICD parameters afterwards.
2009	Gelblum	33	Various	Photons; Electrons (n=1) Photons & electrons (n=1)	6 (photons); 6 MeV (electrons); 6MV & 9MeV	6-86.4	0.01-2.99	Reset in 2 patients treated with 15MV photons, outside RT field	Devices successfully reprogrammed
2010	Ferrara	8	Various	Photons & electrons (95.6%); C0-60 (4.4%)	6; 18 (59%)	8-79.2	>1 (n=2) <1 (n=6)	No malfunctions	-
2011	Croshaw	2	Breast	Photons	6	38.5	1.01, 1.68	No malfunctions	–
2011	Soejima	2	Various	NA	NA	20-74	NA	No malfunctions	-

Appendix A – Table 4

Studies examining the effects of radiotherapy on ICDs *in vivo* (since 1994) - 2

Year	Author	n	Tumour	Beam type	Beam energy (MV)	Tumour dose (Gy)	CIED dose (Gy)	Outcome	Clinical consequence
2012	Makkar	19	Various	Photons; Photons & electrons	6: 16. Both with or without electrons (6-16MeV)	NA	0.921 +/- 0.726	Partial resets in 2 devices after 1.23Gy and 0.04Gy 16MV photons to the ICD, respectively	RT completed successfully in both patients
2013	Dell'Oca	1	Mediastinum	Photons	6	64	<5	No malfunctions	-
2013	Elders	15	Various	Photons; Photons & electrons (n=1)	6-18	16-70	<1	6 malfunctions in 5 RT courses at 10 and 18MV; invalid data (n=2), reset (n=1), inappropriate tachycardia sensing (n=1), reset and trend data error 9 months after the reset (n=1). Distance from device to RT field 5cm and 8cm respectively	RT completed successfully in all patients
2013	Zaremba	5	Thorax	Photons	6 ; 18	37	37	Converting to backup mode (n=1)	None (animal study; all devices explanted after the irradiation)
2014	Ahmed	1	Lung	Photons	15	69.6	52.4	No malfunctions	-
2014	Gossman	40	Various	Photons	Various	NA	<2 in 85% >2 in 15% Not exceeding 6.5	Failure at 0.3Gy (n=1); increase in sensor rate during RT (n=1); irregular heartbeat leading to reprogramming (n=1); twinging in the chest wall resulting in respiratory arrest (n=1)	Not specified in more detail
2015	Zaremba	73	Various	MV photons, kV photons, electrons	9	Various	NA	Reset (n=3), reset and increase in pacing threshold (n=1)	Devices successfully reprogrammed

Appendix B

Critical Appraisal Skills Programme

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Summertown Pavilion, Middle Way Oxford OX2 7LG

CASP Checklist: 10 questions to help you make sense of a Systematic Review

How to use this appraisal tool: Three broad issues need to be considered when appraising a systematic review study:

- Are the results of the study valid? (Section A)
- What are the results? (Section B)
- Will the results help locally? (Section C)

The 10 questions on the following pages are designed to help you think about these issues systematically. The first two questions are screening questions and can be answered quickly. If the answer to both is "yes", it is worth proceeding with the remaining questions. There is some degree of overlap between the questions, you are asked to record a "yes", "no" or "can't tell" to most of the questions. A number of italicised prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

About: These checklists were designed to be used as educational pedagogic tools, as part of a workshop setting, therefore we do not suggest a scoring system. The core CASP checklists (randomised controlled trial & systematic review) were based on JAMA 'Users' guides to the medical literature 1994 (adapted from Guyatt GH, Sackett DL, and Cook DJ), and piloted with health care practitioners.

For each new checklist, a group of experts were assembled to develop and pilot the checklist and the workshop format with which it would be used. Over the years overall adjustments have been made to the format, but a recent survey of checklist users reiterated that the basic format continues to be useful and appropriate.

Referencing: we recommend using the Harvard style citation, i.e.: *Critical Appraisal Skills Programme (2018). CASP (insert name of checklist i.e. Systematic Review) Checklist. [online] Available at: URL. Accessed: Date Accessed.*

CASP
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Section A: Are the results of the review valid?

1. Did the review address a clearly focused question?

Yes ☐
Can't Tell ☐
No ☐

HINT: An issue can be 'focused' In terms of
- the population studied
- the intervention given
- the outcome considered

Comments:

2. Did the authors look for the right type of papers?

Yes ☐
Can't Tell ☐
No ☐

HINT: 'The best sort of studies' would
- address the review's question
- have an appropriate study design (usually RCTs for papers evaluating interventions)

Comments:

Is it worth continuing?

3. Do you think all the important, relevant studies were included?

Yes ☐
Can't Tell ☐
No ☐

HINT: Look for
- which bibliographic databases were used
- follow up from reference lists
- personal contact with experts
- unpublished as well as published studies
- non-English language studies

Comments:

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4. Did the review's authors do enough to assess quality of the included studies?

Yes ☐
Can't Tell ☐
No ☐

HINT: The authors need to consider the rigour of the studies they have identified. Lack of rigour may affect the studies' results ("All that glisters is not gold" Merchant of Venice – Act II Scene 7)

Comments:

5. If the results of the review have been combined, was it reasonable to do so?

Yes ☐
Can't Tell ☐
No ☐

HINT: Consider whether
- results were similar from study to study
- results of all the included studies are clearly displayed
- results of different studies are similar
- reasons for any variations in results are discussed

Comments:

Section B: What are the results?

6. What are the overall results of the review?

HINT: Consider
- If you are clear about the review's 'bottom line' results
- what these are (numerically if appropriate)
- how were the results expressed (NNT, odds ratio etc.)

Comments:

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7. How precise are the results?

HINT: Look at the confidence intervals, if given

Comments:

Section C: Will the results help locally?

8. Can the results be applied to the local population?

Yes ☐
Can't Tell ☐
No ☐

HINT: Consider whether
- the patients covered by the review could be sufficiently different to your population to cause concern
- your local setting is likely to differ much from that of the review

Comments:

9. Were all important outcomes considered?

Yes ☐
Can't Tell ☐
No ☐

HINT: Consider whether
- there is other information you would like to have seen

Comments:

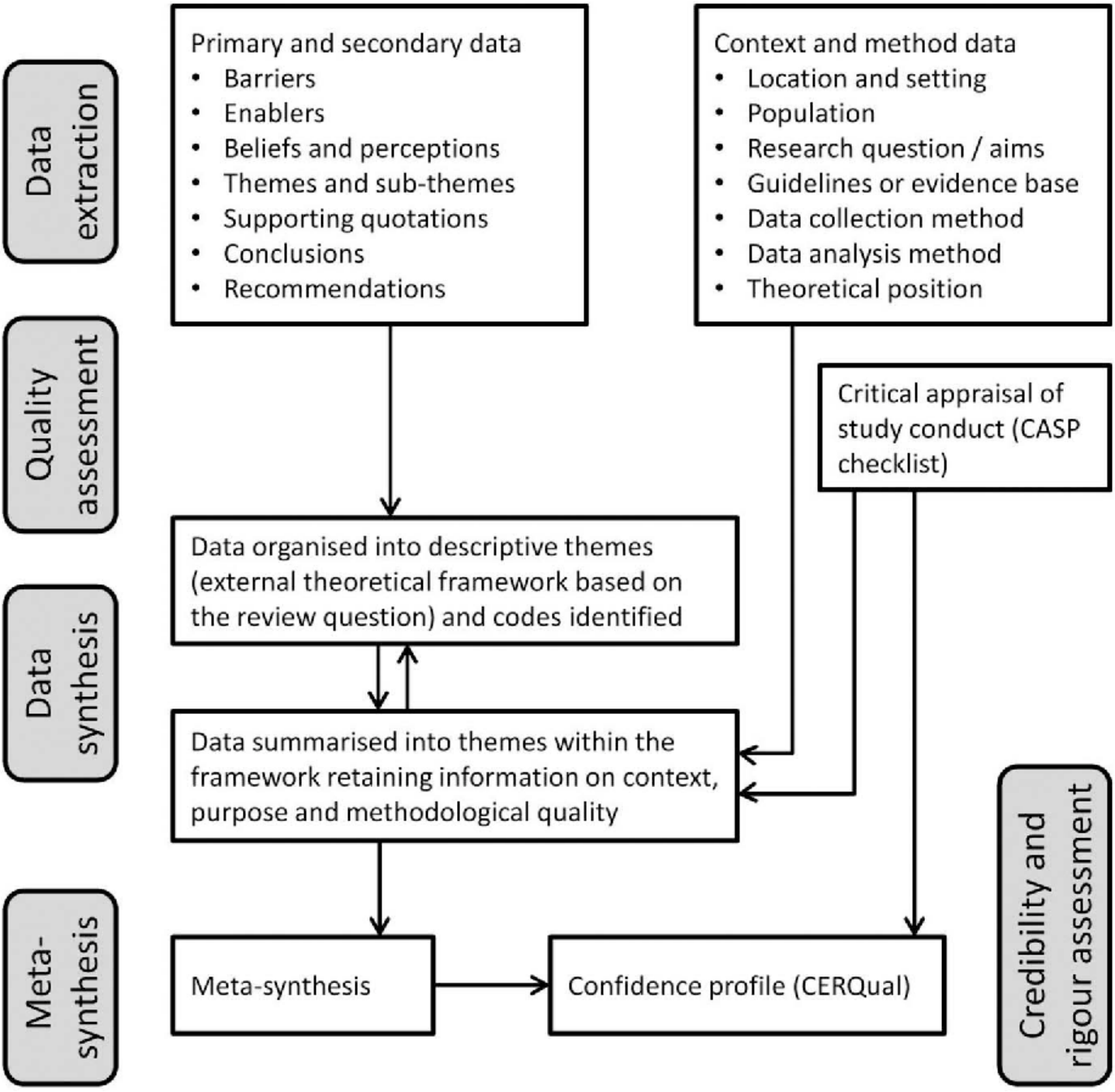
10. Are the benefits worth the harms and costs?

Yes ☐
Can't Tell ☐
No ☐

HINT: Consider
- even if this is not addressed by the review, what do **you** think?

Comments:

Appendix B – Table 2



Appendix C

Appendix C – List of Radiotherapy Departments / Oncology Centres in the UK

Suffolk Oncology Centre

Norfolk & Norwich University Hospital

Mount Vernon Cancer Centre

Peterborough District Hospital

Addenbrooke's Hospital

Southend University Hospital

Colchester Hospital

Cancer Partners UK, Elstree, Hertfordshire

Barts and the London NHS Trust

The London Clinic

Queen’s Hospital - Romford

UCLH

Royal Free Hospital

Imperial College

The Harley Street Clinic

Hammersmith Hospitals

BUPA Cromwell Hospital

Guy’s and St Thomas’s

Royal Marsden

Wimbledon

North Middlesex

Kent Oncology Centre

Oxford

Kent & Canterbury Hospital

Berkshire Cancer Centre

Guildford -Surrey

Portsmouth Haematology & Oncology Centre

Royal Sussex - Brighton

Southampton

Northamptonshire Centre for Oncology

Cancer Partners UK - Portsmouth

Cancer Partners Southampton

Gloucestershire Oncology Centre - Cheltenham

Dorset Cancer Centre – Poole

South Devon Healthcare NHS

Bristol Haematology & Oncology Centre

Royal Cornwall Hospital

Derriford Oncology Centre – Plymouth

Exeter Oncology Centre

Royal United Hospital - Bath

Beacon Centre - Taunton

Middlesbrough

Northern Centre for Cancer - Newcastle

Queen's Centre for Oncology & Haematology – Hull

North Humberside

Lincolnshire

Weston Park Hospital - Sheffield

St James's - Leeds

Rosemere Cancer Centre - Lancashire

Clatterbridge Cancer Centre NHS

Christie Hospital NHS Trust

Cumbria

Staffordshire

Arden Cancer Centre - Coventry

Wolverhampton

Leicester

Queen Elizabeth Hospital - Birmingham

Derby

Nottingham

Spire Hospital Little Aston - West Midlands

Shrewsbury

Velindre NHS Trust

Singleton Hospital - Swansea

North Wales Cancer Treatment Centre

Beaston

Dundee - Tayside

Aberdeen

Edinburgh

Inverness

Belfast

Appendix D

Appendix D – *First e-mail* request for radiotherapy departments – CIED policies

Dear Radiotherapy Service Manager,

I am contacting you to request your assistance in a National Audit I am conducting with the support of the Society and College of Radiographers, into radiotherapy departments' current cardiac device policies. In order to carry out this audit, I would be grateful if I could obtain a copy of your department's policies.

This audit will incorporated into the research project that I am undertaking as part of a PhD study at Velindre Cancer Centre into the effect of radiotherapy on cardiac devices. One of the main objectives is to develop evidence-based clinical guidelines and clinical protocols for the safe administration of radiotherapy to patients who have a cardiac device in situ. Depending on the outcomes, the research may lead to the development and publication of national guidelines as to the safe administration of radiotherapy to these patients.

My research to date has shown that the number of patients with cardiac devices presenting for radiotherapy treatment is increasing. Over the past three decades technological developments have resulted in manufacturers using modern pacemaker components which may be more sensitive to ionising radiation. Pacemaker manufacturers publish their own guidelines regarding radiotherapy tolerances doses based anecdotal experience and research carried out in 1994 by the American Association of Physicists in Medicine. Therefore, pacemaker policies in radiotherapy departments are based on evidence that is eighteen years old carried out on superseded technology. This highlights the clinical need for research to determine the behaviour of modern pacemakers when in or close to the radiotherapy treatment field and to the publication of a clinical policy to reflect this.

Your participation in the audit will greatly assist the research and I look forward to disseminating the results and recommendations to you in the future. All information received will be treated anonymously and no individual hospital will be identified. Please would you send all policies to me at laurenevans44@hotmail.co.uk .

Many thanks for your co-operation regarding my research.
Lauren Evans

Appendix D – *Second e-mail* request for radiotherapy departments – CIED policies

Dear Radiotherapy Service Manager,

I am contacting you in reference to an email sent by the Society and College of Radiographers dated May 2012. This email requested your assistance in the National Audit that is being conducted into radiotherapy departments' current cardiac device policies.

To date I have not received a copy of policies from all departments. In order to obtain a detailed understanding of current working practices, I do require as many department's policies as possible.

If you have already responded to this request, I would like to thank you for your assistance. However, if you have not already done so, I would be extremely grateful if a copy of your policy could be sent to me at laurenevans44@hotmail.co.uk.

Many thanks for your co-operation regarding my research.

Lauren Evans

Appendix D – *Third e-mail* request for radiotherapy departments – CIED policies

Dear Radiotherapy Service Manager,

I am contacting you in reference to two emails sent by the Society and College of Radiographers dated May 2012 and July 2012. These emails requested your assistance in the National Audit of current cardiac device policies in radiotherapy departments.

I presented preliminary findings of this audit at the Society Conference dated 2nd February based on a response rate of 51%. It is necessary that more information is required on existing policies to successfully complete this audit.

To date I have not received a reply from your department. I would be extremely grateful if you would forward a copy of your policy or any existing documentation currently in use. If you do not currently have a policy, would you also inform me.

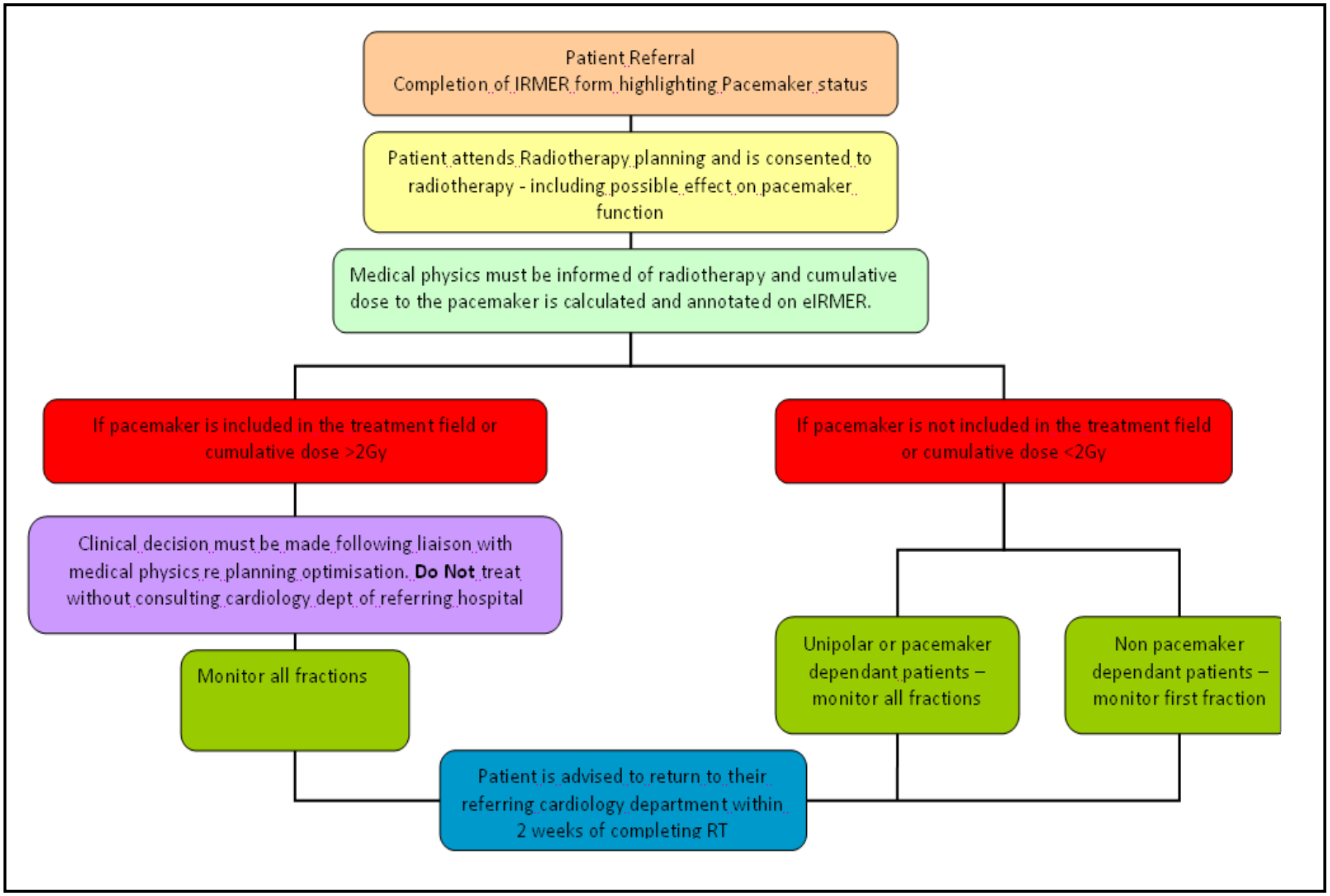
All information can be sent to me at laurenevans44@hotmail.co.uk.

Many thanks for your co-operation.

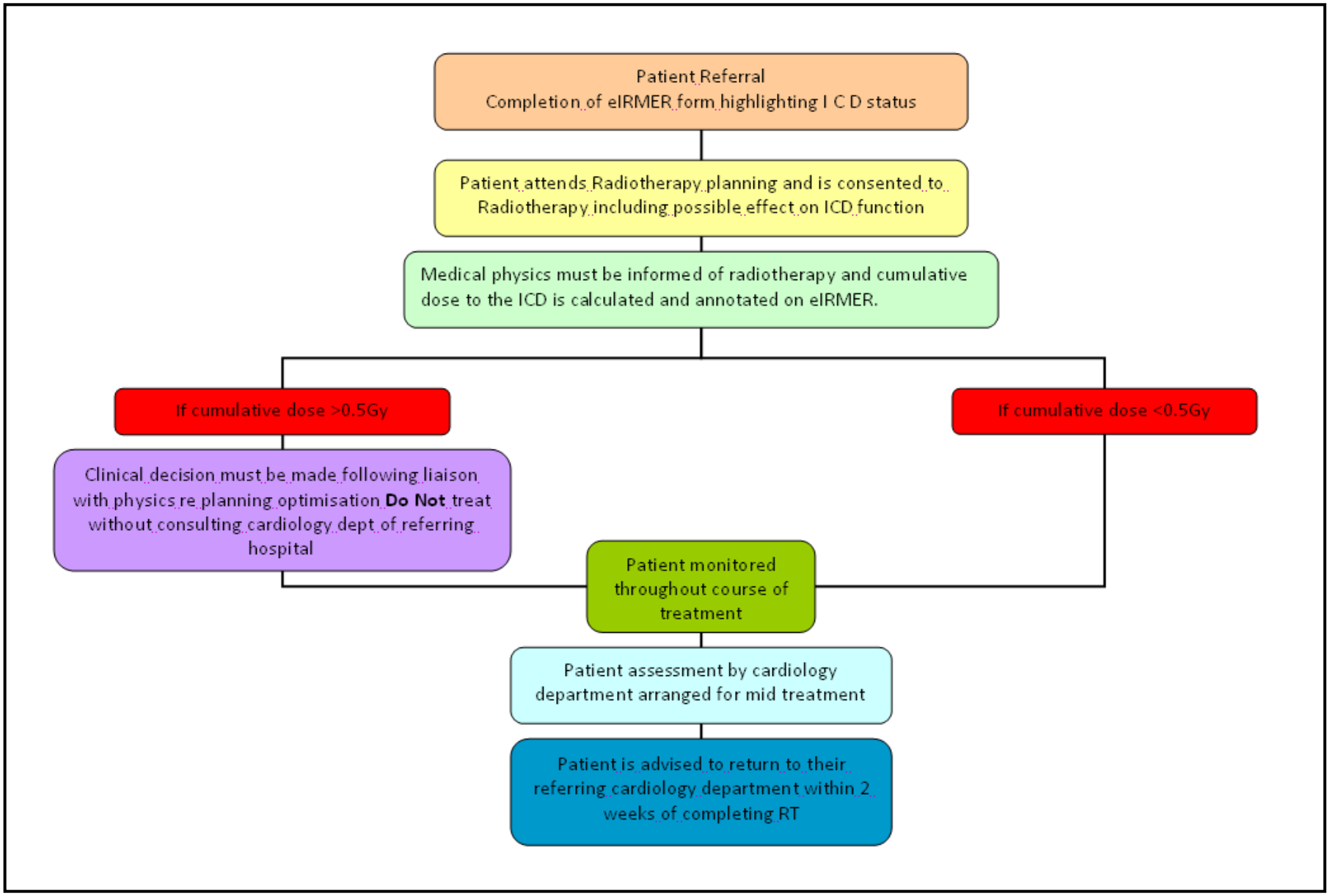
Lauren Evans

Appendix E

Pacemaker patient pathway



ICD patient pathway



Pacemaker / ICD patient pathway

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14
General - Cardiac Devices - Pacemaker and ICD														
Patient referral - Completion of IRMER form – highlight pacemaker / ICD status														
Patient RT planning – consented to RT and possible effect on pacemaker / ICD function														
Medical physics informed of RT - cumulative dose calculated – annotated on eIRMER														
Patient advised to return to cardiology dept – 2 weeks post RT - follow up														
Pacemaker - Pacemaker is involved in radiotherapy treatment field or cumulative dose > 2Gy														
Clinical decision - liaise with medical physics – planning optimisation														
RT not proceed without consulting cardiology dept of referring hospital														
Monitor all fractions of RT														
Pacemaker - Pacemaker is not involved in radiotherapy treatment field or cumulative dose < 2Gy														
Unipolar or pacemaker dependant patient – monitor all fractions of RT														
Non-pacemaker dependant patient – monitor first fraction of RT														
ICD														
Patient monitored throughout course of radiotherapy treatment														
Patients assessed by cardiology dept – mid RT treatment														
ICD - Cumulative dose > 0.5Gy														
Clinical decision - liaise with medical physics – planning optimisation														
RT not proceed without consulting cardiology dept of referring hospital														
Monitor all fractions of RT														

Roles and responsibilities – Pacemakers (1)

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Consultant Oncologist / Specialist Registrar														
eIRMER (RT planning tab) – pacemaker status ticked														
Non-registered patients – F.TP1 – pacemaker information recorded														
Pacemaker / ICD not in RT treatment volume														
If device is in RT treatment volume – cardiologist informed														
Maximum cumulative dose (medical physics) pacemaker not exceed 2Gy / ICD 0.5Gy														
Consent – patient aware of adverse effect of RT on device														
Planning Radiographers														
Annotated – pacemaker prior to scanning														
Pacemaker group aware of all subsequent appointments														
Pacemaker recorded on patient's radiotherapy treatment sheet														
Medical physics informed – F.TP6														
Consultant informed if device within radiotherapy treatment area														
Treatment Radiographers														
Do not commence RT without the presence of a trained radiographer / SHO														
Medical Physics														
Dose estimation information – pacemaker and leads														
Information available 48 hours prior to patient undergoing radiotherapy (unless emergency)														
Any changes to dose estimation – forwarded to pacemaker group														

Roles and responsibilities – Pacemakers (2)

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Appropriately trained radiographers – pacemaker monitoring														
Pacemakers														
Prior to radiotherapy treatment														
Contact referring cardiology dept														
Complete F.TD18 form														
Arrange cardiology follow up appointment														
Assess patient prior to commencing course of RT														
Highlight patient's monitoring need of their RT treatment sheet														
Canisc – pacemaker highlighted under *other* tab selecting *general description*														
Pacemaker not sited within the treatment field – cumulative dose estimation less than 2Gy														
Dose estimation greater than 2Gy – appropriate shielding – clinical decision														
Dose estimation greater than 2Gy – medical physics informed														
Dose estimation greater than 2Gy – cardiologist informed														
On the first day of radiotherapy treatment														
SHO present – if pacemaker is in RT treatment field or concerns regarding patient's condition														
2 appropriately trained radiographers present to assess the patient														
20 sec cardiac tracing – assessed and attached to form F.TD18														
Pacemaker patient checklist placed in front of the radiotherapy treatment sheet														
Assess if further monitoring is required – annotate / sign form F.TD18														

Roles and responsibilities – Pacemakers (3)

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14
During subsequent radiotherapy treatments														
Patient monitored by appropriately trained radiographer														
Completed RT – completed pacemaker details form F.TD18 filed with treatment sheet														
Annotate patient given advice letter F.TD30 and cardiology follow up appointment														

Roles and responsibilities – ICDS (1)

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Appropriately trained radiographers – pacemaker monitoring														
ICD														
Prior to radiotherapy treatment														
Contact referring cardiology dept														
Complete F.TD18 form														
Arrange cardiology follow up appointment														
Assess patient prior to commencing course of RT														
Highlight patient's monitoring need of their RT treatment sheet														
Canisc – pacemaker highlighted under *other* tab selecting *general description*														
ICD is not sited within the RT treatment field – cumulative dose - less than 0.5Gy														
ICD is in the field or dose estimation greater than 0.5Gy - shielding														
ICD is in the field or dose estimation greater than 0.5Gy – medical physics informed														
ICD is in the field or dose estimation greater than 0.5Gy – cardiologist informed														
On the first day of radiotherapy treatment														
Ensure that patient has consented to switch off ICD during RT														
12 lead ECG prior to first treatment – attached to form F.TD18														
2 authorised radiographers / SHO present - monitor patient – staff for subsequent appts														
20 sec cardiac tracing – assessed and attached to form F.TD18														
Switch off ICD during RT														

Roles and responsibilities – ICDs (2)

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14
F.TD18 signed by SHO and trained radiographers														
During subsequent radiotherapy treatments														
Patient monitored by appropriately trained radiographer														
Completed RT – completed pacemaker details form F.TD18 filed with treatment sheet														
Annotate patient given advice letter F.TD30 and cardiology follow up appointment														

Out of hours and emergency patient pathway

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Radiographer – record as much information as possible (device)														
No device information available – treat device as an ICD														
Radiographer complete for F.TD18														
Dose to pacemaker less than 0.5Gy / #														
Dose 5Gy or less - device needs to be more than 1.5cm from any field edge														
Dose 5Gy – 10Gy - device needs to be more than 3.5cm from any field edge														
Pacemaker - SHO present and responsible – patient monitoring during RT treatment														
ICD – doughnut magnet placed over ICD during exposure														
ICD - SHO present and responsible – patient monitoring during RT treatment														
Referred back to radiotherapy planning dept														
Referred back to medical physics – dose estimation														
Referred back to pacemaker group														

Appendix F

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journal homepage: www.clinicaloncologyonline.net

Original Article

A National Audit of Current Cardiac Device Policies from Radiotherapy Centres across the UK

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Abstract

Aims: The number of patients with cardiac implantable electronic devices (permanent pacemakers and implantable cardioverter defibrillators) undergoing radiotherapy treatment is increasing. The aims of this audit were to establish current UK practice regarding the management of patients with implanted cardiac devices undergoing radiotherapy and to compare this practice with current 'gold standard' evidence-based guidelines.
Materials and methods: All UK radiotherapy departments were contacted and asked to provide their current cardiac implantable electronic device policy or to indicate if there was no current policy. A proforma was created to analyse these polices and to compare with current best practice.
Results: In total, 47/67 (70%) radiotherapy departments responded and 45 departmental policies were submitted; 31/45 (69%) policies defined the radiotherapy tolerance dose to permanent pacemakers and 14/45 (31%) defined the monitoring procedure for patients in line with current best practice. Only 5/45 (11%) policies defined the radiotherapy tolerance dose to implantable cardioverter defibrillators and 12/45 (27%) defined the monitoring procedure in line with current best practice.
Conclusion: Most UK cardiac device policies do not reflect current best evidence. Policies are based on research carried out in 1994 by the American Association of Physicists in Medicine. This evidence does not account for advances in cardiac implantable electronic device technology. Further research is urgently needed to establish the effect of radiotherapy on these devices.

Key words: Cardiac device; defibrillator; national survey; pacemaker; policy; radiotherapy

Introduction

The life expectancy of the English and Welsh population has increased by more than 65% in the past century [1]. This has resulted in a higher prevalence of cardiovascular morbidity, leading to an increase in the number of patients with cardiac implantable electronic devices (CIEDs) [2,3]. In addition, the age-standardised incidence of cancer has increased by more than 25% in the past 30 years [1]. It has been estimated that 50–60% of all patients with cancer will require radiotherapy during the course of their illness [4]. Therefore, with an ageing population and an increase in the incidence of both cardiovascular morbidity and cancer, the number of patients with CIEDs presenting for radiotherapy treatment will probably increase [2,5,6].

There are two categories of CIED fitted into patients; permanent pacemakers and implantable cardioverter defibrillators (ICDs). Permanent pacemakers are referred to as 'pacemakers' in this paper. Pacemakers are permanent devices and vary in sophistication. ICDs are more sophisticated devices and have the ability to automatically defibrillate the heart by monitoring the patient's heart rate and delivering the appropriate electrical therapy.

Although most medical treatments pose little danger to the functioning of CIEDs, radiotherapy has the potential to cause device malfunction. Cardiac devices may be affected in two ways; electromagnetic interference (EMI) and direct damage to the circuitry via ionising radiation, both of which may cause temporary and permanent device malfunction [3]. Changes within the device parameters as result of EMI are seen even when the CIED is placed outside the radiotherapy treatment field [7].

Over the past three decades, the design and technology of CIEDs has evolved and the use of complementary metal

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oxide semiconductor circuits has expanded [8]. These are more sensitive to ionising radiation than bipolar semiconductor devices used previously, possibly resulting in increased damage and catastrophic failure of the cardiac conduction system in the device [9,10].

It is not possible to predict the exact behaviour of a CIED when it is in or close to the radiotherapy treatment field [11]. In addition, published results are not consistent in their findings or recommendations. Radiotherapy has been shown to cause malfunction of CIEDs, ranging from inappropriate triggering, device reprogramming or device failure [12–14]. Other investigators have reported a minimal effect of radiotherapy on CIEDs [15].

There is concern that the photon energy of the treatment beam may also be important. Gelblum and Amols [16] discussed the possible effects of neutron contamination from high-energy photon beams. They recommended the use of low-energy beams (<10 MV), but there is little evidence to support this recommendation.

The American Association of Physicists in Medicine (AAPM) [17] published a report in 1994 on the safe use of radiotherapy in patients with permanent pacemakers. The AAPM report is the basis of most of the current CIED departmental radiotherapy policies in the UK (authors' observation). Frizzell [18] published a more contemporary review and a distinction was made between pacemakers and ICDs. Both the AAPM and the Frizzell reports are widely referenced in the literature and in our opinion have the most robust evidence base to support them. Despite this, the AAPM report is now nearly two decades old and does not reflect advances in CIED or radiotherapy technology. However, in the absence of more contemporary evidence-based guidelines on treating CIED patients with radiotherapy, it is reasonable to compare current UK policies with the AAPM recommendations, using the Frizzell update to define current best practice for ICD management.

Below is a summary of the AAPM and Frizzell recommendations:

AAPM Recommendations (pacemakers):

1. Pacemakers should not be placed in the direct (unshielded) therapy beam.
2. The absorbed dose to be received by the pacemaker should be estimated before treatment and limited to 2 Gy.
3. If the total estimated dose to the pacemaker might exceed 2 Gy, pacemaker function should be checked before radiotherapy and possibly at the start of each following treatment week by a cardiologist.
4. Patients should be closely observed during the first radiotherapy treatment on a linear accelerator.

Frizzell Recommendations (ICDs):

1. The absorbed dose to be received by the ICD should limited to 0.5 Gy.
2. A magnet should be placed over an ICD when a patient is exposed to radiation.
3. Notify all patients about the possibility of ICD malfunction, failure or both.

Monitoring recommendations:

1. Patients should be monitored with a continuous electrocardiogram (ECG) strip during the first radiotherapy treatment. This strip should then be reviewed for any evidence of pacing disruption when radiotherapy is being administered.
2. ICD patients should undergo daily monitoring and staff should document any changes in the patient's physical status and any changes in the ECG trace.
3. Monitoring should be carried out by fully trained and competent health professionals. If therapeutic radiographers are monitoring patients, they should receive specific training on the management and monitoring of these patients.
4. If at any point malfunction is suspected or detected, the clinical oncologist and cardiologist should be immediately informed.

Consent recommendations:

1. The patient is aware of potential adverse effects of radiotherapy on CIEDs.
2. The patient is aware the ICD will be deactivated during radiotherapy.

Currently, there are no UK or national guidelines on the use of radiotherapy in patients with CIEDs and most radiotherapy departments have no formal risk management strategy or policy in place [11]. The aims of this audit were to establish current UK practice regarding the management of patients with CIEDs undergoing radiotherapy and to compare this practice with the current 'gold standard' AAPM and Frizzell recommendations.

Materials and Methods

UK radiotherapy centres were identified using the Society and College of Radiographers' database. Between May 2012 and March 2013, all radiotherapy department managers were e-mailed asking them to participate in a national audit. Centres were asked to either provide their current CIED policy or to indicate if there was no policy.

A proforma was created to analyse CIED policies comprising two sections: first, the roles and responsibilities of healthcare professionals; second, treatment and management guidelines. All data collected were anonymised. A database (Microsoft Excel) was created for the entry and analysis of audit data and departmental guidelines were compared. The results are presented as simple frequencies and percentages.

Results

In total, 67 radiotherapy centres were identified in the UK and contacted. Overall, 47/67 (70%) departments responded to the request to provide their policy for inclusion in the audit. Forty-five departments provided their policy and two

departments are currently re-writing their CIED policy and were excluded from the results. Twenty departments did not respond to the request. The analysis was carried out on the 45 polices submitted that are currently in use.

Table 1 summarises the roles and responsibilities of healthcare professionals. Overall, 39/45 (87%) policies require the clinical oncologist to state whether a CIED is present on the radiotherapy referral form; 41/45 (91%) policies require the clinical oncologist to contact the patient's cardiology department before starting radiotherapy; 34/45 (76%) policies require a cardiology assessment; 36/45 (80%) policies require the clinical oncologist to provide relevant information to medical physics to allow the calculation of the estimated cumulative dose to the CIED before starting radiotherapy; 12/45 (27%) policies require patients fitted with CIEDs to be informed of the risks to themselves and their device before starting radiotherapy; 5/45 (11%) policies state that patients fitted with ICDs should be informed about the possibility of ICD malfunction or failure during radiotherapy and must give consent to deactivate the ICD during radiotherapy.

Of note is that in only 29/45 (64%) policies is it mandatory for the planning radiographer to contact the treating consultant if the CIED is within a radiotherapy treatment field or the estimated dose is too high. Less than a third of policies include appropriate monitoring procedures for treatment radiographers in patients with pacemakers or ICDs. There is no requirement for medical physics to calculate the estimated dose to CIEDs and leads in 9/45 (20%) policies.

Table 2 summarises adherence to current guidelines: 31/45 (69%) policies define the radiotherapy tolerance dose to the pacemaker recommended in the AAPM guidelines. Of these, 21/31 (68%) policies require the cardiology department to be contacted to discuss safe management of the patient. In total, 14/45 (31%) policies do not define a tolerance dose limit to the pacemaker and none of these radiotherapy departments contact the patient's cardiology department. Only 5/45 (11%) policies define the radiotherapy tolerance dose limit to the ICD as 0.5 Gy and all five of these radiotherapy departments contact the cardiology department to discuss the management of the patient; 23/45 (51%) policies define a dose limit of >0.5 Gy to the ICD and 17/45 (38%) policies do not define a dose limit. 39/40 (98%) policies that use an incorrect tolerance dose limit or do not define a dose limit do not mandate contacting the patient's cardiology department for advice. 30/45 (67%) policies require a follow-up appointment to be made with the patient's cardiology department after the completion of radiotherapy.

Table 3 summarises the monitoring requirements for patients with CIEDs receiving radiotherapy. Overall, 31/45 (69%) policies do not define monitoring procedures for patients with pacemakers in line with the AAPM guidelines and none mandate the use of appropriately trained staff to monitor patients. Similarly, 33/45 (73%) policies do not define monitoring procedures for patients with ICDs in line with the Frizzell report and none mandate the use of appropriately trained staff to monitor patients.

Table 1
Roles and responsibilities

Roles and responsibilities	Results ($n = 45$ unless stated otherwise)	
	Number of radiotherapy department policies	%
Consultant oncologist		
Identify patient's CIED status and highlight on radiotherapy referral form	39	87
Contact patient's cardiology department before starting radiotherapy treatment	41	91
Request cardiology assessment	34	76
Provide medical physics with information to calculate cumulative radiotherapy dose to CIED	36	80
Dose to the implantable internal pacemaker does not exceed 2 Gy	31	69
Dose to the ICD does not exceed 2 Gy	5	11
Consent – patient aware of potential adverse effects of radiotherapy on cardiac device	12	27
Consent – switch off ICD during radiotherapy	5	11
Planning radiographers		
Annotated patient's CIED status	34	76
CIED included in scan if in/close to the radiotherapy treatment field	35	78
Medical physics informed of patient's CIED status	35	78
Contact consultant if CIED is within radiotherapy treatment field or estimated dose too high	29	64
Treatment radiographers		
Appropriate monitoring procedure for patients with pacemakers	14	31
Appropriate monitoring procedure for patients with ICDs	12	27
Medical physics		
Dose estimation calculated for CIEDs and leads	36	80

CIED, cardiac implantable electronic device; ICD, implantable cardioverter defibrillator.

Table 2
Adherence to American Association of Physicists in Medicine (AAPM) and Frizzell guidelines

Guidelines	Results ($n = 45$ unless stated otherwise)	
	Number of radiotherapy department policies	%
Pacemakers – AAPM guidelines		
2 Gy radiotherapy tolerance dose to device stated	31	69
Requirement to contact cardiology if radiotherapy dose to pacemaker exceeds 2 Gy	21 (of 31)	68
No radiotherapy tolerance dose stated	14	31
Do not contact cardiology	14 (of 14)	100
Cardiology follow-up made after radiotherapy completed	30	67
ICDs – Frizzell Report		
0.5 Gy radiotherapy tolerance dose to device stated	5	11
Requirement to contact cardiology if radiotherapy dose to ICD exceeds 0.5 Gy	5 (of 5)	100
1 Gy radiotherapy tolerance dose to device stated (exceeding 0.5 Gy tolerance dose)	9	20
Do not contact cardiology if radiotherapy dose to ICD exceeds 1 Gy	9 (of 9)	100
2 Gy radiotherapy tolerance dose to device stated (exceeding 0.5 Gy tolerance dose)	14	31
Do not contact cardiology if radiotherapy dose to ICD exceeds 2 Gy	13 (of 14)	93
No radiotherapy tolerance dose stated	17	38
Do not contact cardiology if no radiotherapy tolerance dose is stated	17 (of 17)	100
Cardiology follow-up made after radiotherapy completed	30	67

ICD, implantable cardioverter defibrillator.

Discussion

The number of patients with CIEDs undergoing radiotherapy treatment is increasing [2,5,6]. There is limited published research on the effect of radiotherapy on CIEDs, but there is evidence to show radiotherapy at low doses can cause malfunction or failure with potentially life-threatening consequences [10]. Given this risk, all radiotherapy centres should have policies in place to support the safe radiotherapy treatment of patients with CIEDs.

This audit used the AAPM guidelines and Frizzell report as the benchmark to compare UK radiotherapy departments' current CIED policies, as in the opinion of the authors, these guidelines had the most robust evidence base to support them [17,18].

The first question we wanted to answer was how many UK radiotherapy centres have a CIED policy in routine use. All radiotherapy department managers were asked to provide their current policy for analysis. The request yielded a response rate of 70%; 45 respondents provided their policy and two centres stated that they are currently re-writing their policy. A third follow-up e-mail has been sent from the Society of Radiographers on behalf of the researchers asking radiotherapy departments to forward their policy or to inform the researchers if they do not have one. This will allow a more detailed national picture to be established in the future, but a response rate of 70% was felt high enough to proceed with this review. At this point, it is not known whether the remaining 20 radiotherapy departments who have not responded have a policy, but it is possible that up

Table 3
Monitoring

Clinical practice – monitoring of patients with cardiac devices	Results ($n = 45$ unless stated otherwise)	
	Number of radiotherapy department policies	%
Pacemakers – AAPM guidelines		
Appropriate monitoring procedure	14	31
Appropriate staff used to monitor patients	14	31
Close observation of patient using cardiac monitor on first fraction of radiotherapy	14	31
Subsequent monitoring requirements assessed and annotated	14	31
ICDs – Frizzell report		
Appropriate monitoring procedure	12	27
Appropriate staff used to monitor patients	12	27
12 lead continuous strip ECG before first fraction of radiotherapy	12	27
Deactivate ICD with magnet during radiotherapy	12	27
Continuous strip ECG monitoring for all subsequent treatments	12	27
Document any change in patient's status	12	27

AAPM, American Association of Physicists in Medicine; ECG, electrocardiogram; ICD, implantable cardioverter defibrillator.

to 30% of UK radiotherapy centres have no policy for managing patients with CIEDs. Given the potential risk from radiotherapy to patients with CIEDs, it is concerning that a significant proportion may not have a policy to guide healthcare professionals. The lack of an over-arching national policy on this therapy area is not specific to the UK. An American report suggests that 12% of US oncology departments have neither a formal risk management strategy nor a cardiac device policy and that only 15% have a written policy [11].

The audit results highlight significant differences between policies in the roles and responsibilities of healthcare professionals involved in the patient pathway and the management of patients with a CIED receiving radiotherapy. From the results of the audit, in 87% of radiotherapy departments the treating clinical oncologist determines CIED status and highlights it on the radiotherapy referral form. This means that in 13% of the policies included in this review, it is left to radiographers to identify whether a CIED is present. Anecdotal evidence from this audit shows that in some cases, a CIED is not discovered until a patient attends for radiotherapy. This results in treatment being delayed or treatment proceeding without safety measures in place. It is not known how many patients with CIEDs undergo radiotherapy without the knowledge of the therapeutic radiographers, but this potentially dangerous scenario is less likely if the treating oncologist determines early on in the treatment pathway that a device is present and informs the planning and treatment teams. Worryingly, in only 29/45 (64%) policies is it mandatory for the treating consultant to be contacted if the CIED is within a radiotherapy treatment field or the estimated dose is too high. In most cases, this communication would probably happen even in the absence of policy. However, given the potential harm to the patient, this should be explicit. There is clearly a need for policies in use to include monitoring procedures for treatment radiographers in patients with pacemakers or ICDs. These procedures are currently included in less than one-third of policies and it is vital that patients having treatment are monitored to minimise the chance of harm. There is no requirement for medical physics to calculate the estimated dose to CIEDs and leads in 9/45 (20%) policies. Without this estimation being made before radiotherapy starts, patients may be exposed to doses of radiation that exceed the limits recommended by AAPM and Frizzell.

Patients consenting for any type of treatment need to be informed of potentially serious side-effects related to that treatment. Nearly three-quarters of policies do not mandate discussion of potential damage to the CIED during and after radiotherapy in the treatment consent process. Given the lack of contemporary research in this area, it is not possible to quantify this risk of damage or harm at present, but consideration should be given to discussing potential complications in all patients with a CIED. ICDs are probably susceptible to radiotherapy damage at lower doses than pacemakers and ICD patients should be informed about the possibility of malfunction or failure during radiotherapy treatment as the consequences may be devastating. ICD patients also need to be told in advance of radiotherapy that their device will be deactivated using a magnet during treatment.

The AAPM report recommended that the cumulative radiotherapy dose to the pacemaker be limited to less than 2 Gy [17]. In the audit, only 31/45 (69%) radiotherapy departments limit the cumulative dose to the pacemaker to 2 Gy and of these, only 21/31 (68%) require communication with the cardiology department if the dose exceeds 2 Gy. It is concerning that nearly a third of policies define no tolerance dose to the pacemaker. There is evidence that even low cumulative doses of radiotherapy may damage CIEDs and patients are probably being put at risk of harm with the current policies in use.

The Frizzell report recommended a lower radiotherapy tolerance dose of 0.5 Gy for ICDs and that they should be deactivated before radiotherapy by placing a magnet over the device to prevent inappropriate therapy or shock delivery as a result of accidental sensing of EMI interference [18]. Worryingly, the audit shows that only 5/45 (11%) radiotherapy departments limit the ICD dose to 0.5 Gy, 23/45 (51%) radiotherapy departments specify a higher ICD tolerance than recommended and 17/45 (38%) do not state a radiotherapy tolerance dose. That means that in most centres with a cardiac device policy, ICDs are potentially exposed to doses of radiotherapy that may affect function and cause serious harm to the patient.

In addition, it is of significant concern that only 6/45 (13%) CIED policies differentiate between pacemakers and ICDs and subsequently apply radiotherapy tolerance dose limits to both types of device. In these policies, ICDs are subject to the same radiotherapy tolerance dose limits and the same monitoring procedures as pacemakers. As a result, ICDs are almost certainly being subjected to radiotherapy doses beyond tolerance and ICD malfunction has potentially life-threatening consequences.

The AAPM and Frizzell reports recommend that all patients with CIEDs be monitored with a continuous ECG strip during their first radiotherapy treatment for any evidence of pacing disruption [17,18]. In addition, they should be monitored by an appropriately trained health professional. The audit shows that over two-thirds of policies do not mandate the monitoring procedures defined by AAPM and Frizzell and less than one-third require the use of an appropriately trained health professional to carry out the monitoring. Therefore, a significant number of patients with CIEDs are undergoing radiotherapy with no monitoring and in those that are monitored most of the staff involved may not have appropriate training to interpret ECG or clinical changes.

Conclusion

This audit of CIED policies is based on a 70% response rate from radiotherapy centres in the UK. It cannot be definitive in its conclusions, but important themes have emerged nevertheless. It is clear that policies differ between radiotherapy centres. In addition, a significant proportion of

policies do not adhere to current established tolerance doses for CIEDs. As a consequence, it is very likely that patients are being put at significant risk of harm. We are carrying out urgently needed research to further define the effect of radiotherapy on modern cardiac devices. This research will underpin the development of contemporary evidence-based guidelines on the use of radiotherapy in patients with these devices.

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Appendix G

Summary – Effect of ionising radiation on pacemakers at 6MV and 10MV

DEVICE	First malfunction	RT Dose (Gy)	Other malfunctions	RT Dose (Gy)	Point of Failure (POF)	RT Dose (Gy)
6MV						
PM X2	**3 – Sensing**	3Gy	**3 – Sensing**	3Gy ➔ 5G ➔	**1 – Pacing pulse**	120Gy 120Gy
PM X3	**1 – Pacing pulse**	120Gy			**1 – Pacing pulse**	120Gy
PM X4	**1 – Pacing pulse**	70Gy	**2 – Pacing frequency** **3 – Sensing**	70Gy ➔ 90Gy ➔	**4 – Telemetry**	120Gy
PM Y2	**6 – Lead impedance changes**	80Gy	**6 – Lead impedance changes**	80Gy ➔	**4 – Telemetry**	90Gy
PM Y3	**2 – Pacing frequency**	44Gy	**2 – Pacing frequency**	44Gy ➔	**4 – Telemetry**	92Gy
PM Y4	**3 – Sensing**	10.5Gy	**3 – Sensing**	10.5Gy ➔	**3 – Sensing** **5 – Battery**	120Gy
PM Z2	**4 – Telemetry**	20.5Gy	**2 – Pacing frequency** **4 – Telemetry**	20.5Gy ➔ 90Gy ➔	**4 – Telemetry**	120Gy
PM Z3	**4 – Telemetry**	23Gy			**4 – Telemetry**	23Gy
PM Z4	**5 – Battery**	12Gy	**5 – Battery**	12Gy ➔	**4 – Telemetry**	13.5Gy

10MV						
PM X5	**4 – Telemetry**	28Gy			**4 – Telemetry**	28Gy
PM X6	**2 – Pacing frequency**	2.5Gy	**1 – Pacing pulse**	20Gy ➔	**1 – Pacing pulse**	90Gy
PM X7	**4 – Telemetry**	17Gy	**3 – Sensing**	30Gy ➔ 56Gy ➔	**4 – Telemetry**	100Gy
PM Y5	**3 – Sensing**	4.5Gy	**3 – Sensing**	5Gy ➔ 50Gy ➔	**3 – Sensing** Device failure Unable to sense **5 – Battery** Device failure Elective replacement indication (ERI)	 70Gy 70Gy
PM Y6	**3 – Sensing**	7Gy	**3 – Sensing**	18Gy ➔	**3 – Sensing**	90Gy
PM Y7	**3 – Sensing**	52Gy			**3 – Sensing**	52Gy
PM Z5	**3 – Sensing**	41Gy		41Gy ➔	**3 – Sensing**	120Gy
PM Z6	**4 – Telemetry**	21Gy	**3 – Sensing** **4 – Telemetry**	21Gy ➔ 90Gy ➔	**4 – Telemetry**	90Gy
PM Z7	**4 – Telemetry**	8.5Gy	**4 – Telemetry**	29Gy ➔	**5 – Battery**	120Gy

Summary - Effect of ionising radiation on ICDs at 6MV and 10MV

DEVICE	First malfunction	RT Dose (Gy)	Other malfunctions	RT Dose (Gy)	Point of Failure (POF)	RT Dose (Gy)
			6MV			
ICD X2	**3 – Sensing**	60Gy	**3 – Sensing**	70Gy →	**1 – Pacing pulse**	100Gy
ICD X3	**7 – Shock**	45Gy	**3 – Sensing**	46Gy →	**1 – Pacing pulse** **7 – Shock**	70Gy 70Gy
ICD Y2	**3 – Sensing**	4Gy	**3 – Sensing** **7 – Shock** **5 – Battery**	5G → 5G → 40Gy →	**3 – Sensing** **7 – Shock**	90Gy 90Gy
ICD Y3	**3 – Sensing** **1 – Pacing pulse** **4 – Telemetry**	0.5Gy 0.5Gy 0.5Gy			**1 – Pacing pulse**	1Gy
ICD Z2	**3 – Sensing**	1.5Gy	**3 – Sensing**	1.5Gy →	**1 – Pacing pulse** **7 – Shock**	3.5Gy 3.5Gy
			10MV			
ICD X4	**5 – Battery**	120Gy			**3 – Sensing**	120Gy
ICD X5	**7 – Shock**	10Gy	**4 – Telemetry**	20Gy →	**7 – Shock**	80Gy
ICD Y4	**3 – Sensing**	5Gy	**3 – Sensing** **4 – Telemetry**	5Gy → 6Gy →	**1 – Pacing pulse**	15Gy
ICD Y5	**4 – Telemetry** **5 – Battery**	12.5Gy 12.5Gy	**3 – Sensing** **4 – Telemetry**	12.5Gy → 14Gy →	**1 – Pacing pulse**	120Gy
ICD Z3	**7 – Shock**	8.5Gy	**3 – Sensing**	9Gy →	**7 – Shock** **1 – Pacing pulse**	10Gy 10Gy

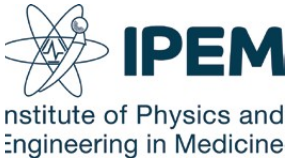
Summary – Effect of EMI on CIEDs – Pacemakers

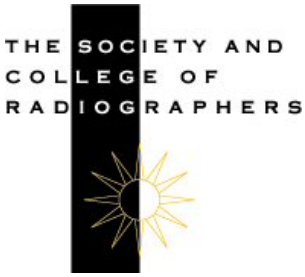
DEVICE Pacemakers	CIED malfunctions observed		At what point CIED malfunction observed
6MV			
PM X9	#1 - #3	**3 – Sensing**	During EMI exposure
	#4	**3 – Sensing**	During EMI exposure
		1 – Pacing pulse	During EMI exposure
	#5 - #6	No CIED malfunction observed or recorded	
	#7 - #9	**1 – Pacing pulse**	During EMI exposure
	#10	**1 – Pacing pulse**	During EMI exposure
PM X10	#1 - #7	No CIED malfunction observed or recorded	
	#8 - #10	**2 – Pacing frequency**	Beam ON / During EMI exposure
10MV			
PM X11	#1 - #10	**2 – Pacing frequency**	Beam ON / During EMI exposure
PM X12	#1 - #9	**1 – Pacing pulse**	During EMI exposure
	#10	**1 – Pacing pulse**	During EMI exposure

Summary – Effect of EMI on CIEDs – ICDs

DEVICE Pacemakers	CIED malfunctions observed		At what point CIED malfunction observed
6MV			
ICD X7	#1 - #8	**2 – Pacing frequency**	Beam ON
	#9 - #10	**5 – Battery**	Post beam OFF
ICD X8	#1 - #6	**1 – Pacing pulse**	During EMI exposure
	#7	**3 – Sensing**	During EMI exposure
	#8 - #10	**1 – Pacing pulse**	During EMI exposure
10MV			
ICD X9	#1 - #5	No CIED malfunction observed or recorded-	
	#6 - #10	**7 – Shock**	During EMI exposure
ICD X10	#1 - #3	No CIED malfunction observed or recorded-	
	#4 - #6	**2 – Pacing frequency**	Beam ON
	#7 - #10	**2 – Pacing frequency**	Beam ON

Appendix H





Radiotherapy Board

Management of cancer patients receiving radiotherapy with a cardiac implanted electronic device: A clinical guideline

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Overview

A national review of cardiac device policies in use in radiotherapy departments across the UK in 2013 reported that most policies do not reflect current best evidence.[1] The Radiotherapy Board[a] formed a multidisciplinary working party comprising clinical oncology, cardiology, therapeutic radiography and medical physics expertise to develop evidence-based guidelines for the management of cancer patients receiving radiotherapy with a cardiac implanted electronic device.

[a] The Radiotherapy Board was established in 2013 by The Royal College of Radiologists (RCR), the Society and College of Radiographers (SCoR), and the Institute of Physics and Engineering in Medicine (IPEM) to provide guidance, oversight and support for the continuing development of high-quality radiotherapy services for cancer patients in the UK.

Contents

1. Introduction

The number of cancer patients with cardiac implantable electronic devices (CIEDs) receiving radiotherapy is increasing.[2-4] There are two main categories of CIED: permanent pacemakers and implantable cardioverter defibrillators (ICDs). Electronic monitoring devices (eg implantable loop recorders) have no direct connection to the heart and are not covered in this guideline. Most permanent pacemakers (referred to as 'pacemakers' in this document) are implanted in patients who either have inappropriate bradycardia, or who are at risk of bradycardia. Bradycardia pacemakers generally only pace the heart when the patient's heart rate is excessively slow (usually <50 beats/minute), otherwise the pacemakers simply monitor and therefore an electrocardiogram (ECG) may appear "normal" and not show any pacemaker activity. Cardiac resynchronisation pacemakers coordinate the sequence of cardiac contraction and are used in patients with heart failure. As such, these pacemakers tend to pace the heart continuously and an ECG usually shows paced beats. ICDs are more sophisticated devices; in addition to normal pacing capabilities (for bradycardia and/or for resynchronisation), ICDs have the ability to monitor the patient's cardiac rate and rhythm, and deliver shock therapy when certain criteria are met. The simplest shock criteria involve heart rate; thus when sensed heart rate exceeds a pre-programmed value (usually >220 beats/minute), shock therapy is delivered. Inappropriate shock therapy may arise when the ICD senses the cardiac rhythm incorrectly.

Although most medical treatments pose little danger to the functioning of CIEDs, radiotherapy has the potential to alter device function. CIEDs may be affected in two ways - electromagnetic interference (EMI) and direct damage via ionising radiation - both of which may cause temporary or permanent device malfunction.[5] Over the past three decades, the design and technology of CIEDs has evolved. The use of complementary metal oxide semiconductor (CMOS) circuits within CIEDs has increased.[6] These are more sensitive to ionising radiation than the bipolar semiconductor devices previously used, with the potential of increased damage and catastrophic device failure.[7,8] CIEDs are also now more complex in design, they are smaller, have thinner housing, less shielding and have limited battery capacity. These CIEDs use random access memory (RAM) to hold patient-related data. Ionising radiation can damage the RAM and can lead to complete loss of CIED function.[9]

It is not possible to predict the exact behaviour of a CIED when it is within or close to a radiotherapy treatment field.[10] In addition, published results are not consistent in their findings or recommendations. Radiotherapy has been shown to cause malfunction of CIEDs, ranging from inappropriate triggering and device reprogramming to device failure.[10-13] However, other investigators have reported minimal effect of radiotherapy on CIEDs.[14-17]

The American Association of Physicists in Medicine (AAPM) published a report in 1994 on the safe use of radiotherapy in patients with permanent pacemakers.[18] The AAPM report is the basis of most of the current CIED departmental radiotherapy policies in the UK.[1] Frizzell published a more contemporary review in which a distinction was made between pacemakers

and ICDs.[19] Both the AAPM and the Frizzell reports are widely referenced in the literature and, in our opinion, have the most robust evidence base to support them. The AAPM report is now nearly two decades old and does not take into account subsequent advances in CIED or radiotherapy technology and treatment delivery.[1] A Dutch update of the 1994 AAPM guidelines was published by Hurkmans et al, in 2012[6] and in 2015 Gauter-Fleckenstein et al published the DEGRO/DGK guidelines.[9] Both papers have been referenced in these guidelines where appropriate.[6] In the absence of more contemporary research on safely treating CIED patients with radiotherapy, it is reasonable to use the AAPM recommendations, the Frizzell review, the Dutch update and DEGRO/DGK guidelines as the basis of a UK guideline document.

Currently, there are no UK guidelines on the use of radiotherapy in patients with CIEDs. A national review of current cardiac device policies from radiotherapy centres across the UK reported that 30% of UK radiotherapy centres have no policy for managing patients with CIEDs.[1] Results showed that policies differ between radiotherapy centres and a significant number of policies do not adhere to current established tolerance doses for CIEDs. In the departments where there is a CIED policy, the majority do not reflect best evidence.[1] There is limited published research on the effect of radiotherapy on CIEDs, but there is evidence to show that radiotherapy even at low doses can cause malfunction or failure with potentially life-threatening consequences.[11] Given this risk, all radiotherapy centres should have policies in place to support the safe delivery of radiotherapy in patients with CIEDs.[1]

In 2014, a multidisciplinary working party was established with the aim of providing national guidance for clinicians, therapy radiographers and medical physicists on the management of cancer patients with a CIED who are receiving radiotherapy.

This document reviews the evidence and literature to determine current ‘gold standard’ practice and provides recommendations for the management of cancer patients who have a CIED and are receiving radiotherapy.

2. Summary of recommendations

- CIEDs should not be placed directly in the radiotherapy treatment beam
- The cumulative radiotherapy dose received by a pacemaker should not exceed 2Gy
- Patients with rate-adaptive pacemakers should be reviewed by cardiology and consideration given to temporary deactivation of the sensor whilst receiving radiotherapy
- The cumulative radiotherapy dose received by an ICD should not exceed 0.5Gy
- The photon beam energy should be $\leq$10MV
- The dose contribution from on-treatment verification imaging should be taken into account when calculating cumulative radiotherapy dose

- The patient's cardiologist should be informed in advance of any planned radiotherapy for advice on monitoring during radiotherapy and subsequent follow-up
- Patients with CIEDs should be fully informed of the potential short- and long-term risks of radiotherapy. This should be included in patient information available from the cardiology department in addition to radiotherapy patient information
- Patients should be allocated an appropriate risk categorisation group as defined in Table 1
- Monitoring requirements based on the patient's risk categorisation group should be implemented
- Appropriately trained staff should be involved in CIED monitoring during radiotherapy

3. Patient management

The management of CIED patients undergoing radiotherapy is summarised in Table 2. The roles and responsibilities of staff involved in the management of these patients is summarised in Table 3.

3.1 Before radiotherapy

All patients should be screened for the presence of a CIED as part of the radiotherapy planning process. Once these patients have been identified, CIED information should be annotated as stated on the patients' CIED identification card. Staff should be aware that some cardiologists place the CIED on the patients' right side if they are left-handed. Anecdotal evidence from a national review showed that in some cases, a CIED is not discovered until a patient attends for radiotherapy.[1] This results in treatment being delayed or proceeding without safety measures in place. Planned radiotherapy treatment details should be recorded as per standard practice. The cardiology team should be informed as soon as possible to facilitate patient review before radiotherapy with the aim of establishing CIED functionality. The purpose is to detect any possible change in pacing-dependency of the patient. If an examination of technical CIED function has not been conducted within the previous three months, it is recommended that it should be carried out prior to the patient commencing radiotherapy. The cardiologist should also recommend appropriate CIED monitoring during and after radiotherapy. Patients with rate-adaptive CIEDs must be reviewed by cardiology before a planned course of radiotherapy begins and consideration given to deactivating the sensor.

3.1.1 Radiotherapy planning

If the CIED is near or in the anticipated treatment field or volume, it should be included in the planning computed tomography (CT) scan. This will allow accurate estimation of the cumulative radiotherapy dose received by the CIED. The CIED should not be in the planning target volume (PTV) in order to minimise the dose to the device. Radiotherapy beam energy no greater than 10MV should be used to avoid neutron contamination.[6,9,20] The medical physics team should be informed of the presence of a CIED and every effort

should be made in the planning process to limit the cumulative dose to the device.

3.1.2 Risk group

It is not possible to predict the exact behaviour of any given CIED when it is in, or in close proximity to, the radiotherapy treatment field.[9] Research indicates that the risk of CIED malfunction increases as the cumulative radiation dose to the CIED increases. In addition, the risk to the patient is greater if the patient is pacing-dependent. These include patients whose pacemaker is pacing all the time (and who are at risk of asystole if the pacemaker malfunctions) and patients with a resynchronising pacemaker where the patient may be at risk of increased heart failure symptoms in the event of device malfunction.

Patients with a pacemaker should be allocated a risk group based on their pacing dependency and estimated cumulative radiotherapy dose received. In 2015, Gauter-Fleckenstein et al proposed a risk categorisation that incorporates these two parameters (Table 1)**.**[9]

Low risk patients:

- Pacemaker independent, and the device is anticipated to receive a cumulative radiotherapy dose of less than 2Gy

Medium risk patients:

- Pacemaker dependent and the device is anticipated to receive a cumulative radiotherapy dose of less than 2Gy
- Pacemaker independent and the device is anticipated to receive a cumulative radiotherapy dose of between 2Gy and 10Gy

High risk patients:

- Pacemaker dependent and the device is anticipated to receive a cumulative radiotherapy dose of between 2Gy and 10Gy
- All patients (pacemaker dependent and independent) and the device is anticipated to receive a cumulative radiotherapy dose of more than 10Gy

Patients with an ICD in situ should be regarded as high risk. The estimated cumulative radiotherapy dose to the ICD should not exceed 0.5Gy.

For all CIEDs, the potential dose received from on-treatment verification imaging should also be taken into account. This is especially important with ICDs, which have a much lower recommended maximum cumulative radiotherapy dose of 0.5Gy.

In patients identified as being medium or high risk, the clinical oncologist should liaise with medical physics to discuss how to optimise the patient's radiotherapy plan and limit the cumulative dose to the CIED. If after optimisation of the radiotherapy plan the estimated cumulative dose exceeds those outlined above then a review of management options should take place. If radiotherapy is felt to be the most appropriate management option, it is

recommended that the clinical oncologist should liaise with the cardiology department.

3.1.3 Consent

Patients consenting for any type of treatment need to be informed of potentially serious side effects related to that treatment. During the consent process the clinical oncologist should discuss the potential damage to the CIED during and after radiotherapy. Patients should be told they will be subject to close monitoring during treatment and further follow-up after radiotherapy has finished. Given the lack of contemporary research in this area, it is not possible to quantify this risk of damage or harm at present, but discussion of potential complications should take place for all patients with a CIED. Patients with rate-adaptive CIEDs may have their sensor deactivated for the duration of radiotherapy treatment. It is important that the implications and risks of this are fully discussed with the patient by the cardiology team before any planned radiotherapy. ICDs are considered susceptible to radiotherapy damage at lower doses than pacemakers. For this reason, all ICD patients should be informed about the possibility of malfunction or failure resulting from radiotherapy treatment as the complications may be life threatening. ICD patients should be informed in advance of radiotherapy that their device will be deactivated using a magnet during treatment.[9,19,20]

3.2 During radiotherapy

All patients with CIEDs should be monitored with a continuous ECG strip during their first radiotherapy treatment.[9,18-20] This strip should then be reviewed for any evidence of pacing disruption when radiotherapy is being administered. Particular attention should be given to any pacing discrepancies when the radiation beam is turned on and off. If the patient is classified as low risk (cumulative dose to the cardiac device is <2Gy and the patient is non-pacemaker dependent) and there are no changes on the ECG monitoring, further monitoring is not required during the remainder of the radiotherapy treatments. If the patient is classified as medium or high risk (cumulative dose to the cardiac device is >2Gy or the patient is pacemaker dependent or has an ICD) they will require ECG monitoring throughout the course of their radiotherapy.[6] Patients who have an ICD require daily monitoring owing to their device being deactivated during radiotherapy treatment. The patient should be observed during treatment with audiovisual monitoring. Monitoring staff should document any changes in the patient's physical status, and any changes in the ECG trace should be documented and reviewed after every radiotherapy treatment. The minimum level of training received by monitoring staff should include Immediate Life Support (ILS) and appropriate resuscitation equipment should be available at all times. If therapeutic radiographers are monitoring patients, they should receive specific training on the management and monitoring of these patients. If at any point malfunction is suspected or detected, the clinical oncologist and cardiologist should be immediately informed.

ICDs have a much lower cumulative radiotherapy dose limit of 0.5Gy.[9,19,20] ICDs should be deactivated prior to the patient's daily radiotherapy treatment by placing a magnet over the device to prevent inappropriate therapy or shock

delivery as a result of accidental sensing of radiation interference. When deactivating ICDs, there should be the ability to externally pace the patient if appropriate. Defibrillation devices available should be able to deliver external pacing and staff with Advanced Life Support (ALS) training or an ability to deliver external pacing should be available.

3.3 After radiotherapy

The importance of both short- and long-term follow-up monitoring for patients who have a CIED and have received radiotherapy was highlighted in a paper by Last.[5] Patients should have their cardiac device checked within two weeks of completion of their radiotherapy and then one, three and six months after treatment. Devices exhibiting signs of dysfunction should be followed up with increased frequency. This will allow discrimination to be made between a temporary dysfunction that may occur owing to a build-up of charge within the semiconductor and more permanent circuitry damage.[21] Should any additional changes be observed during the follow-up period then immediate device revision is likely to be necessary.

Table 1:

Risk categorisation determined by dependence and cumulative radiotherapy dose to pacemaker

	< 2Gy	**2 – 10Gy**	**> 10Gy**
Pacing independent	Low risk	Medium risk	High risk
Pacing dependent	Medium risk	High risk	High risk

***Table 2**:*
Summary of management of CIED patients receiving radiotherapy

Before radiotherapy
Consultant clinical oncologist highlights CIED status
CIED information annotated as stated on the patient device identification card: • Type of device: eg bradycardia pacemaker, resynchronising pacemaker, ICD or combined pacemaker/ICD, resynchronising pacemaker/ICD • Manufacturer • Make • Model • Date of implantation • Implantation site • Patient dependence on CIED
Radiotherapy treatment details recorded: • Radiotherapy treatment site • Radiotherapy prescription • Radiotherapy treatment technique
Clinical oncologist should liaise with patient's cardiology department regarding: • Monitoring requirements • Requirement for device reprogramming or deactivation • Follow-up and review appointments
CIED to be included in CT planning scan if close to anticipated radiotherapy treatment field
Medical physics calculates estimated cumulative radiotherapy dose to the CIED
Patients allocated a risk categorisation
Patients with CIEDs should be fully informed on the potential short- and long-term risks of radiotherapy and consent appropriately

During radiotherapy	
Low risk patients	Day one of radiotherapy – audio-visual and ECG monitoring by appropriately trained staff
	Appropriately trained staff determine patient's monitoring requirements for subsequent radiotherapy treatments
Medium risk patients	Audio-visual and ECG monitoring by appropriately trained staff for every fraction of radiotherapy treatment
	Weekly CIED check by patient's cardiology department
High risk patients	Potential CIED relocation
	Audio-visual and ECG monitoring by appropriately trained staff for every fraction of radiotherapy treatment
	Weekly CIED check by patient's cardiology department
ICD patients	Day one of radiotherapy – 12 lead ECG should be performed by an appropriately trained staff member as a baseline
	Appropriately trained staff member must deactivate the ICD during radiotherapy treatment by placing the specialist magnet over the ICD
	Audio-visual and ECG monitoring by appropriately trained staff for every fraction of radiotherapy treatment
	Weekly ICD check by patient's cardiology department
After radiotherapy	
CIED device check-up, two weeks after radiotherapy treatment by cardiology department	
Cardiology follow-up one, three and six months after radiotherapy treatment or as advised by cardiology department	

Table 3:
Roles and responsibilities of staff involved in the management of CIED patients receiving radiotherapy

Clinical oncologist
Identify patient's CIED status and highlight on radiotherapy referral form
Contact patient's cardiology department before commencing their radiotherapy treatment
Request cardiology assessment / CIED device check
Provide medical physics with information to calculate cumulative radiotherapy dose to CIED
Check the dose to the pacemaker does not exceed 2Gy
Check the dose to the ICD does not exceed 0.5Gy
Consent – patient aware of potential adverse effects of radiotherapy on CIED
Consent – patient aware that ICD will be switched off during radiotherapy
Planning radiographers
Annotate patient's CIED status
CIED included in CT planning scan if in/close to the radiotherapy treatment field
Medical physics informed of patient's CIED status
No direct placement of CIED in radiotherapy beam
Limitation of radiotherapy beam energy to 10Mv
Contact consultant clinical oncologist if the CIED is within the radiotherapy treatment field or the estimated cumulative dose is too high
Appropriately trained radiographers
Assess patient prior to commencing their radiotherapy treatment
Highlight patient's monitoring requirements

Monitor the patient during their radiotherapy treatment
If the patient has an ICD, deactivate the device during each fraction of radiotherapy treatment
Arrange follow-up appointment with the patient's cardiology department
Treatment radiographers
Do not commence patient's radiotherapy treatment without ensuring correct procedure has been followed
Do not commence patient's radiotherapy treatment without the presence of the appropriately trained staff to monitor the patient
Read and be conversant in CIED department policy
Medical physics
Calculate estimated cumulative radiotherapy dose to the CIED and leads prior to the patient commencing radiotherapy treatment. Previous radiotherapy courses received must be taken into consideration

4. Evidence review

4.1 Methodology

A multidisciplinary working party was established to provide guidance for the management of cancer patients with a CIED who are receiving radiotherapy. The Cochrane Library and Medline via OVID were searched for articles, guidelines and systematic reviews. The search was performed in January 2014, combining search terms 'radiotherapy' or 'radiation therapy', 'pacemaker', 'ICD'. In addition 'hand searching' of relevant clinical journals, guidelines and meeting abstracts was carried out.

4.2 CIED technology

The number of patients with CIEDs undergoing radiotherapy treatment is increasing.[2,3,4] Although most medical treatments pose little danger to the functioning of CIEDs, radiotherapy has the potential to cause device malfunction.[5] The design and technology of CIEDs has evolved, allowing improved efficiency and functioning. Over the past three decades the use of complementary metal-oxide semiconductor circuits in cardiac devices has expanded.[6] These are more sensitive to ionising radiation than the older bipolar semiconductor devices used previously, possibly resulting in damage to the hardware and software components.[7] Damage could be transient, with dropped beats, transient inhibition, altered sensitivity, increased or decreased pulse width and frequency or triggering of pacemakers. Severe damage caused by radiation may lead to catastrophic failure of the cardiac conduction system in the device.[8]

4.3 Pacemakers

The AAPM report recommends that the maximum dose to a pacemaker should be limited to less than 2Gy.[18] A study by Mouton et al supported the AAPM recommendations.[8] In their in vitro study, ninety-six patients having thoracic radiotherapy whose pacemakers were adjacent to the radiotherapy treatment field exhibited a range of short- and long-term side effects. Results showed that one pacemaker exhibited clinically significant disturbances at a dose rate of 0.2Gy/min at a cumulative dose of only 0.15Gy, two pacemakers exhibited defects at a cumulative dose of 1Gy and nine pacemakers failed at a cumulative dose of 2Gy.[8] Hurkmans et al directly irradiated nineteen new pacemakers; the commonest damage reported was loss of output.[11] In contrast, in the Mouton study only one pacemaker malfunctioned below 50Gy, suggesting modern pacemakers may be relatively radioresisitant.[8] The authors concluded that the AAPM recommendations were still valid. Importantly, in the Mouton study, pacemakers were not returned to the manufacturers for a more detailed analysis after irradiation, so potentially significant damage may have been missed. There is little in the academic literature on the effect of radiotherapy on rate-adaptive CIEDs. It is the authors' observation (unpublished) that they may be influenced by radiotherapy, causing temporary increased sensor rate and tachycardia. Other potential effects of radiotherapy on CIEDs include temporary loss of sensing, temporary device inhibition, temporary loss of capture and device reset [St Jude Medical – Effect of Therapeutic Radiation on St Jude Medical

Implantable Cardiac Rhythm Devices, October 2013]. This observation is also recognised in the Frizzell review.[19]

4.4 ICDs

Frizzell published a more contemporary review of CIEDs and radiotherapy, concluding that the AAPM recommendations were no longer comprehensive as ICDs were not discussed.[19] ICDs are more sophisticated and have the ability to automatically defibrillate the heart by monitoring the patient's heart rate and deliver the appropriate electrical therapy. Frizzell recommended a lower radiotherapy tolerance dose of 0.5Gy for ICDs. This tolerance dose is partly based on work by Hurkmans et al who directly irradiated 11 ICDs. This study observed that the dose at first malfunction was as low as 0.5Gy.[19] It is also recommended that ICDs should be deactivated prior to each fraction of radiotherapy by placing a magnet over the device to prevent inappropriate therapy or shock delivery as a result of accidental sensing of Electromagnetic Interference (EMI).

4.5 Beam energy

Gelblum et al reported on 33 patients with ICDs receiving radiotherapy. Two ICDs were reset to the factory settings during treatment for pelvic cancers with 15MV photon beams.[20] Elders et al reported on 15 patients with ICDs who underwent radiotherapy treatment on linear accelerators with beam energies of between 6 and 18MV. In total, six ICD malfunctions were found, and all occurred with beam energies $\geq$ 10MV.[22] Both authors postulated that the cause of the ICD malfunctions was related to neutron production with higher energy beams. This has lead to other guidelines recommending that photon beam energy is kept to $\leq$10MV when treating patients with CIEDs.[6]

4.6 CIED leads

No published guidelines make reference to lead dose. The consensus view is that leads are relatively insensitive to radiation damage compared to CIEDs.[6] However, there is no evidence to inform dose constraints to CIED leads and so, in the authors' view, every effort should be made to keep the leads out of the treatment field. If this is not possible, then the dose to the lead should be kept as low as possible.

4.7 On-treatment verification imaging

No published guidelines make recommendations on the potential contribution of imaging techniques to the CIED cumulative dose. Murphy et al reported that the dose from a kilovoltage cone beam CT scan is likely to be in the region of 10-80mGy.[23] Kan et al reported mean skin doses of 6.4cGy per kilovoltage cone beam CT chest scan.[24] Even using the lower limit of 10mGy from Murphy et al, it is possible that daily cone beam CT in a 20-fraction radical lung treatment may contribute as much as 0.2Gy. Using the Kan et al skin dose estimates, it is possible the CIED may get significantly more than 0.2Gy. An estimation of the dose contribution from the image verification method used should be made and this should be taken into consideration when allocating CIED patients to a risk group.

5. Audit procedure

Radiotherapy centres should conduct a regular audit looking at guideline implementation.

The following compliance standards should be included in the audit:

- Radiotherapy tolerance doses used for the specific CIEDs
- Classification of patient risk category
- Adherence to patient management pathway and implementation
- Adherence to monitoring procedures
- All staff members aware of their roles, responsibilities and scope of practice

6. Implementation

Radiotherapy centres should circulate this document to all relevant staff. Consideration should be given on how best to implement the recommendations and audit adherence to these recommendations. Adaptation of the guideline may be appropriate to best reflect local practice and expertise.

7. Staff and department requirements

- All staff involved in the requesting, planning and delivery of radiotherapy should be aware of the guideline and their role in ensuring appropriate and safe management of patients with CIEDs
- Communication links between the radiotherapy and cardiology departments are vital. Staff should be aware of who to contact and how to seek advice
- Monitoring staff should receive specific training on the management of CIED patients
- The radiotherapy department is responsible for training the staff
- The radiotherapy department is responsible for the availability of appropriate equipment for monitoring of patients

8. Conclusion

This is a guideline on the safe management of patients with a CIED receiving radiotherapy. It is based on current best evidence, and should be used and adapted to best suit local practice in radiotherapy departments.

9. Pacemaker manufacturer documents

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Medtronic:

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St. Jude Medical:

St. Jude Medical (2014) Effects of Therapeutic Radiation on St. Jude Medical Implantable Cardiac Rhythm Devices

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Appendix I

Public Health England

Protecting and improving the nation's health

Safer Radiotherapy

Radiotherapy Newsletter of Public Health England
May 2015 Issue 16

Welcome to the 16th issue of *Safer Radiotherapy*. The aim of the newsletter is to provide a regular update on the analysis by PHE of radiotherapy error (RTE) reports. These anonymised reports are submitted on a voluntary basis through the National Reporting and Learning System (NRLS) of NHS England or directly to PHE, to promote learning and minimise recurrence of these events.

Safer RT is designed to disseminate learning from RTEs to professionals in the radiotherapy community to positively influence local practice and improve patient safety.

Now published three times a year, *Safer RT* will contain key messages and trends from the preceding four-month period of RTE reports.

Any comments and suggestions for inclusion in the newsletter would be gratefully received. They should be sent to **radiotherapy@phe.gov.uk**.

Thanks to all contributors to this issue. The next issue of *Safer RT* will be published in September 2015 and will be available at **https://www.gov.uk/government/collections/medical-radiation-uses-dose-measurements-and-safety-advice**.

Helen Best
Editor

INSIDE THIS ISSUE

Patient Safety in Radiotherapy Steering Group (PSRT)

As highlighted in issues 14 and 15 of *Safer RT*, the PSRT continues to develop the learning from RTEs and their analysis.

The draft causative factor taxonomy is currently being piloted across ten clinical sites. The final taxonomy will be made available for use across the radiotherapy community to support trends analysis.

In parallel, work on refining the pathway coding is underway (see page 3). Comments from across the radiotherapy community have already been received. In addition, it is proposed that this work will include the introduction of safety barriers, also known as critical control points or detection methods. These include any process steps whose primary function is to prevent the occurrence of errors.

Once agreed by the PSRT, this will be shared with the pilot sites for comment.

The Radiotherapy Team is based at PHE CRCE Chilton

EDITORIAL HEADLINE

Development of the Patient Safety Incident Management System (DPSIMS) Project

The NRLS is a database of patient safety incident reports submitted by NHS organisations across England and Wales, and directly by patients, specifically for the purposes of learning. Hospitals regularly upload incident reports from their local systems to the NRLS, where they are analysed by national patient safety experts to spot trends, specific incidents of concern or emerging risks to patient safety. Radiotherapy departments include the TSRT trigger code in reports so that these might be highlighted for national analysis by PHE and lessons shared with the professional community.

The DPSIMS Project (previously known as the NRLS Development Project) was started in 2014. It is a three-year project to specify and procure a replacement for the NRLS, to support the ability of the NHS to learn and improve on the basis of reported experience.

Engagement to date has included a survey, focus group and workshops for patient advocates and professional users of the NRLS, providing an opportunity to influence the future of patient safety reporting and learning. More recently, a series of clinical site visits to explore the potential impact of various options for the NRLS successor system on local level provision has been conducted with ten sites, the findings of which will be published in the coming weeks.

Further information can be found at **http://www.england.nhs.uk/ourwork/patientsafety/dpsims-dev/**.

RTE Data Analysis: December 2014 to March 2015

Data Analysis

Submissions from 56 NHS UK RT departments contributed to this issue's full data analysis, for 1 December 2014 to 31 March 2015, which is available at **https://www.gov.uk/government/collections/medical-radiation-uses-dose-measurements-and-safety-advice**. This is a slight increase from 52 at the last analysis, reflecting the strong reporting culture that continues in the UK RT community.

The analysis includes data on primary process coding and severity classification of the RTEs. A breakdown of primary process codes by classification levels is also included.

New NHS radiotherapy providers are welcome to contact radiotherapy@phe.gov.uk for advice on how to submit data.

Classification of RTEs

Of those RTEs reported for the period December 2014 to March 2015, 1772 out of 1851 reports (95.7%) were classified as minor radiation incidents, near misses or other non-conformances (see Figure 1). This is consistent with previous analyses. These are lower level incidents which would have no significant effect on the planning or delivery of individual patient treatments.

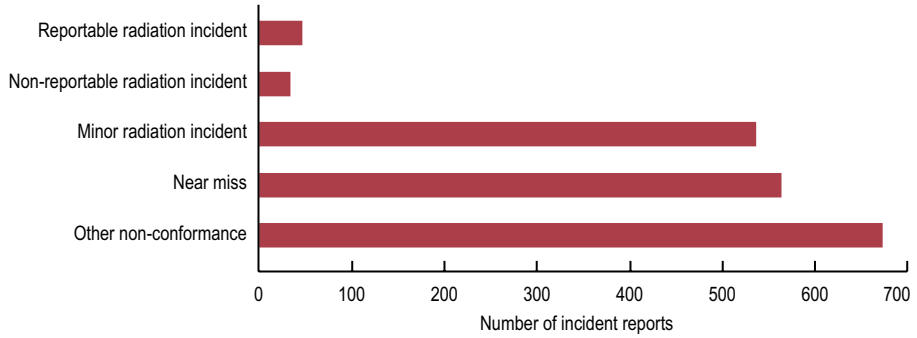
Reportable radiation incidents (level 1) made up 46 (2.5%) of all reports. Pretreatment 'positioning of patient' comprised 6 (13%) and treatment 'on-set imaging: approval process' comprised 5 (10.9%) of all level 1 RTEs reported for this time period. Non-reportable radiation incident reports (level 2) made up 33 of all reports (1.8%). 'On-set imaging: approval process' and 'movements from reference marks' each comprised 4 (12.1%) of all level 2 RTEs.

Of the 536 minor radiation incidents (level 3) reported, 119 (22.2%) of this subset were related to 'on-set imaging: production process', making it the most frequently occurring code in this classification. The second most frequently occurring type of incident, at 64 (11.9%), was 'use of on-set imaging'. On-treatment imaging is discussed further in issue 12 of *Safer RT*.

The most commonly occurring RTE process code in the near miss (level 4) classification was treatment 'on-set imaging: approval process', with 46 reports (8.1%).

Within the non-conformance (level 5) classification, 'bookings made according to protocol' had 49 reports (7.3%), making this the most frequently occurring RTE in this classification.

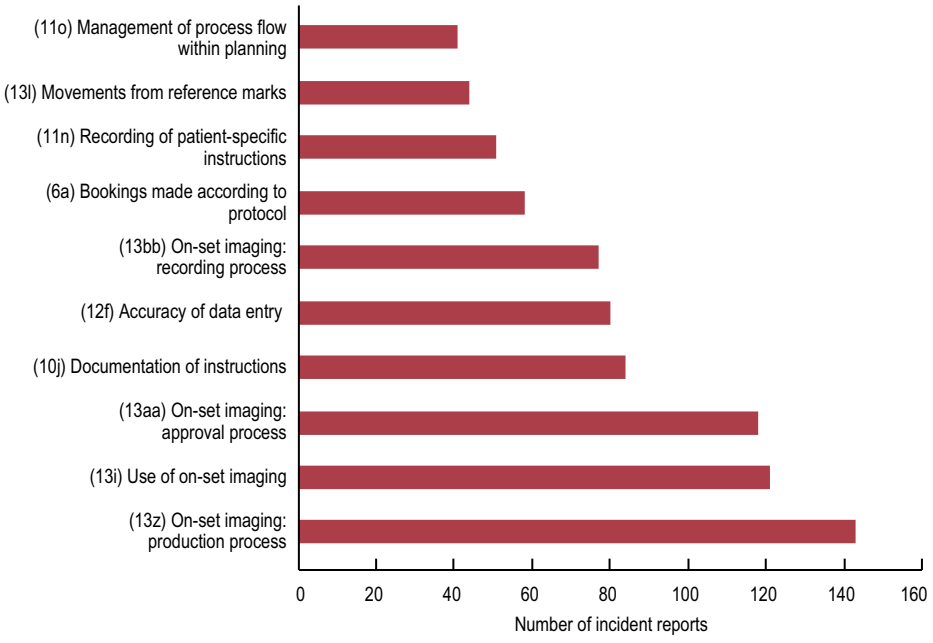
Figure 1 ***Classification breakdown of RTE reports using the TSRT9 trigger code, December 2014 to March 2015 (1851 reports)***



Primary Process Code

The main themes (points in the patient pathway where the majority of reported RTEs occurred) for this dataset are shown in Figure 2. Imaging process codes contributed to 459 of the reports in the main themes (56.1%), making up 24.7% of all reports in this reporting period. Of note, 'on-set imaging: production process' contributed to 143 of the reports in the main themes (17.5%). This will be discussed further in the *Error of the Month*.

Figure 2 ***RTE main themes (817 out of 1851 reports), for December 2014 to March 2015 (with process code indicated)***



The data analysed is submitted by the RT community. If you have any suggestions on how the process coding can be refined, please email the Radiotherapy Team at **radiotherapy@phe.gov.uk**.

Consistency Checking

Consistency checking on the application of the TSRT classification and pathway coding by local RT departments is undertaken by PHE staff on all RTE reports.

Classification

The classification or severity of the event was amended for 31 (1.6%) reports in this reporting period. The amendments were made from 25 (80.6%) reports classified as near misses and 6 (19.4%) reports classified as non-conformances. Of the near misses reclassified, the majority (24) were changed to minor radiation incidents. If an RTE includes an unintended exposure, including on-set imaging, this will be classified as a minor radiation incident or above.

Classification allocated by department	Text description	Reclassification in consistency checking	Comments
Near miss	Images taken for planning procedure, no confirmed diagnosis, departmental protocol requires confirmed diagnosis. Patient ultimately not for radiotherapy treatment	Reportable radiation incident	Although no treatment given, planning images taken before confirmed diagnosis, resulting in unnecessary dose
Near miss	Digital moves completed in incorrect direction, on-set images acquired showing incorrect move. Re-set and moved in correct direction and repeated on-set imaging	Minor radiation incident	Although treatment in correct area, additional on-set imaging taken

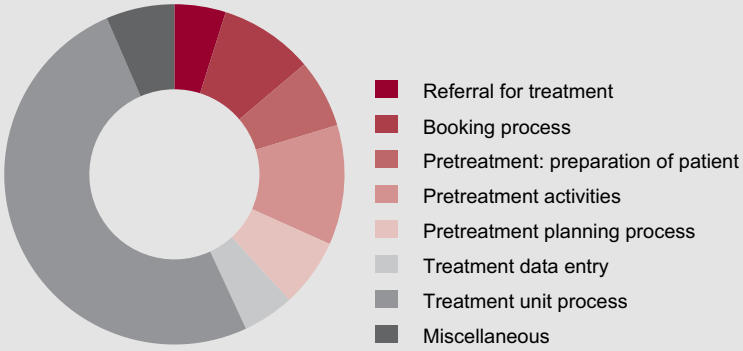
Primary pathway coding

The pathway coding was amended for 127 (6.8%) reports in this reporting period.

The amendments were made on reports associated with the entire patient pathway. Of these, 78 (61.4%) were coded locally from 'other' process codes. PHE staff attributed existing pathway codes to these reports. This suggests there is a need to reduce the ambiguity of some of the terms used in the pathway coding. Reports locally coded as 'other' which could not be amended to existing pathway codes made up 82 (4.4%) of the reports in this reporting period.

This highlights the need for refinement of the pathway coding to reflect current practice. This work is currently being undertaken.

Original pathway codes for amended reports, December 2014 to March 2015



For this reporting period the most frequently changed pathway coding was found in the treatment unit process, at 62 (50.4%) reports.

Pathway coding allocated by department	Text description	Newly assigned pathway code
Treatment unit, setting of couch position (13q)	Skin blemish used instead of tattoo	ID of reference marks (13k)
Pretreatment activities, positioning of patient (10b)	Consultant unavailable for set-up as requested	Availability of staff with competency appropriate for procedure (20a)

ERROR OF THE MONTH

On-set imaging

TSRT Process Code: On-set imaging: production process (13z)

This code accounted for 143 (7.7%) RTEs reported from December 2014 to March 2015. It has been the most commonly occurring RTE since June 2014. The majority of these reports, 138 (96.5%), were lower level incidents having little or no effect on the planning or delivery of individual patient treatments.

This RTE is associated with the incorrect production of on-set imaging. The main themes highlighted within these reports included exposed images being unusable due to over-exposure, the incorrect field size exposed or unsuitable positioning of the image panel. This RTE is also associated with equipment malfunction; such errors should also be reported locally and to the MHRA and the relevant manufacturer.

How can we minimise the risk of this RTE occurring?

Points to consider

1. Produce and follow clearly defined and up-to-date protocols
2. Clearly define individual responsibilities
3. Ensure staff are adequately trained, competent and appropriately entitled in the use of the technology
4. Ensure adequate instructions are available on the clinical requirement of imaging
5. Capture image parameters on day 1 and action if further optimisation is required
6. Ensure on-set imaging has been optimised
7. Put in place contingency plans in case of equipment failure
8. Investigate repeat incidents. Consider removal of equipment from practice
9. Monitor locally reported RTEs to identify further preventive action
10. Audit repeated failure to review and update procedures

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GUEST EDITORIAL

Radiotherapy Management of Cancer Patients with a Cardiac Implanted Electronic Device: A Clinical Guideline

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A national review of cardiac device policies being used in radiotherapy departments across the UK was carried out in 2013. This reported that most policies do not reflect current best evidence[1]. To address this, the Royal College of Radiologists, the Society and College of Radiographers and the Institute of Physics and Engineering in Medicine formed a multidisciplinary working party. This group, comprising clinical oncology, cardiology, therapeutic radiography and medical physics experts, has developed evidence-based guidelines for the management of cancer patients receiving radiotherapy with a cardiac implanted electronic device (CIED).

The number of cancer patients with CIEDs receiving radiotherapy is increasing[2]. Most medical treatments pose little danger to the functioning of CIEDs. However, radiotherapy has the potential to alter device function[3]. There is limited published research on the effect of radiotherapy on CIEDs, but there is evidence to show that radiotherapy even at low doses can cause malfunction or failure[4].

The American Association of Physicists in Medicine (AAPM) published a report in 1994 on the safe use of radiotherapy in patients with pacemakers[5]. A later review was produced by Frizzell et al in 2009 and, in 2012, Hurkmans et al updated the AAPM guidelines[6,7]. The AAPM report does not take into account advances in CIED technology and radiotherapy treatment technology and delivery. Despite this, it still forms the basis of most CIED departmental radiotherapy policies in the UK[1].

The multidisciplinary working party has developed a UK guideline which reviews the evidence, defines current 'gold standard' practice and provides recommendations for the safe delivery of radiotherapy in patients who have a CIED.

Summary of recommendations

- CIEDs should not be placed directly in the radiotherapy treatment beam
- the cumulative radiotherapy dose received by the pacemaker should not exceed 2 Gy
- patients with rate-adaptive pacemakers should be reviewed by cardiology and consideration given to temporary deactivation of the sensor while receiving radiotherapy
- the cumulative radiotherapy dose received by an implantable cardiac defibrillator (ICD) should not exceed 0.5 Gy
- the photon beam energy should be less than 10 MV
- the dose contribution from on-treatment verification imaging should be taken into account when calculating cumulative radiotherapy dose
- patients should be allocated an appropriate risk stratification group
- the patient's cardiologist should be informed in advance of any planned radiotherapy for advice on monitoring during radiotherapy and subsequent follow-up
- patients with CIEDs should be fully informed of the potential short- and long-term risks of radiotherapy: this should be included in the patient information available from the cardiology department in addition to radiotherapy patient information

Conclusion

The guideline has been developed to support the safe management of patients with a CIED receiving radiotherapy. It is based on current best evidence, and can be adapted to suit local practice in radiotherapy departments. We are conducting research to further define the effect of radiotherapy on modern CIEDs.

References

1 Lester JF et al. Clin Oncol 2014; 26: 45–50.
2 Brooks N et al. Br J Cardiol 2005; 12: 192–8.
3 Last A. Br J Radiol 1998; 71: 4–10.
4 Hurkmans CW et al. Radiother Oncol 2005; 76: 93–8.
5 Marbach JR et al. Med Phys 1994; 21: 85–90.
6 Frizzell B. Comm Oncol 2009; 6: 469–71.
7 Hurkmans CW et al. Radiother Oncol 2012; 7: 198.

DATES FOR THE DIARY

8–9 June	UKRO, Coventry
28 September	BIR, IR(ME)R update
23 October	BIR, RTE study day
September	*Safer Radiotherapy,* Issue 17