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To investigate the safe levels of radiotherapy administered to patients who have an implanted cardiac device.

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Summary

With an ageing UK population, the number of patients with cardiac pacemakers presenting for radiotherapy treatment is increasing. Research has shown that in clinical practice there are a variety of different pacemakers in use. Over the past three decades manufacturers have increasingly used a variety of pacemaker components which are subsequently more sensitive to ionising radiation. Therefore, this project aim is to investigate the safe levels of radiotherapy administered to patients who have an implanted cardiac device. While it is accepted that pacemaker manufacturers publish their own guidelines regarding radiotherapy tolerance doses to their cardiac devices, research has also shown that there are no national guidelines and most radiotherapy departments have no formal risk management strategy in place or a cardiac pacemaker policy. The policies that are in place are based on manufacturers' guidelines and anecdotal experience from the United States of America and were published in 1994. Due to this there is a clinical need for research based in the United Kingdom to determine the behaviour of a given cardiac device when it is in or close to the radiotherapy treatment field.

Background and Objectives of study

Introduction to study:

With an ageing UK population, the number of patients with cardiac pacemakers presenting for radiotherapy treatment is increasing. Life expectancy of the population has increased by more than 65% in England and Wales over the past century (Office of National Statistics, 2004). One consequence of this increase in longevity is the increase in prevalence of cardiovascular morbidity (Kalache and Keller, 2000). This in turn is leading to an increase in the number of patients with cardiac pacemakers (Last, 1998). The age-standardised incidence of cancer has increased by more than 25% in the past 30 years (Office of National Statistics, 2004). It has been estimated that 50–60% of all patients with cancer will require radiotherapy at some point during the course of their illness (The Royal College of Radiologists, 1998).

Purpose of Research:

Research shows that in clinical practice there are a variety of different pacemakers in use, for example implantable internal pacemakers and implantable cardioverter defibrillators (Marbach et al, 1994). Implantable internal pacemakers, such as bipolar pacemakers, are permanent cardiac devices and they vary in sophistication. Implantable cardioverter defibrillators (ICDs) are more sophisticated devices and they have the ability to automatically defibrillate the heart, by constantly monitoring the heart rate and

delivering appropriate electrical therapy. Pacemakers are usually placed in a subcutaneous pocket over the pectoral muscles in the left infraclavicular region. The pacemaker leads that lie in contact with cardiac musculature, deliver electrical impulses to the heart and carry the signals back to the pacemaker generator (Fischer and Ritter, 1998).

Research has shown that over the past three decades manufacturers have increasingly used complementary metal-oxide semi-conductors (CMOS) circuits in their pacemakers, which 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 pacemaker (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 pacemakers. Nevertheless, 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, 1996).

It is not possible to predict the exact behaviour of any given pacemaker when it is in, or in close proximity to the radiotherapy treatment field (Solan et al, 2004). The American Association of Physicists in Medicine report by Marbach et al in 1994 recommend that the maximum dose to the pacemaker should be limited to less than 2 Gy. Subsequent retrospective data has resulted in further recommendations being issued by Moulton et al in 2002. 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. Their results showed that one of the irradiated pacemakers exhibited clinically significant disturbances at a cumulative dose of only 0.15 Gy, two pacemakers exhibited defects at a dose of 1 Gy and nine pacemakers failed at a cumulative dose of 2 Gy. Therefore there is a significant risk when irradiating patients with cardiac pacemakers (Moulton et al, 2002). While it is accepted that pacemaker manufacturers publish their own guidelines regarding radiotherapy tolerance doses to the pacemaker, research has also shown that there are no national guidelines and most radiotherapy departments have no formal risk management strategy in place or a cardiac pacemaker policy (Solan et al, 2004). The policies that are in place are based on manufacturers' guidelines and anecdotal experience from the United States of America and were published in 1994. Due to this there is a clinical need for research based in the United Kingdom to determine the behaviour of a given pacemaker when it is in or close to the radiotherapy treatment field.

Primary Research Questions

1. What is the effect of radiotherapy on pacemaker function?
2. At what radiotherapy dose does the implanted cardiac device exhibit clinical malfunctions?
3. At what radiotherapy dose does the implanted cardiac device fail at?

Pacemaker failure is the inability of an implanted artificial pacemaker to perform its intended function of regulating the beating of the heart. It can be defined as failure to sense and/or failure to pace the heart (Reinhart et al, 1981).

There are two main types of pacemaker clinical malfunction:

- Minor malfunctions – these can be transient and pose little risk to the patient.
 - For example prolonged change of interference or 'safety mode pacing'
 - Minor malfunctions can occur at doses as low as 2Gy
- Significant malfunctions – cause definite risk to the patient.

- For example extreme fixed rate output, prolonged pacemaker inhibition and total shutdown.
- This will require immediate replacement of the damaged pacemaker
- Significant failure is in the range of 15-36Gy

Dissemination Strategy

- Through peer review journals (in Radiography, Clinical Oncology and Cardiology).
- National and International presentations:
 - Society of Radiographers - Radiotherapy Conference 2011
 - UKRO 2011
 - ESTRO 2011
 - Pacemaker Manufacturers Annual Conference (St. Jude Medical – Stockholm and Biotronik – Berlin)
- Velindre Cancer Centre (Radiographers and Medical Physics):
 - CPD 'lunch and learn' sessions
 - Presentation - clinical audit of VCC adherence to their Cardiac Pacemaker Policy
 - Presentation of research proposal and aim of the research project
 - Present findings and results of research project
 - Present how the research project will form National Guidelines
- Link with Radiography students (Cardiff University)
 - Presentation - Overall summary and aim of the research project
 - How I have been involved in research since graduating from Cardiff University
 - Engage their involvement in the research project
- Work with the pacemaker manufacturers to produce radiotherapy tolerance doses for the cardiac devices
- Work with the Society of Radiographers to produce clinical guidelines for the profession

Method

Using a quantitative methodology, the research will adopt an experimental approach to data collection. The primary issues for this experiment are the conditions of the devices and the environmental factors that exist.

Device conditions:

20 pacemakers from four different manufacturers (Biotronik, Boston Scientific, Medtronic and St. Jude Medical) will be tested in this study. All the devices will be new (no used devices will be included in the study, as they might have a history of use, which could influence results).

Pacemakers programmed accordingly:

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

Environmental conditions:

- Room temperature will be recorded
- Room pressure will be recorded
- Linear accelerator energy – 6Mv

The devices will be connected to a simulator which will replicate the electrical behaviour of a paced heart. The simulator will establish the demand function of the device and test electrocardiogram monitors. It will differentiate between natural sinus beats and paced beats and it will also define the refractory period of the device. The output pulse across the load will be monitored using an oscilloscope and an ECG machine. A stepped attenuator giving a range of millivolt settings was used to give pre-set amplitude inhibition pulses. TLDs will be placed directly on the device and on the nearest edge of the radiotherapy treatment field. In order to mimic clinical practice, the cardiac device will be placed in a phantom and tissue equivalent bolus material will be placed on top of it, such that the middle of the device is located at the maximum dose depth (1.6cm). The device being studied will be positioned precisely along the projected central ray of the primary radiation beam.

The linear accelerator to be used will be Varian linear accelerators with 120 MLC and portal imaging with an x-ray energy of 6Mv, set at a dose rate of at a rate of 600 MU/min. The phantom containing the device will be mounted with the plane of the device at the isocentre. The x-ray field collimators will be opened to encompass the device within the primary x-ray beam.

In order to determine at which point a device exhibits a certain malfunction, the devices will be irradiated to a total dose of 50Gy in 25 fractions (increasing dose by 2Gy per fraction). After every 5 fractions (increasing dose delivered by 10Gy every 5 fractions) the device will be subjected to functionality baseline tests to determine if the device is still operating. If these tests prove that no adverse damage has been caused to the device, they will be returned to the hospital and irradiated for another 10Gy (in 5 fractions). This process will continue until the device has received a cumulative dose of 50Gy. If at any point the devices exhibit signs of damage or any adverse effects they will be sent away to the specific

pacemaker manufacturer. The manufacturers will extensively test and analyse the device and provide a full service report. Thereafter, the devices will be returned to the hospital and irradiated to their definite point-of-failure (120Gy).

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

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