THE DOSIMETRIC IMPACT OF IV CONTRAST WHEN PLANNING RADIATION THERAPY FOR RADICAL LUNG CANCER

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A Thesis submitted in partial fulfillment of the requirements for the Masters of Health Science at Unitec Institute of technology, Auckland, New Zealand 2010
ABSTRACT

The purpose of this study is to investigate the need to account for the presence of Intravenous (IV) contrast on planning computered tomography (CT) scans of the thorax for the radical treatment of lung cancer.

This study required the relationship between CT numbers and relative electron densities (RED) to be also investigated. Research in this area has concluded that CT numbers of high atomic number materials, such as contrast, currently cannot be accurately converted to RED for use in planning. This study therefore used the current CT-RED conversion file to investigate the impact of contrast on calculations in the thorax.

Previous authors who have conducted research on the impact of IV contrast on planning calculations have used many different experimental methods. The validity of many of these previous studies comes into question due to the experimental designs selected. For this reason, this study has been designed to use a research method which is meant to represent the actual clinical situation more accurately.

The optimal experimental design for investigating the dosimetric effect of IV contrast in a clinical situation is the pre-test/post-test design. As current protocol at the research location is to take pre- and post-IV contrast scans, both were available for data analysis. Assessment involved comparing dose calculations on contrast-containing CT scans to non-contrast scans. For each patient entered into this study, a plan was completed using both the non-contrast and contrast CT scans, keeping the monitor units (MUs) delivered constant. Dose Volume Histogram (DVH) data from each plan was collected for analysis. Variables recorded included: lung V5, 20 and 30, mean lung dose (MLD), spinal cord maximum dose, heterogeneity index, conformity index.
Previous researchers have found that the impact of IV contrast on dose calculations in the head and neck region was insignificant. However, significant differences have been found using phantoms and in some small studies performed on other anatomical sites. Many of these studies did not accurately reproduce real clinical situations as they employed experimental methods that forced relative electron densities to represent contrast enhancement on non-contrast CT scans. This limits the extent to which results from these studies can be applied to clinical situations.

This study found no significant differences between the plans produced on the contrast scans and non-contrast scans.
ACKNOWLEDGEMENTS

I would like to firstly acknowledge and thank my supervisors, Dr John Poletti and Dr Jenny Cox for their help and support over the long course of this thesis. Without their guidance and feedback this would not have been possible.

Dr Patries Hurst input has been invaluable, thank you so much for the many discussions and brainstorming sessions you have done with me, as well as practical help with tables and graphs!

The medical physicists of Midcentral health have been great sounding boards and a wealth of help, especially Keith Croft, Tania Groudeva and Iordan Kostourkov. Sarah Mc Dermott a visiting physics technician also was extremely helpful in sharing her recent thesis and helped me take many of the measurements required – thank you all so much.

Pauline McChesney – where would I be without your ruthless proofreading and helpful suggestions, thank you.

To all my friends and family, thanks for the encouragement in my postgraduate study, without it I don’t think I would have got this far.
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CHAPTER 1. INTRODUCTION

1.1 AIM:

The purpose of this study is to investigate whether there is a need to account for the presence of IV contrast on planning CT scans of the thorax for radical radiation therapy for lung cancer. The current protocol for the treatment of lung cancer at my place of work and many other departments in New Zealand is to take two scans, one prior to the administration of IV contrast and then one immediately following the administration. These images are then fused and used to aid in the delineation of the planning targets. The data sets are then separated and planning takes place on the non-contrast CT scan data.

Primary Aim:

- Investigate the differences produced in the dosimetry when planning in the presence of IV contrast compared to scans with no IV contrast present.

Sub Aims:

- Investigate the accuracy of the CT number – RED conversion for IV contrast.

- Quantify any errors caused by the CT-RED conversion.

- Make recommendations to the research centre, and other radiation therapy departments considering the use of IV contrast in radiation therapy planning of the thorax, on the optimal method for planning in the presence of IV contrast.

This study begins by exploring and reviewing previous research in this area. A full literature review is done on previous studies and the optimal process for conducting this type of research is discussed. Some background information on CT numbers and Relative Electron Densities (RED) is given. Two main experiments were then conducted, an investigation into
the CT-RED number conversion which is then followed by the main experiment; the investigation into the effect of contrast on the CT-RED conversion and the degree at which this impacts on dose calculations. These experiments are then flowed by the results and a discussion of these. Finally some conclusions and recommendations are made.

1.2 BACKGROUND

In New Zealand, lung cancer is the most common cause of cancer death for males and the third most common for females ("Cancer: New registrations and deaths 2005", 2008). Whilst surgery is a potentially curative treatment for early stage lung cancers, only 20% of cases at diagnosis are suitable for surgery as often lung cancer patients have multiple co-mortalities and radical surgery is not an option (Cowdy, 2008). Approximately 70% of patients presenting with lung cancer already have locally advanced or metastatic disease, so chemotherapy, radiation therapy or a combination of the two are often treatment choices (Molina, et al., 2008).

Statistics show that cure rates in lung cancer are poor ("Cancer: New registrations and deaths 2005", 2008), despite extensive research into the best methods to treat these cancers. Radiation Therapy (RT) is often a treatment of choice due to its lower toxicity and less invasive approach compared to chemotherapy or surgery. One large Radiation Therapy Oncology Group (RTOG) study investigating the use of radiation therapy alone as a treatment option only achieved a 10-month median survival and a 5% 5-year survival rate (Molina, et al., 2008). Research into stereotactic and hyperfractionated treatments is looking more promising but these still require further work before they become a standard practice (Haasbeek et al., 2008) (Sher, et al., 2008).

At my place of employment, MidCentral Health Ltd, the current standard of care for radical radiation therapy for lung cancer is a course of radiation using 60-66Gy in 30-33 fractions ("Protocol for radiation treatment of Non-small Cell lung cancer", 2003). IV contrast for CT
simulation maybe used at the Oncologists’ request to aid in the contouring of the planning
target volume (PTV). The protocol currently requires the plan calculations be done on a
normal CT scan without the presence of IV contrast to reduce any perceived errors occurring
due to the presence of the contrast on the scan.

In order to understand these recommendations and concerns a good understanding of the
process in which the treatment planning system (TPS) uses the CT numbers to relate relative
electron densities (RED) and the factors that influence these is required. The next chapter is
an introduction to this area of physics along with the aims of the radiation therapy process.
CHAPTER 2. BACKGROUND

2.1 RADIATION THERAPY FOR LUNG CANCER

The delivery of radiation therapy to the lung has evolved greatly over the years and its complexity has increased dramatically. Standard treatments delivered in the 1980-90’s consisted of parallel opposed pairs (POP) of treatment beams, which whilst delivering the required dose to the tumor, often gave high doses to surrounding structures (Cowdy, 2008). As research progressed and new techniques were developed treatments progressed to three dimensional conformal therapies (3DCRT). This modern method allowed higher doses to be delivered to the planning target volume (PTV) and helped minimize dose to the organs at risk (OAR). With this ability to more accurately deliver radiation therapy the need to more accurately define the PTV and OAR increased.

The aim of radiation therapy planning is to deliver the prescribed dose to the target volume whilst minimising dose to surrounding sensitive structures. In order to achieve this accurately, PTVs and OARs need to be clearly identifiable on CT images. The use of contrast-enhanced CT scans in radiation therapy planning has enabled more accurate delineation of planning target volumes and sensitive structures (Lees, et al., 2005).

Radiation therapy treatment planning systems (TPS) use the data from planning computed tomography (CT) scans to provide information on the patient’s size, the location of structures and information on the density of any inhomogeneities present. TPS use the information about these inhomogeneities to calculate the way radiation may interact with the tissue, and the resultant dose to the patient/structures can then be accurately calculated.
The aim of simulation, prior to treatment planning, is to place the patient in the treatment position and obtain images that ‘simulate’ the patient’s external and internal anatomical position during treatment to enable accurate treatment planning (Washington & Leaver, 1996). Intravenous contrast, used in planning CT scans, is present during the CT planning scan but not during the actual treatment of the patient. The presence of this contrast on the planning CT scan may alter the electron density of the tissues. The contrast presence during the scan for planning and absence during treatment would be expected to lead to significant inaccuracies in planning calculations and this effect needs to be quantified.

One current practice is to take pre- and post-intravenous (IV) contrast CT scans. This method has been designed to incorporate the benefits of IV contrast for visualisation of anatomy whilst reducing the perceived errors in dose calculations that may be caused by the presence of the IV contrast. The two scans are ‘fused’ and the contouring of OAR and PTV is done using the IV contrast scan. The scans are then separated and the planning is done on the non-contrast scan only.

The assumption is that the contrast will affect the RED to a degree in which the planning calculations are inaccurate. This is the basis of this investigation and a good understanding of how this may occur is needed and information on what degree RED are affected by IV contrast is required. The following section reviews the physics behind these calculations.

2.2 CT DATA AND RADIATION THERAPY TREATMENT PLANNING

Computed tomography involves the measurement of the radiation attenuation of an object. Information is gathered by passing radiation through an object and measuring the intensity of that beam after it has been attenuated by the object in its path. This information is then converted to an electrical signal that is reconstructed into an image using convolution and
back projection algorithms (Seeram, 2001). CT images are made up of pixels; each pixel is assigned a CT number which is related to the linear attenuation coefficient of that tissue ($\mu$) (Seeram, 2001). CT numbers are determined using the following equation:

**Equation 1. CT number**

$$\mu_t/\mu_w$$

CT number = --------- . K,

$$\mu_w$$

where $\mu_t$ is the attenuation coefficient of the tissue and $\mu_w$ is the attenuation coefficient of water and $K$ is a constant $= 1000$ (Seeram, 2001).

Because CT numbers are derived using a kilovoltage photon beam and radiation therapy is delivered using a megavoltage photon beam, a relationship between CT numbers and the attenuation properties of tissues when they interact with photos of megavoltage energies is necessary (Plessis, et al., 1998). Kilovoltage beams are significantly affected by photoelectric attenuation, which is highly influenced by atomic number ($Z$). Therefore the data produced during the CT process is largely a result of interactions influenced by the atomic number for the materials present. Soft tissue has a $Z \sim 7.5$, and contrast media has a $Z \sim 53$ due to its iodine content (IAEA, 2005).

Megavoltage energies in the range of 4-18 MeV are most commonly used for radiation therapy treatment. These treatment energies have mean photon energies of 2-6 MeV that are mostly affected by Compton scatter as they pass through human tissue, with a small percentage of pair production at the higher energies (IAEA, 2005). With these energies, the
degree of attenuation is more dependent on electron density (Washington & Leaver, 1996) (see Graph 1). This difference in photon interactions probably will result in different attenuation coefficients. Therefore a relationship is needed between the CT numbers and electron densities. This is achieved by the use of electron density conversion files that are often described in relation to water (relative electron densities – RED) (Plessis, et al., 1998).

Graph 1. The effect of atomic number and photon energy on radiation interactions

(IAEA pg: 37, 2005)

CT –RED conversion has been proved accurate for the conversion of matter such as soft tissue which has a relatively small atomic number range. The issue and main area of debate is the ability to convert higher atomic number materials such as contrast or metal to RED accurately (Coolens & Childs, 2003). As CT numbers are obtained as a function of the mass density and atomic number, and RED is a function of mainly the mass density, a high CT number (such as for contrast or metal) may be a result of either high atomic number or mass density, therefore the accuracy of such number is debated. This is investigated in experiment one.
Lung cancer is a serious problem causing many deaths per year in New Zealand. Radiation therapy is an important treatment method for this condition. The use of CT scanning to accurately define the treatment volume is the standard method of simulation for radiation therapy planning. It is established that contrast can aid in the accurate delineation of the PTV and OAR, and that contrast may in fact impact on the accuracy of the dose calculations. Other researchers have investigated this problem. The following is a review of the previous research in this area.
The literature review begins with a review of the experimental research done into the influence of the contrast on dose calculations, using mostly phantoms. This is then followed by review of research done on specific body sites including head and neck, abdomen and thorax. The optimal methods for performing this type of research is reviewed as well as indices that may indicate the impact on the resultant plans. Finally, research into the accurate conversion of CT-RED number is investigated.

3.1 EXPERIMENTAL RESEARCH INTO THE INFLUENCE OF CONTRAST ON DOSE CALCULATIONS:

In 2001, Ramm, Damrau, Mose, Manegold, Rahl and Bottcher performed an investigation into the influence of contrast agents on dose calculations. The researchers used a phantom filled with water containing cylinders of various dimensions containing differing concentrations of contrast media. The researchers scanned this phantom and applied basic planning techniques. The researchers investigated a number of variables: the concentration of the contrast used, the diameter of cylinder containing the contrast and the treatment planning technique, 2 field vs 4 field beam arrangement (Ramm et al., 2001).

This study found that the use of contrast media led to a change in the MUs calculated. They found that the difference increased linearly with the molarity of the contrast and the diameter of the cylinders containing contrast. The researchers also found that with increasing beam numbers, dose inaccuracies decreased. They found significant differences in the MUs produced when the contrast was in vessels larger than 5cm in diameter and in a
concentration that increased the CT numbers by more than 500 Housfeild units (HU) (Ramm et al., 2001).

These conclusions, whilst beneficial in providing information on the impact of different possible variables, are not relevant to actual clinical situations. The researchers performed many tests and analysed large amounts of data, but the data is not strictly representative of the physiological uptake of contrast media in human tissues, and used planning techniques that are no longer commonly used for radical cases. A further study has shown that, under normal conditions, IV contrast will not increase the CT number of tissue by more than 500 and, apart from the heart itself, blood vessels in the human body do not normally exceed 5cm in diameter (Lees, et al., 2005).

The effect of the presence of IV contrast in lung tissue was investigated by Lees, Holloway, Fuller and Forstner (2005). These researchers felt that an investigation using actual patients would be unethical, so elected to use an anthropomorphic phantom. This thorax phantom was made up of similar electron density materials to the actual tissues found in the human thorax.

The researchers performed two investigations. Firstly, they inserted straws of various concentrations of contrast into the ‘lungs’ of the phantom in an area said to represent the tumour mass. This was then scanned and a simple plan consisting of three beams was applied to the data obtained from the scan. This was then repeated without the presence of contrast in the straws. The resultant MUs from both plans were compared and differences (<1.5%) were deemed insignificant (Lees, et al., 2005).

This first investigation may not be clinically relevant. The researchers suggest that this is simulating the uptake of the contrast media in the tumour mass; however tumour vascularity varies dependent on tumour type and the presence or absence of necrosis. This
study also completely ignores the possibility of IV contrast present in the large blood vessels in the mediastinum and the uptake in the small blood vessels of the lungs, which may impact significantly on MU calculations.

### 3.2 RESEARCH ON THE EFFECT OF IV CONTRAST ON HEAD AND NECK RADIATION THERAPY PLANNING:

Two recent studies on the use of intravenous (IV) contrast-enhanced CT scans for intensity modulated radiation therapy (IMRT) planning of the head and neck region have concluded that the presence of contrast on the CT images does not result in clinically significant errors in dose calculations (Choi et al., 2006; Liauw, et al., 2005). Both sets of researchers agree that the use of IV contrast is essential for the accurate and extensive contouring required for IMRT planning. Both studies used similar experimental methods.

Liauw and colleagues (2005) did a small study on five patients having IMRT for head and neck carcinomas. This research was done using only contrast-enhanced CT scans. The organs at risk (OAR) and planning target volumes (PTVs) were contoured, along with the contrast-containing vessels visible in the neck region. The IMRT plans were completed on the contrast scan then repeated on the same scan, with the density of the contrast-containing vessels altered. The differences in the plans produced were then analysed (Liauw, et al., 2005). A major flaw in this experiment design is the ‘forcing’ or altering of the density of the contoured vessels only. Altering the density in the vessels alone does not completely eliminate the effect of the presence of contrast in other tissues, which may have an effect on dose calculations. For an accurate evaluation of the effects of the intravenous contrast on dose calculations, scans before and after contrast administration should be compared.
Choi and colleagues (2006) performed a slightly larger study investigating the effects of IV contrast on fifteen patients receiving IMRT to the head and neck. These patients were scanned without the contrast, then immediately rescanned in the same position after the administration of IV contrast. The IMRT plan was completed on the contrast scan, then the exact same parameters were applied to the non-contrast scan and the plan re-calculated. A comparison and analysis was then made (Choi et al., 2006). One would assume that the comparison between the two scans would be more akin to the real occurrence when the patient attended for treatment without the presence of any IV contrast.

Both studies concluded that the presence of IV contrast made no clinically significant impact on the dose calculation to the OAR or the PTVs. They found minor changes in the MUs calculated but concluded that these small differences were insignificant (Choi et al., 2006; Liauw, et al., 2005).

Ramm et al. (2001) concluded that, with an increase in the beam numbers, the effect of IV contrast on dose calculations decreases. IMRT uses a large number of beams, so perhaps this is the reason for this apparent insignificant impact on MU calculation. Ramm et al., (2001) also concluded that the diameter of the vessels containing the contrast impacted on the MU calculations. Head and neck sites have relatively small blood vessels, and these may have less effect than the larger vessels found in the thorax and abdomen, which were not investigated in the Choi et al., (2006) or Liauw et al., (2005) studies.
3.3 RESEARCH ON THE EFFECT OF IV CONTRAST IN OTHER RADIATION THERAPY PLANNING SITES:

Lees, Holloway, Fuller and Forstner (2005) conducted a 2-phase study on the effect of IV contrast on dose calculations in lung tissue; their first investigation involved a phantom as described earlier in this review. Lees et al.’s (2005) second investigation involved the manipulation of the electron densities on the scan of an actual patient, forcing the electron density of the lungs to a mean electron density calculated from six patients’ contrast-enhanced lung scans (Lees, et al., 2005).

This was designed to simulate the actual density changes due to the absorption of contrast agents in the smaller vessels of the lung tissue. This study found that the RED of non-contrast lungs was on average 0.23, whereas with the contrast-enhanced lungs, the RED was increased to 0.38. The same plan was applied to the normal and the forced density scans; the results were then analysed. The MUs calculated and the mean lung doses were compared and the conclusion stated that the differences were minor and insignificant (Lees, et al., 2005).

This study failed to investigate the impact of the large vessels of the heart and lungs being filled with the contrast. The Ramm et al., (2001) study concluded that the size of the vessels containing the contrast related to the degree of errors in dose calculations. This study also forced the RED of the lungs to the average RED for six normal lung scans. One could assume that lung cancer patients have lungs that may vary in RED after the uptake of IV contrast, due to changes in the vascularity of the lungs as a result of their pathology.

An earlier Australian study (Miller & Joon, 2002) researched this topic using an experimental design that more accurately mimicked the actual situation when IV contrast is no longer present for treatment. Scans were taken pre- and post-contrast, and the same plans were
compared on both scans. This study was however limited by a small sample size of just 10 patients (Miller & Joon, 2002).

This study introduced another variable – the breath hold. The reason for introducing this second variable is unclear, as radiation therapy treatment is usually given in a ‘free breathing’ situation, and scanning in a ‘breath hold’ situation is not representative of actual treatment, unless gated treatment is an option. Currently in New Zealand and Australia, gated treatment is not often used. The design of this research is such that you cannot separate the effects of breath hold and IV contrast, and this makes the comparison difficult.

There were many flaws in Miller and Joon’s (2002) experimental design. The evaluation was done by keeping the doses the same, and evaluating the differences in MUs needed to deliver this dose in contrast/breath hold scans, versus non-contrast/free breathing scans (Miller & Joon, 2002). Whilst this did show that there can be significant changes in the number of MUs required to deliver the same dose, the clinical significance of this is not able to be clearly distinguished. It would have been more clinically significant to keep MUs constant and evaluate the resultant changes in dose delivered. Another flaw of this article is the lack of information on the type and concentration of contrast media used. Previous studies have shown that these variables can affect dose distributions (Ramm et al., 2001).

Another Australian study (Rudolph et al., 2007) was an investigation into the effects of IV contrast on planning stomach cancer patients. This study reviewed ten cases of stomach cancer; the patients had a non-contrast scan immediately followed by a contrast-enhanced scan. This study used a variety of methods, including dose volume histogram (DVH) analysis, plan subtraction and estimations of biological endpoints, to evaluate the differences between the non-contrast plans and the contrast plans. The conclusion of this study found that the difference between the two plans was insignificant and that the non-contrast scan was not required (Rudolph et al., 2007). This study used a similar method to Miller and Joon...
(2002), and kept the dose delivered constant and varied the MUs required to deliver this
dose. In order to confirm the insignificance of the impact of IV contrast, an absolute dose
comparison is needed to compare the actual clinical significance of the presence of IV
contrast at the time of planning.

A recent study reviewed was that of Shibamoto, et al., (2007). These researchers
investigated the impact of contrast materials over a number of sites including whole brain,
head and neck, mediastinum, whole pelvis and abdomen. Unfortunately, this study is limited
by its use of very small study sets for each site of only 5 patients, each of whom had a range
of different cancers at different stages and grades.

These patients received both pre and post IV contrast CT scans and planning was performed
on the contrast data set, then copied to the non-contrast set. The planning techniques used
were simple parallel opposed pairs. This study, like others reviewed, kept the dose constant
and analysed the MU differences required pre and post-contrast to deliver the prescribed
dose. The researchers found in most cases the differences were insignificant except in upper
abdominal patients who required an increase in MU by an average of 3.2% and, in one case,
by 7.6% to deliver the same dose post-contrast compared to the pre-contrast data. The
researchers stated a number of possibilities for this difference, including the presence of the
liver and spleen which up took a lot of the IV contrast, coupled with differing anatomical
positions between the two CT scans due to the effect of the patient breathing throughout
the scanning process (Shibamoto et al., 2007).
3.4 INVESTIGATING THE IMPACT OF IV CONTRAST:

One of the main weaknesses of previous studies on the impact of IV contrast on dosimetric calculations for planning radiation therapy has been the methods used to compare the two plans. The majority of the studies reviewed decided to investigate the differences in the MUs required to deliver the prescribed dose with or without the presence of IV contrast on the planning CT (Choi et al., 2006; Liauw, et al., 2005; Miller & Joon, 2002; Rudolph et al., 2007; Shibamoto et al., 2007).

The aim of this study is to investigate the possibility of planning on a CT scan containing IV contrast, then applying that plan in the clinical setting without concern that the dose delivered has been miscalculated due to the presence of the IV contrast on the planning scan. Therefore, the most relevant way to investigate this possible miscalculation would be to keep the MUs consistent between the plans, and investigate the differences in the dose delivered. This method would then enable the results to demonstrate the differences that occur as a result of planning on a CT scan with IV contrast, then delivering the MUs calculated on that plan to a patient without the presence of IV contrast. This method should demonstrate the clinical impact of a department’s decision to plan in this manner.

3.5 COMPARING PLANS:

When comparing two plans, there are many variables that can be used to assess the differences and quantify the plans’ conformity with the aims of treatment. Since the development of 3DCRT planning, many quantitative indices have been postulated as optimal tools for evaluating radical lung plans (Armstrong, 2007; McGibney, et al., 2003). For this study, the most commonly reported indices have been chosen to provide information on the variations between the two plans; one with IV contrast present and one without.
• **Lung dose** including reporting on V5, V20, V30 and mean lung dose (MLD)

• **Spinal Cord** - maximum point dose

• **Heterogeneity index** (HI)

• **Conformity index** (CI)

### 3.5.1 LUNG DOSE

Radiation-induced pneumonitis is a major limiting factor in the delivery of optimal radiation therapy to the lung. Many studies have shown that total lung V20 and mean lung dose (MLD) are good variables for demonstrating the risk of radiation pneumonitis (Chang et al., 2006; Kocak et al., 2007; Seppenwoolde et al., 2003).

A lung V20 is the volume of the total lungs that receives 20Gy or more. Whilst studies show a range of recommendations for limiting the V20, from 28-17%, my place of employment has decided to use a planning recommendation to limit lung V20 to 20% ("Protocol for radiation treatment of Non-small Cell lung cancer", 2003). V30 and V5 have also been chosen as variables in this study to investigate any smaller differences in lung dose variation as a possible result of planning on a plan with IV contrast present.

Mean Lung dose (MLD) is the most recommended measure for predicting radiation pneumonitis. The risk of radiation pneumonitis increases linearly with increasing MLD (Chang et al., 2006). Chang et al., (2006) recommends that MLD be kept below 17Gy.
3.5.2 SPINAL CORD DOSE

The spinal cord variable used in this study is the maximum point dose. This has been selected as the spinal cord is an important serial sensitive structure to consider when planning radical radiation therapy in the thorax (ICRU, 1999). The function of a serial sensitive structure is damaged when any part of that structure surpasses the tolerance dose for that tissue. The tolerance of the spinal cord is reported by Emami et al., (1991) with a TD5/5 of 50Gy to 5-10cm length or 47Gy to a 20cm length. However, as the spinal cord is a serial structure, a maximum point dose is preferred as an optimal reporting tool (Emami et al., 1991). My place of employment has decided to recommend that, when planning radiation therapy to the thorax, the maximum point dose to a spinal cord should aimed to be kept below 45Gy ("Protocol for radiation treatment of Non-small Cell lung cancer", 2003)

3.5.3 CONFORMITY AND HETEROGENEITY INDEX

The final two variables selected for this study are the conformity index (CI) and the heterogeneity index (HI). The conformity index is the volume of tissue enclosed by the 95% isodose curve, or the ‘treated volume’, divided by the volume of the PTV (Armstrong, 2007). The method of finding the CI has been described by the TROG 03.04 ‘RADAR’ trial (TROG, 2004). To calculate a CI, a new structure called the CI box is created with a margin on the PTV to encompass the 95% isodose curve. CI is calculated using the following equation:

Equation 2. conformity index

A. = total volume of PTV

B. = Volume of the 95% within the CI box

\[ CI = \frac{B}{A} \]
The conformity index is a measure often used to assess if a plan is ‘optimal’. The ideal CI would equal 1; however, this is not a realistic aim for thorax plans. The larger the CI, the less conformal the plan is and the more normal tissue is unnecessarily irradiated to the dose required to achieve the aim of treatment. Armstrong (2007), strongly recommends the use of a CI when comparing plans in which technology or technique need accurate comparison. Chang, Zhang & Cox (2007) argue that whilst CI is an important variable to assess, it must be balanced in thorax plans with other variables such as the lung V5 and MLD (J. Y. Chang, et al., 2007).

The heterogeneity index (HI) is a ratio between the maximum dose and the prescribed dose; this should be kept as close to one as possible. ICRU 50/62 recommends that the dose across the PTV should be kept between -5% and +7% of the prescribed dose.

### 3.6 CT-NUMBER TO RED CONVERSION

Studies show that CT numbers can vary significantly; for example, Coustantinou and Harrington (as cited in Schneider, et al., (1996)) found that the CT number of a homogenous material can vary between 1-2%. They also found that accuracy is dependent on the location of a material within the image, and errors can reach 3% in the periphery of a CT image. Coustantinou and Harrington also found that CT numbers can vary greatly between scanners and a variation of up to 10% can be found between different CT scanners. However, because these differences are referring to CT numbers, and TPS convert these to RED, which has a much smaller range of numbers (0~1.7) than CT numbers (-1000 ~1000), a variation of up to 10% in CT numbers would equate to very minor, perhaps insignificant, changes in RED.
Plessis, et al., (1998) found that CT number intervals of 30 for soft tissues and 100 for bone would result in insignificant changes in dose calculations in TPS (Plessis, et al, 1998). Chu, et al., (2000) did a similar investigation and found that a change of CT number of 20 in soft tissue and 250 in bone resulted in less than a 1% change in MU calculations (Chu, et al., 2000). Thomas (1999) did further investigations into the range of RED values required to make a 1% or less change in the dose and produced the following table:

**Table 1. Percentage change in tissue maximum ratio (TMR) per cm of depth and the change in depth required to produce a 1% change in TMR used to calculate the range of RED that would give a dose correction factor within 1% of those calculated for typical inhomogeneities**

<table>
<thead>
<tr>
<th>RED Experiment</th>
<th>Cobalt</th>
<th>6 MV</th>
<th>10 MV</th>
<th>21 MV</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Change in TMR per cm of depth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 cm</td>
<td>4.0</td>
<td>3.0</td>
<td>2.4</td>
<td>0.7</td>
</tr>
<tr>
<td>10 cm</td>
<td>5.4</td>
<td>3.6</td>
<td>3.0</td>
<td>2.3</td>
</tr>
<tr>
<td>Change in depth to produce 1% change in TMR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 cm</td>
<td>2.5 mm</td>
<td>3.3 mm</td>
<td>4.2 mm</td>
<td>14.3 mm</td>
</tr>
<tr>
<td>10 cm</td>
<td>1.9 mm</td>
<td>2.8 mm</td>
<td>3.3 mm</td>
<td>4.3 mm</td>
</tr>
<tr>
<td>Range of relative electron density for ±1% in dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>0.24–0.28</td>
<td>0.23–0.30</td>
<td>0.22–0.30</td>
<td>0.21–0.31</td>
</tr>
<tr>
<td>Fat</td>
<td>0.90–1.00</td>
<td>0.88–1.02</td>
<td>0.87–1.03</td>
<td>0.84–1.06</td>
</tr>
<tr>
<td>Liver</td>
<td>1.03–1.07</td>
<td>1.02–1.08</td>
<td>1.01–1.09</td>
<td>1.00–1.10</td>
</tr>
<tr>
<td>Humerus</td>
<td>1.31–1.47</td>
<td>1.28–1.50</td>
<td>1.26–1.52</td>
<td>1.22–1.56</td>
</tr>
<tr>
<td>Cranium</td>
<td>1.34–1.68</td>
<td>1.25–1.79</td>
<td>1.23–1.79</td>
<td>0.56–2.46</td>
</tr>
</tbody>
</table>

(Thomas, 1999, pg 783)

Whilst investigating contrast calculations using the XiO planning system, it was discovered that the system would ‘cap’ the CT-number to RED conversion at a CT value of 1152 equating to an RED of 1.71. Upon further investigation, it was noted that the planning system was labeling areas of IV contrast as having an RED of 1.71 (the highest limit) – therefore, the actual RED could be much higher and the planning system was not accurately accounting for the IV contrast. The CT number -RED experiments in this thesis were formulated to attempt to account for this inaccuracy in the planning system.
3.7 RESEARCH IN CT-RED CONVERSION

A number of researchers have investigated methods for finding accurate RED of higher atomic number materials. Coolens & Childs (2003) investigated two methods for obtaining a CT-RED conversion file for metallic materials. Firstly, they calculated theoretical electron densities of the materials to be tested using atomic composition, then calculated the electron density using CT numbers and compared the results. These two methods did not result in RED of the same value for each material and highlight that there is a need for a better way to determine RED of higher atomic number materials. Coolens & Childs (2003) second experiment involved stoichiometric calibration; this also failed to achieve a match between the theoretical electron densities and those obtained using stoichiometric calibration using CT numbers.

Ramm (2001) investigated how high atomic number contrasts such as barium affect dose calculations in 3D treatment planning. Ramm found that using CT to measure the Hounsfield numbers of various concentrations of barium sulphate did not produce a linear graph, and accounted this to the beam-hardening effect of CT scanning materials of high atomic number. The problem of beam-hardening in CT using kilovoltage may be avoided using MVCT; this is a possibility currently being investigated by other researchers.

Plessis et al. (1998) investigated the use of CT numbers to establish material properties needed for Monte Carlo calculation of dose distributions and found that in order to make dose calculations accurate to 1%, CT number intervals of 30 in soft tissue and 100 in bone can be used. As the RED of the tissue increased (i.e. from soft tissue to cortical bone), the influence of the change in CT number on dose calculation accuracy decreased. Extrapolating this on to much higher RED materials such as IV contrast and metal, one may assume even larger intervals in CT numbers could be used and still maintain dose calculation accuracy of
1%. Unfortunately, Plessis and his fellow researchers did not investigate this with higher density materials.

A theme occurring from these studies is that the relationship between high RED materials and CT numbers cannot be assumed to be linear. Unfortunately, one solution commonly used in radiation therapy departments to account for high RED materials is to simply extend the CT-RED conversion file linearly, based only on tests of lower atomic number tissues. Whilst this is relevant for most situations in radiation therapy planning where patients are mostly made up of low atomic numbers, when high atomic number materials such as iodine or barium based contrasts or metallic implants such as hip replacements are present, our dose calculations may be becoming less accurate. Thomas (1999) warns of the inaccuracies that occur when you try and apply currently used equations to relate CT-numbers and RED in higher atomic number materials such as metal implants (Thomas, 1999).

The need to accurately represent the RED of higher atomic number materials is important as most departments now use CT data and 3D planning techniques (Saw et al., 2005). The increasing addition of IV contrast use in obtaining planning images also necessitates accurate CT-RED conversion files.

An experiment was needed to determine the effective RED of much higher atomic number materials, as previous studies have proven that directly relating CT numbers to known or theoretical REDs of tissues of higher atomic number materials can lead to inaccuracies (Thomas, 1999). This experiment, conducted to help support the results of the main thesis, is described in chapter 4.
3.8 LITERATURE REVIEW AND SUMMARY

The review of this literature has shown that solid conclusions on the impact of IV contrast on planning calculations are still not achieved. Researchers are confident that the impact on areas such as the head and neck are minimal, but there is still some doubt and debate in the areas with larger blood vessels such as the thorax. This has lead to this investigation on the impact of contrast when planning radical lung cancer treatment.

Research into the conversion of CT number to RED has also shown this is an area where inaccuracies exist and can be difficult to quantify. This has lead to experiment one – the CT-Number conversion investigation in Chapter 4. The literature review has highlighted the optimal method for the main experiment and indicated the appropriate indices for assessment of the plans. The main experiment is conducted in Chapter 5.
CHAPTER 4. CT NUMBER-RED CONVERSION INVESTIGATION

4.1 AIM:

- Investigate the relationship between CT numbers and RED for IV contrast and higher atomic number materials

4.2 METHOD

4.2.1 PART ONE:

Standard calibration conditions for 6MV photons were set up on a treatment unit using a 10x10 cm field, 100cm source to axis distance (SAD), with a dose point measured at 5cm depth in plastic water. Different materials were placed in the beam path and the dose at the 5cm depth was recorded when 100 MU were delivered.

Figure 1. Experiment one set up

Dose delivered at 5cm depth after 100 MU delivered was measured

Different materials placed in beam path
**Table 2. Measured dose delivered per 100 MU post absorption by various materials**

<table>
<thead>
<tr>
<th>Date:</th>
<th>13/10/2008</th>
<th>Measured by:</th>
<th>Aitang and Hannah</th>
<th>Gantry:</th>
<th>zero</th>
</tr>
</thead>
<tbody>
<tr>
<td>Machine:</td>
<td>LA1 6MV</td>
<td>Field size:</td>
<td>10cm by 10cm</td>
<td>Collimator:</td>
<td>zero</td>
</tr>
<tr>
<td>Depth:</td>
<td>5cm</td>
<td>Temperature:</td>
<td>21.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phantom:</td>
<td>Plastic water</td>
<td>Pressure:</td>
<td>771mmHg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Materials:</th>
<th>Readings(nC)</th>
<th>Average(nC)</th>
<th>Dose at 5cm depth(cGy)</th>
<th>Output at dmax(cGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plastic water</td>
<td>20.19</td>
<td>20.19</td>
<td>20.19</td>
<td>95.3</td>
</tr>
<tr>
<td>Steel</td>
<td>4.34</td>
<td>4.334</td>
<td>4.337</td>
<td>20.5</td>
</tr>
<tr>
<td>Lead</td>
<td>7.758</td>
<td>7.751</td>
<td>7.7545</td>
<td>36.6</td>
</tr>
<tr>
<td>Brass</td>
<td>10.17</td>
<td>10.17</td>
<td>10.17</td>
<td>48.0</td>
</tr>
<tr>
<td>Contrast</td>
<td>17.04</td>
<td>17.04</td>
<td>17.04</td>
<td>80.4</td>
</tr>
</tbody>
</table>

100.1
4.2.2 PART TWO:

Using the same set up as the treatment measurements, the phantom with the various materials was then CT scanned. The scan was taken using the ‘extended CT number scale’ option available on the Siemens scanner.

Table 3. Hounsfield numbers and Xiao’s derived RED of measured materials

<table>
<thead>
<tr>
<th>Material</th>
<th>Average Hounsfield number</th>
<th>Standard deviation</th>
<th>Derived RED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steel</td>
<td>5692.63</td>
<td>95.6</td>
<td>&gt;10.24 (Xio limit)</td>
</tr>
<tr>
<td>Lead</td>
<td>5188.186</td>
<td>219.5</td>
<td>6.7</td>
</tr>
<tr>
<td>Brass</td>
<td>5123.22</td>
<td>146.8</td>
<td>6.35</td>
</tr>
<tr>
<td>IV contrast</td>
<td>3921.7</td>
<td>28.3</td>
<td>1.35</td>
</tr>
</tbody>
</table>

The standard calibration conditions were then modeled in the planning system (CMS Xio, Version 4.4) using the scanned data for each of the materials tested. The RED of the material was then forced to various REDs until the dose at the 5cm point in the plastic water was achieved using the set 100 MUs.

Graph 2. Derived RED to CT values showing non-linear relationship
4.2.3 RESULTS AND DISCUSSION:

This small experiment has shown that with the addition of higher atomic number materials, the relationship between RED and CT numbers can no longer be called linear, and that there is potential error in using a linearly extended RED-CT conversion table to estimate the effect of IV contrast in planning calculations. Looking further at the data collected in this experiment, there appear to be two different effects occurring between the two groups of materials, low atomic number and high atomic number.

Graph 3. Derived RED to CT values showing low and high atomic number differences

![Derived RED to CT Values showing low and high atomic number differences](image)
Further investigation is therefore needed to investigate the RED-CT number relationship of IV contrast.

**4.2.4 PART THREE:**

To further investigate the CT – RED curve created by IV contrast, further experiments were required using various strengths of IV contrast. Measurements of the dose at a point were taken when 100 MU was delivered through a vessel containing mixtures of 100%, 66%, 50%, 33% and 20% Omnopaque 350 IV contrast diluted in distilled water as per the following diagram.

*Figure 2. Experiment two set up*
Initially, the data was used to discover the potential errors in the dose calculations performed by XiO using the current CT-RED conversion table; the measured doses at the isocentre were compared with the calculated doses at the isocentre.

Table 4. Dose measurements delivered per 100 MUs after being absorbed by various concentrations of omnipaque 350 contrast, using 6MV

<table>
<thead>
<tr>
<th>concentrations of contrast</th>
<th>100.0</th>
<th>66.0</th>
<th>50.0</th>
<th>33.0</th>
<th>20.0</th>
<th>0.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>measurements in nC at 6MV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>11.460</td>
<td>11.620</td>
<td>11.650</td>
<td>11.640</td>
<td>11.720</td>
<td>14.000</td>
</tr>
<tr>
<td>3</td>
<td>11.460</td>
<td>11.613</td>
<td>11.640</td>
<td>11.630</td>
<td>11.713</td>
<td>14.000</td>
</tr>
<tr>
<td>dose (cGy) per 100MU</td>
<td>55.43693</td>
<td>56.19986</td>
<td>56.35631</td>
<td>56.30793</td>
<td>56.68374</td>
<td>67.77597</td>
</tr>
</tbody>
</table>

Table 5. Dose measurements delivered per 100 MUs after being absorbed by various concentrations of omnipaque 350 contrast, using 15MV

<table>
<thead>
<tr>
<th>concentrations of contrast</th>
<th>100.0</th>
<th>66.0</th>
<th>50.0</th>
<th>33.0</th>
<th>20.0</th>
<th>0.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurements in nC at 15MV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table six shows that the potential error in these examples between XiO’s calculated dose and the measured dose is approximately 11% for 6 MV and 12% for 15 MV.

Table 6. Comparing XiO’s calculated doses with measured doses after being absorbed by various concentrations of Omnipaque 350, using 6MV

<table>
<thead>
<tr>
<th>IV contrast%</th>
<th>Averaged measured dose with 100MU</th>
<th>Averaged XiO’s calculated dose (unforced REDs)</th>
<th>differences</th>
<th>% difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>55.4</td>
<td>61.5</td>
<td>6.1</td>
<td>11</td>
</tr>
<tr>
<td>66</td>
<td>56.2</td>
<td>63.2</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>50</td>
<td>56.4</td>
<td>63.6</td>
<td>7.2</td>
<td>13</td>
</tr>
<tr>
<td>33</td>
<td>56.3</td>
<td>64.3</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>20</td>
<td>56.7</td>
<td>65.3</td>
<td>8.6</td>
<td>15</td>
</tr>
<tr>
<td>0</td>
<td>67.8</td>
<td>68.6</td>
<td>0.8</td>
<td>1</td>
</tr>
<tr>
<td>ave</td>
<td>56.2</td>
<td>63.58</td>
<td>7.38</td>
<td>11</td>
</tr>
<tr>
<td>SD</td>
<td>0.48</td>
<td>1.41</td>
<td>0.96</td>
<td></td>
</tr>
</tbody>
</table>

Table 7. Comparing XiO’s calculated doses with measured doses after being absorbed by various concentrations of Omnipaque 350, using 15MV

15MV

<table>
<thead>
<tr>
<th>IV contrast%</th>
<th>Averaged measured dose with 100MU</th>
<th>Averaged XiO’s calculated dose (unforced REDs)</th>
<th>differences</th>
<th>% difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>66.2</td>
<td>76.1</td>
<td>9.9</td>
<td>15</td>
</tr>
<tr>
<td>66</td>
<td>66.9</td>
<td>77.6</td>
<td>10.7</td>
<td>16</td>
</tr>
<tr>
<td>50</td>
<td>67.1</td>
<td>77.9</td>
<td>10.8</td>
<td>16</td>
</tr>
<tr>
<td>33</td>
<td>67.2</td>
<td>78.4</td>
<td>11.2</td>
<td>17</td>
</tr>
<tr>
<td>20</td>
<td>67.4</td>
<td>79.3</td>
<td>11.9</td>
<td>18</td>
</tr>
<tr>
<td>0</td>
<td>88.2</td>
<td>82</td>
<td>-6.2</td>
<td>-7</td>
</tr>
<tr>
<td>ave</td>
<td>66.96</td>
<td>77.86</td>
<td>10.9</td>
<td>12</td>
</tr>
<tr>
<td>SD</td>
<td>0.46</td>
<td>1.18</td>
<td>0.73</td>
<td></td>
</tr>
</tbody>
</table>
Graph 4. XiO’s calculated dose compared with measured doses per 100 MU for 6 MV

Graph 5. XiO’s calculated dose compared with measured doses per 100 MU for 15 MV
A 11-12% inaccuracy is large and this is under controlled experimental conditions; therefore a way to correct for this inaccuracy needs to be determined. Although a complete correction is not possible, due to many influencing factors such as contrast size and concentration, a more accurate CT-RED conversion table could be created to provide data that may model a more realistic CT-RED conversion with higher atomic number substances.

4.2.5 PART FOUR:

In order to determine a more realistic CT-RED conversion graph, experiment one was repeated on the 2nd set of data and the RED of the various concentrations of Omnipaque 350 was forced until the dose at the point calculated by XiO equaled that of the measured dose at the point.

Table 8. Average Hounsfield numbers and derived RED for various concentrations of Omnipaque 350 contrast

<table>
<thead>
<tr>
<th>concentration of contrast %</th>
<th>Average HU</th>
<th>SD</th>
<th>derived RED</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>2931.4</td>
<td>111.9823</td>
<td>2.8</td>
</tr>
<tr>
<td>66</td>
<td>2240.5</td>
<td>173.2854</td>
<td>3.1</td>
</tr>
<tr>
<td>50</td>
<td>1871.8</td>
<td>49.05281</td>
<td>3.2</td>
</tr>
<tr>
<td>33</td>
<td>1359.7</td>
<td>14.57586</td>
<td>3.3</td>
</tr>
<tr>
<td>20</td>
<td>904.9</td>
<td>7.156194</td>
<td>3.1</td>
</tr>
</tbody>
</table>

One would assume that as percentage contrast concentration increased, the RED would also increase. This experiment has shown that this is not the case; it has shown that a change in HU of nearly 2000 makes a change in RED of only 0.2-0.3. If we look at the known data of low atomic number material, a change in 0.2-0.3 RED is a change of ~650 HU, showing that the relationship is not linear.
4.3 DISCUSSION AND CONCLUSION:

These experiments have shown that the assumption that the RED-CT number file can be extended linearly to account for higher atomic numbers is incorrect. An attempt has been made to determine a suitable graph for relating the CT number and RED of IV contrast; this has proven difficult and beyond the scope of this masters thesis in Health Science. I have been able to determine the error produced currently by the use of the standard CT-RED conversion file (un-extended) and found this to be in the realms of 10-12%. However, this error is for a single beam at standard calibration conditions. The Ramm et al. (2001) studies, which are discussed further in this document, concluded that with an increase in beam numbers, the effect of IV contrast on dose calculations decreases. A 10-12% error with one beam should decrease with the increasing beam numbers used in 3D conformal Radiation therapy planning, as used in this study.

Plessis, et al., (1998), and Chu. et al., (2000) did studies, discussed previously, that showed large changes in CT numbers in higher atomic number materials resulted in smaller changes in RED, and that these changes produce very little difference in MU calculations (1%).

The potential error here has been investigated and attempts made to quantify it. It is certainly an area that requires further investigation. For the purposes of the main experiment, in chapter 5, the decision to use the capped standard CT-RED conversion file was made. This is justified as this represents the clinical situation as it stands, and the use of current technology. The impact of planning on a capped conversion file will be demonstrated in the experiment and will yield the required results and show the impact of using calculations based on this conversion file on the scan without contrast present.

In the next chapter the main experiment is conducted.
CHAPTER 5. AN EXPERIMENT TO MEASURE DOSIMETRIC IMPACT OF IV CONTRAST ON LUNG PLANS

5.1 EXPERIMENTAL METHOD

Previous authors who have conducted research on the impact of IV contrast on planning calculations have used many different experimental methods. The validity of many of these previous studies comes into question due to the experimental designs selected. For this reason, this study has been designed to use a research method that is meant to represent the actual clinical situation more accurately so that accurate conclusions on the effect of the IV contrast can be drawn.

The optimal experimental design for this situation is the pre-test/post-test design. This method enables investigations into the impact of the IV contrast on the dose calculations to be accurately assessed. The study has been designed to imitate what would happen in the clinical setting if only one scan had been taken with IV contrast present. As the additional non-IV contrast scan is also obtained, this research design allows the impact of a plan optimised on an IV contrast data set to be assessed by placing the plan on to the non-IV contrast CT data set. This enables an analysis to be carried out to assess any dosimetric differences between the ‘IV contrast CT plan’ and the ‘non-IV contrast CT plan’. This design will reproduce the clinical situation of only one CT scan, with IV contrast, may be taken, and the patient being treated without the presence of IV contrast in their body.

Ethics approval for this research was sought and gained from the Central Regional Ethics Committee (CEN/07/36/EXP).
5.2 SUBJECTS

All patients from November 2007 till November 2008, who were referred to the department for radical radiation therapy to the lung, and deemed suitable to receive IV contrast, were reviewed for this study (refer to Appendix 4. Contrast-Enhanced CT Scanning for Radiation Therapy Planning – departmental protocol). One patient was excluded when the CT scan showed extensive disease, rendering the patient unsuitable for radical treatment. Another patient was excluded as the IV contrast was not administered according to the protocol, resulting in images with very little IV contrast present.

Patients with any type, stage or grade of lung cancer and who were prescribed a dose of 48 Gy or more to be delivered using a 3D conformal technique were included in this study.

5.3 METHODOLOGY

5.3.1 CT SCAN:

All patients were imaged using the RCTS standard IV contrast Radical Chest CT scan process (Thompson, 2006) on a Siemens 6-slice ‘Emotion’ helical scanner (Siemens Medical Solutions Inc., Forchheim, Germany).
The patients were positioned supine in the department’s standard ‘Wingboard’ position, which includes thorax immobilisation using a custom-made wingboard, which places both arms above the head and supported in a cradle (see figures 3 & 4). Arm positions are recorded using a graduated scale along the ‘wings’ of the support. The patients also had a knee rest utilised for comfort.

*Figure 3. Custom wingboard*

*Figure 4. Patient positioning*
An initial topogram was taken from the level of the oral cavity to 5cm inferior to the diaphragm. The first scan was performed as per protocol: a helical CT using 3 mm collimation extending from 5cm superior to the apex of the lungs to 5cm inferior to the base of the lungs in a free breathing state; this scan is then reconstructed into 4mm slices at 4mm increments (Thompson, 2006). An initial isocentre was selected using Siemens dosimetrist virtual simulation software (Siemens Medical Solutions Inc., Forchheim, Germany) and this position marked on the patient’s skin. Immediately following the initial scan, IV contrast consisting of 100 ml of Omnipaque 350 was given, and a second scan using the same parameters as the first was performed with a standard 40-second time delay after the administration of the contrast (Thompson, 2006).

### 5.3.2 CONTOURING:

The two CT scans, one with and one without the presence of IV contrast, were fused together using Coherence dosimetrist software (Siemens Medical Solutions Inc., Forchheim, Germany). A Radiation Therapist (RT) contoured the patients’ skin surface, lungs and spinal cord. The lungs are contoured using a 3D algorithmic procedure in the dosimetrist software, which has been set to contour the lungs based on a threshold range of Hounsfield units once the RT selects the tissue to be identified as lungs. The skin surface contour included the couch top and wingboard so that the electron density of these can be accurately accounted for; this removes the requirement for any ‘couch factors’ to be added in the planning process. This is the department’s normal practice and removes any risk of human error when inputting factors, and allows for accurate representation of the actual treatment set up in the planning system.
Utilizing the fused data sets, the Radiation Oncologist (RO) was able to contour the gross tumour volume (GTV) onto the non-IV contrast scan using information from the IV contrast scan; this was done using the ‘blending’ tool in the Coherence dosimetrist software to change the mixing ratio of the non-contrast and the contrast data set so that the RO was able to visualise the contrast data set and then change the mixture to see the non-contrast data set. ROs typically contoured onto the non-contrast data set, then checked this GTV contour on the contrast data set prior to accepting it as their final contour. When the data sets were un-fused, the contours remained only on the non-contrast data set.

The clinical target volume (CTV) and planning target volume (PTV) were then created using 3D auto margins around the GTV. The sizes of these margins were determined individually by each radiation oncologist on a ‘patient by patient’ basis, using the radiation oncologists personal experience of what would make a suitable margin incorporating the setup and internal margins (ICRU, 1999). The two data sets were then separated and the non-contrast data set sent to the treatment planning system - CMS’s XiO (Computerised Medical Systems Inc., Missouri, USA).

The researcher then repeated this contouring on the contrast-enhanced data set using the same methods described above. As each scan is taken at different times, there inevitably were some differences between the pre- and post-IV contrast scans. When contouring on the contrast-enhanced CT, the researcher tried to mimic the contouring on the non-contrast CT as closely as possible. As with any manual task on slightly different data sets, there will be some unavoidable differences in this contouring, which is a weakness of this method.
5.3.3 PLANNING:

Each patient’s plan was performed by a RT and approved by the RO, according to normal protocol. This included the use of a pre-determined relative electron density conversion file for the Emotion scanner installed in the department, 3mm grid spacing, superposition algorithm and 3D conformal technique on the XiO planning system. This included the use of multiple beams and segments or ‘beams within beams’. All plans were done using the non-contrast data set only. Once the plan was complete, the researcher saved the plan as a ‘template’. Templates copy the plan’s parameters and allow these to be applied to different data sets. The template from the original plan was then placed on the contrast-enhanced data set and the plan ‘re optimised’ by the researcher. Weightings and field sizes were adjusted to suit, and dose volume histograms (DVH) produced. The new plan, as optimised by the researcher, was then re-saved as a template and placed back on the non-contrast data set. The monitor units (MUs) were changed to reflect the MUs calculated for the contrast plan. This was to demonstrate the effect of the plan that was optimised on the contrast data set on the non-contrast data set, which represents the actual state of the patient at treatment. Dose Volume Histograms (DVHs) were produced and data collected for analysis.

5.3.4 DATA COLLECTION:

DVH graphs were produced using a bin width of 10cGy and a sampling resolution of 0.1cm for the specified tissue. The following data was obtained and recorded from both the non-contrast plan and the contrast-enhanced plan:

- Lung V5, V20 and V30
- Mean lung dose (MLD)
- Maximum spinal cord dose
• Conformity index (CI)

• Heterogeneity index (HI)

The method of finding the CI has been described by the TROG 03.04 ‘RADAR’ trial (TROG, 2004). To calculate the CI, a new structure called the CI box was created with a margin on the PTV to encompass the 95% isodose curve. CI was calculated using the following equation:  

\[ CI = \frac{B}{A} \]

where:

\[ A = \text{total volume of PTV} \]

\[ B = \text{Volume encompassed by the 95\% isodose within the CI box} \]

The heterogeneity index (HI) is a ratio between the maximum dose and the prescribed dose, which should be kept as close to one as possible. The clinically significant maximum (CSM), as defined by ICRU 50/62 (ICRU, 1993, 1999), was used as the maximum dose. This, divided by the dose deemed the minimum required to achieve the aim of treatment (95\% of the prescribed dose), is the HI.

\[ HI = \frac{CSM}{95\% \text{ RX dose}} \]

The following data was also collected for each patient:

• tumour type (pathology)

• location (lobe of lung or mediastinum level)

• Stage and grade

• size (in cm³) of the PTV

• Radiation prescription
5.3.5 DATA ANALYSIS:

As this is a pre/post test experiment, the appropriate statistical analysis would be the testing of the paired data using the “paired sample t test”. When you have two sets of measurements, before and after a treatment, the null hypothesis is:

\[ H_0: \text{there is no difference in the value } X \text{ before } (X_1) \text{ and after } (X_2) \text{ treatment} \]

If the p value is more than the threshold \( p=0.05 \), then we can accept the null hypothesis that there is no difference between the two scans.
5.4 RESULTS

5.4.1 LUNG V5

Table 9. Lung V5 results, showing % of total lung volume receiving 5 Gy or more with and without contrast

<table>
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<th>Non-con</th>
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</tr>
</thead>
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<tr>
<td></td>
<td></td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>HT01</td>
<td>30.9900</td>
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</tr>
<tr>
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<td>57.3300</td>
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</tr>
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<td>49.1400</td>
<td>51.0800</td>
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<td>56.6700</td>
<td>57.6700</td>
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$P = 0.369577$

Graph 6. Graphical representation of Percentage of total lung volume receiving 5 Gy or more with and without contrast
5.4.2 LUNG V20

Table 10. Lung V20 results, showing the % of lung receiving 20 Gy or more with and without contrast

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<tbody>
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<td></td>
<td>Non-con %</td>
<td>Con %</td>
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<td>HT01</td>
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<td>11.35</td>
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<td>HT02</td>
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<td>HT03</td>
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<td>HT05</td>
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<td>6.73</td>
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<td>24.89</td>
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<td>HT10</td>
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\[ P = 0.380234 \]

Graph 7. Graphical representation of Lung V20 results, showing the % of lung receiving 20 Gy or more with and without contrast
5.4.3 LUNG V30

Table 11. Lung V30 results, showing the % of lung receiving 30 Gy or more with and without contrast

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</thead>
<tbody>
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<td></td>
<td>Non-con</td>
<td>Con</td>
<td></td>
</tr>
<tr>
<td>HT01</td>
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<td>10.42</td>
<td></td>
</tr>
<tr>
<td>HT02</td>
<td>19.84</td>
<td>21.31</td>
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</tr>
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<td>HT03</td>
<td>17.67</td>
<td>18.44</td>
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</tr>
<tr>
<td>HT04</td>
<td>25.81</td>
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</tr>
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<td>HT05</td>
<td>14.84</td>
<td>14.88</td>
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<td>HT06</td>
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<td></td>
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<td>28.17</td>
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\[ P = 0.381287 \]

Graph 8. Graphical representation of Lung V30 results, showing the % of lung receiving 30 Gy or more with and without contrast
### 5.4.4 Mean Lung Dose

**Table 12. Mean lung dose results with and without contrast**

<table>
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<tr>
<th>pt</th>
<th>MLD Non-con cGy</th>
<th>MLD Con cGy</th>
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<td>HT01</td>
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<td>878</td>
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<tr>
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</tr>
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<td>HT04</td>
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<td>1879</td>
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<td>HT05</td>
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<td>1110</td>
</tr>
<tr>
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</tr>
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</tr>
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*Graph 9. Graphical representation of Mean lung dose results with and without contrast*

\[ P = 0.389309 \]
5.4.5 SPINAL CORD MAXIMUM DOSE

Table 13. Maximum spinal cord dose results with and without contrast

<table>
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<td></td>
</tr>
<tr>
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<td>2095</td>
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</tr>
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P = 0.816146

Graph 10.). Graphical representation maximum spinal cord dose results with and without contrast
5.4.6 Conformity Index

Table 14. Conformity index results with and without contrast

<table>
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<td></td>
<td>Non-con</td>
<td>con</td>
<td></td>
</tr>
<tr>
<td>HT01</td>
<td>1.35</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
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<td>1.34</td>
<td>1.51</td>
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<td>1.56</td>
<td>1.55</td>
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\[ P = 0.902765 \]

Graph 11. Graphical representation of Conformity index results with and without contrast
### 5.4.7 Heterogeneity Index

**Table 15. Heterogeneity index results with and without contrast**

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\[ P = 0.198941 \]

**Graph 12. Graphical representation of Heterogeneity index results with and without contrast**
5.5 SUMMARY OF MAIN EXPERIMENT

The experiment was conducted as planned, although subject numbers were less than anticipated. A total of 15 patients were available for analysis. Measurement were recorded and reported as above. No statistical differences were demonstrated between the plans produced on the contrast and non contrast CT data sets. These results are discussed in chapter 6.
CHAPTER 6. DISCUSSION

This section will attempt to interpret the results, discuss the limitations of the study and possible errors induced. Finally some recommendations are made for further study.

The purpose of this study is to either validate or negate the current practice at the research centre of taking two CT scans, one with and one without the presence of contrast. Previous research was reviewed and the validity of the reported results was doubted due to varying research methods, small study numbers and the anatomical sites studied.

One would expect to see a systematic error as a result of the contrast presence, showing an increase in dose delivered on the non contrast scan compared to the dose calculated using the contrast enhanced CT scan. This would be due to the assumption that the higher density contrast would absorb more radiation in the planning calculations, yet due to it not being present at the treatment delivery, there would be less absorption leading to increased dose delivered. This is not the case in these results. The results show differences in both directions and this seems to demonstrate a non systematic cause. The source of these possible random errors is discussed along with a discussion on the overall results.

6.1 INTERPRETATION OF RESULTS

The results show that there are no statistically significant differences between the plan optimising variables calculated on the pre- and post-IV contrast scans, hence it may not be necessary to account for the presence of IV contrast on the planning CT scan. This supports the results of previous researchers in this area (Lees, et al., 2005, Shibamoto et al., 2007).
6.2 RESEARCH METHODS

There was doubt around the results of previous research due to the methods employed by the researchers. This experiment was conducted in a more clinically relevant way, to assess the differences and potential error introduced by IV contrast being present in planning CT scans. This was modeled off the methods used by Choi (2006) and colleagues. The pre- and post-test experimental method meant that the plan optimising variables could be assessed on the same patient in the same positions, with and without the contrast present. Previous researchers have used various methods to recreate this situation, forcing REDs and using anthropomorphic phantoms (Lees et al., 2005, Liauw et al., 2005). This study used both pre and post IV contrast scans, placing the same plan on each, and analysed the differences. This method is more akin to the clinical situation where planning would be done on a contrast enhanced CT scan and treatment delivered to the patient with out contrast present. The results of this study are therefore more valid due to the realistic testing environment.

The current method employed in my department of using two scans, pre- and post-contrast, does introduce a number of errors however. The two CT scans, although taken in the same treatment position, are taken in a ‘free breathing state’ and this results in images obtained in different phases of the breathing cycle. This difference makes accurate ‘fusing’ of the two scans difficult. The radiation oncologist then contours the gross tumour volume (GTV) and creates the clinical target volume/ planning target volumes (CTV/PTV) based on the contrast-enhanced CT data set. This is the volume that the Radiation Oncologist (RO) requires to be irradiated to achieve the aim of treatment (ICRU, 1999). This could mean that the locations of these planning targets are not exactly the same on the non-contrast data set, which is used for planning, and its location in relation to the OAR is important when optimising radiation therapy. This is especially evident with radical lung cases where the effect of
physiological movement due to respiration and heartbeat is unavoidable without the use of expensive and complicated gated CT scanning and treatments.

The errors induced due to these physiological changes between the two scans may account for some of the random errors in the results obtained. The results fluctuate between patients, some showing higher doses with contrast whilst other show higher doses without the contrast present.

Miller and Joon (2002) attempted to use ‘breath hold’ CT scans to minimize the likelihood of movement between CT scans with and without contrast for their study. This experimental method did not relate to the clinical situation in which treatment is delivered in a free breathing state. Miller and Joon found that the number of MUs needed to deliver the same dose to the PTV changed when contrast was present on a scan. Unfortunately the method of their experiment, in keeping the dose constant and changing the MUs, makes comparison with this research difficult.

This research’s method of keeping the MUs constant between the two calculation sets was different to previous researchers; this was done to produce results that gave an accurate account for any potential miscalculations in dose delivered. Dose differences are more clinically relevant than MU changes. Dose volume histograms were used to determine dose differences between plans. The variables used in this experiment are the most commonly used variables for assessing the optimisation of a thorax plan; V5, V20, V30, MLD, spinal cord maximum, CI and HI. This produced results which are clinically relevant.

Another important difference in the research method used in this study is the planning technique. Previous studies have used very simple planning techniques and did not report the algorithm used in planning calculations. Ramm’s 2001 study used basic planning techniques utilising 2-4 fields. Modern planning techniques, as used in this study, often use
more beams than this. Ramm (2001) found that with an increase in beam numbers the effect of the contrast on dose calculations decrease. This can also be supported by the fact that the studies using IMRT in the head and neck area, also found no statistical differences in dose calculations in the presence of contrast (Choi et al., 2006). It is likely those results could be due to the large number of beams utilised with IMRT. This research utilized Superposition calculations algorithms for dose calculations which is the most up to date technology available at the research centre.

6.3 SITE STUDIED

A major difficulty when reviewing the literature was the sites studied when investigating the Impact of IV contrast on dose calculations. The majority of previous studies done have been done in the head and neck area (Choi et al., 2006; Liauw, et al., 2005). It was proposed that the thorax would be a site in which the contrast would have more of an effect on dose calculations. This was based on studies done by Ramm et al. (2001) who found that the larger the vessel was containing contrast, the larger the effect on dose calculations. The thorax contains much larger blood vessels and the heart which fill with contrast during a contrast enhanced CT scan. The head and neck studies reviewed all showed that there was no influence due to the contrast present in the small blood vessels in the head and neck (Choi et al., 2006).

This prediction of a greater influence in the thorax planning scans was also supported by smaller studies in which upper abdominal areas showed some differences in the MUs required to be delivered to deliver the same dose in the absence of contrast when planned on contrast scans (Shibamoto et al., 2007). These studies hypothesised that this increase in need for MUs in the presence of contrast was due to the larger organs such as liver and
kidneys up taking large amounts of IV contrast, this could also be similar to the heart and major blood vessels containing contrast. However the results of this study have not shown this.

Additional problems with previous studies in which the impact of IV contrast was attempted to be investigated in the Thorax was the use of phantoms which could not clinically represent the true physiological intake of contrast in the thorax. This study addressed this issue by using real patient’s scans with and without contrast.

6.4 RED-CT NUMBER CONVERSION FILES

Reviewing the published literature on previous experiments in the area of the effect of contrast on dose calculations showed that the problem of CT-RED conversion of higher atomic number materials is often not considered. This study has considered this issue.

The CT-RED experiments conducted were successful in demonstrating that the relationship between CT numbers and RED in higher atomic number substances is not linear. Current modeling should not be used when trying to relate high atomic material CT numbers to RED for planning purposes. The results show that the XiO planning system with its current CT-RED conversion file will ‘cap’ the RED at 1.71 for all CT values higher than 1152, which is approximately the density of cortical bone. Experiments done showed that with no correction for this fact, using a single beam at standard calibration conditions, contrast induced a measured error in the realms of 10-15%. These results must be viewed with caution. This does demonstrate that when a single beam is passed through a volume of contrast, errors are possible, however in the clinical situation, only small amounts of contrast are present for the planning scan also beams are not usually directed straight.
through the high uptake areas such as the heart and multiple beams are used, all of which reduce these errors significantly, as shown in the results of the main experiment.

Initially there was concern that if the CT-RED conversion files were inaccurate, the results of the main experiment of this thesis would be invalid. Upon further consideration of this situation, it is proposed that this is not of concern for this study. With a capped RED conversion file the TPS will assign the maximum RED to any densities higher than the cap level, this would mean the TPS models the radiation interactions based on the maximum RED of 1.71 and not the actual RED of the contrast. This may mean the TPS is underestimating the absorption of the radiation by the contrast. If the case was that the contrast was present for the treatment, this would be a concern, however in this study the contrast is not actually present for the treatment hence any underestimation of absorption is not of concern.

As this study has shown that the differences between the contrast and non contrast scans are not significant, then the fact that the modeling of the contrast in the TPS is not completely accurate is of no concern, because ultimately the differences between the calculations are not significant.

This study used the capped RED file, and has shown that there is no statistical difference between the calculated dose in the presence of the contrast and the calculated dose without the contrast present. As it is the current method to use a capped RED file and attempts to extend this were unsuccessful, the results from this study are still valid. Caution must be used if a non capped RED file is used to produce plans based on contrast scans, as this study has not compared the dose calculated using an extended RED file.

Previous published research does not discuss the use of capped RED files and hence it is difficult to relate their results. CT-RED conversion files are an important consideration when
planning in contrast presence. Personal investigation into the CT–RED conversion files used by other departments has shown some departments simply extend their CT-RED file linearly. Experiments conducted in this study have shown that this is not accurate for higher atomic number materials. If calculations in the presence of contrast are done using this sort of file, errors are possible.

6.5 CLINICAL APPLICATION

The main conclusion of the experiment is that there is no difference between the two data sets, one prior to and one following the application of a ‘change’. These results have been obtained using the same set of circumstances and conditions, hence any differences seen, or not seen in this case, are valid.

The results of this study support those of previous researchers in this area and other anatomical sites (Lees, et al., 2005, Shibamoto et al., 2007). There is statistically no significance between the pre- and post-contrast scans results. This supports the actions of radiation therapy departments conducting only the one CT scan – with the presence of contrast and planning on this scan.

Hence there is no justification for the two scans to be taken. Taking two CT scans (with and without contrast) ultimately doubles the patient dose from imaging, following the ALARA principle radiation therapists are required to keep dose to patients to a minimum, taking unnecessary scans goes against this principle.

Other possible sources of the random results shown, need to be considered. The studies subjects were of various sizes, with tumors in various locations in the thorax. This variable could also be impacting on the results. The use of larger subject numbers of more similar sites could reduce these errors.
6.6 LIMITATIONS OF THE STUDY

There are a number of limitations to this study, the main one being in the contouring of the target volumes. The Radiation Oncologists contoured the targets onto the non-contrast scan, using the contrast scan to aid in this. The researcher then attempted to accurately reproduce this contouring on the contrast scan. Errors were introduced, as exact replication was not possible.

A further limitation is the study numbers. Initially this study aimed to enroll 40 patients, however only 15 were successfully included in this study. A number of reasons account for this; firstly a reduction in the number of lung patients being treated radically in the department in which this study was conducted due to an increase in PET scanning as part of the diagnostic work up. PET scanning has meant more patients are being deemed not suitable for radical treatment due to the presence of metastases that have previously gone undetected when using standard diagnostic techniques. Secondly, the number of patients deemed ‘fit’ for IV contrast scans was less than expected. This is most probably due to the damaging effects of previous chemotherapy making patients unsuitable to receive contrast and also the poor performance status of many lung cancer patients. Lastly, one patient was excluded from the study as the aim of treatment changed to palliative after the scan and another was excluded as the contrast scan was not executed according to protocol and the volume of contrast administered was too small.

6.7 RECOMMENDATIONS FOR FURTHER INVESTIGATION

Areas for investigation include:

- Further investigation using a larger patient cohort should provide more solid evidence that there is no significant difference between contrast and non-contrast scans.
• The impact on the production of Digitally Reconstructed Radiographs (DRRs) due to the presence of contrast.

• The ability to use Megavoltage Cone Beam (MVCB) scans with contrast present to determine the true RED of the Contrast and the impact on dose calculations.
CHAPTER 7. CONCLUSION AND RECOMMENDATIONS

This study has achieved its aims. It was intended to:

1. Investigate the CT number – RED conversion for IV contrast

2. Quantify any errors caused by the CT-RED conversion

3. Make recommendations to the research centre, and other Radiation Therapy departments considering the use of IV contrast in radiation therapy planning of the thorax, on the optimal method for planning in the presence of IV contrast.

The CT-RED number conversion investigation proved difficult but ultimately proved there is concern with simply extending RED conversion files linearly as many departments do.

Investigations to quantify the possible degree of error showed with a single beam this could be in the realms of 10-15%, but based on other research this potential error should be less due to the beam numbers used in modern treatment techniques.

The results show there is no statistically significant difference between the two plans with or without the IV contrast present.

Recommendations can be made that only one planning CT scan needs to be taken, and that the presence of IV contrast on that scan will not influence the dose calculations significantly.
REFERENCES


25 September 2007

Hannah Thompson
10 Halcombe Road
Feilding
New Zealand

Dear Hannah

Thank you for submitting your research proposal ‘The Effect of the Presence of IV Contrast on Planning CT scans for Radical Radiation Therapy to the Lung’

The proposals committee of the School of Health Science has considered and approved your proposal, subject to you meeting some requirements to the satisfaction of your supervisors and Programme Director (Dr Fred Murphy) (or Discipline Leader Assoc Prof Jill Yelder). The requirements are listed below. Please send the revised final proposal with the signed confirmation of approval form (enclosed with this letter) to the School before you begin your research project.

Requirements (you must address these points in a revised version of the proposal):

1. Literature Review (para 3, p.8): The readers acknowledge that there may be little published literature that specifically relates to the intended research question. However, you should indicate the basic search strategy (list databases and give examples of key words) used – this provides confidence for the reader that there is indeed little indexed literature, rather than the possibility that there is literature but you’ve simply not identified it. You’ve identified at least 4 studies (two for thorax and two head and neck). You need to critically review these studies (and any others) in your literature review.

2. (p.11) Please provide further rationale for your intended sample size. In the absence of previous studies or pilot work from which effect sizes can be determined, you may like to consider calculating a sample size ‘on the fly’ – meaning you would run some sample size calculations using the first 10 subjects – this would enable you to estimate a more accurate sample size. (see http://www.sportsci.org/resource/stats/index.html for further info; http://www.psycho.uni-duesseldorf.de/aap/projects/ipower/ provides free software to assist in calculations)
3. (p. 12 para 1) Please clarify the nature of the relationship with the Australian researchers undertaking similar work. How are you planning on using the results from the other site?

Suggestions (offered as general observations, no immediate action required)

1. We note that much of the proposal is written in the first person. While acceptable for a proposal you'll need to use the third person in preparing your dissertation.

Please note that after you have addressed the requirements you may need to make changes to your proposal for ethics approval.

Your principal supervisor is John Poletti and Assoc Prof Jenny Cox (University of Sydney) is acting as an external advisor.

Please be aware that ethical approval may be required for your research once you have finalised your proposal. To determine the need for ethics application and approval, we recommend that you read the Guidelines for Ethical Approval in the Research folder on the Blackboard site Postgraduate Students Resources, to identify any ethical issues that may arise. Discussion with your supervisor or the ethics committee (email: ethics@unitec.ac.nz) may also assist in this decision process. This will help determine the need, or otherwise, for a full application for ethical approval. In particular you will need to consult with your supervisors about the need for ethics approval from your local Palmerston North ethics committee.

Please contact us if you have any questions, or if we can assist you in your research, by contacting me by email address rmoran@unitec.ac.nz

We wish you every success in completing your research project.

Yours sincerely,

Robert Moran
School of Health Science Proposals Committee: Acting Convener

cc:

Principal Supervisor: John Poletti
Associate Supervisor: Dr Jenny Cox
Head of School: Maurice Drake
Programme Director: Dr Fred Murphy
Programme Administrator: Anne Keal
Postgraduate Academic Administrator: Carla Sutton
2. MID CENTRAL HEALTH RESEARCH COMMITTEE APPROVAL

MidCentral Health

Regional Cancer Treatment Services
Research Centre: Radiotherapy Dept.
Palmerton North Hospital, Parkhome Street,
Palmerton North
Private Bag 11639, Palmerton North
Ph: 64 6 350-0036    Fax: 64 6 350-0433

September 7, 2007

Hannah Thompson
Clinical Tutor RT
Radiation Oncology
MidCentral Health

Dear Hannah

Ref: your study on: "An Investigation into the Dosimetric Impact of the presence of IV contrast on Planning CT scans for Radical Radiation Therapy to the Lung"

At our recent meeting of the RCTS Research and Protocol Committee on 29 July 2007 we discussed your above research proposal, and are pleased to advise that the committee fully supports your study.

We wish you well with your study and would appreciate any ongoing updates of your progress – along with a copy of the final report.

Yours sincerely

[Signature]

Richard Isaac
Chairman of the RCTS Research and Protocol Committee
Regional Cancer Treatment Service
Research and Protocol Committee

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Copies to: Penny O'Leary, Company Manager, director, Principal Investigator, Clinical
3. HEALTH AND DISABILITY COMMISSION CENTRAL REGIONAL

ETHICS APPROVAL

Central Regional Ethics Committee
Ministry of Health
Level 2, 1-3 The Terrace
PO Box 5013
Wellington
Phone (04) 496 2465
Fax (04) 496 2181

19 November 2007

Hannah Thompson
19 Halcombe Road
Feilding

Dear Hannah

CEN/07/36/EXP
The Effect of the Presence of IV Contrast on Planning CT scans for Radical Radiation Therapy to the Lung.
Ms Hannah Thompson

The above study has been given ethical approval by the Central Regional Ethics Committee. A list of members of this committee is attached.

Approved Documents

- Information sheet and consent form Student ID# 1231123, Hannah Thompson, MidCentral Health

Certification

The Committee is satisfied that this study is not being conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is being carried out.

Accreditation

The Committee involved in the approval of this study is accredited by the Health Research Council and is constituted and operates in accordance with the Operational Standard for Ethics Committees, April 2006.

Final Report

The study is approved until 16 November 2008. A final report is required at the end of the study. The report form is available on http://www.health.govt.nz/ethicscommittees and should be forwarded along with a summary of the results. If the study will not be completed as advised, please forward a progress report and an application for extension of ethical approval one month before the above date.

Requirements for SAE Reporting

The Principal Investigator will inform the Committee as soon as possible of the following:
- Any related study in another country that has stopped due to serious or unexpected adverse events
- Withdrawal from the market for any reason
- All serious adverse events occurring during the study in New Zealand which result in the investigator breaking the blinding code at the time of the SAE or which result in hospitalisation or death.
- All serious adverse events occurring during the study worldwide which are considered related to the study. Where there is a data safety monitoring board in place, serious adverse events occurring outside New Zealand may be reported quarterly.

All SAE reports must be signed by the Principal Investigator and include a comment on whether he/she considers there are any ethical issues relating to this study continuing due to this adverse event. It is assumed by signing the report, the Principal Investigator has undertaken to ensure that all New Zealand investigators are made aware of the event.
Amendments
All amendments to the study must be advised to the Committee prior to their implementation, except in the case where immediate implementation is required for reasons of safety. In such cases the Committee must be notified as soon as possible of the change.

Please quote the above ethics committee reference number in all correspondence.

The Principal Investigator is responsible for advising any other study sites of approvals and all other correspondence with the Ethics Committee.

It should be noted that Ethics Committee approval does not imply any resource commitment or administrative facilitation by any healthcare provider within whose facility the research is to be carried out. Where applicable, authority for this must be obtained separately from the appropriate manager within the organisation.

Yours sincerely

Jiska van Bruggen
Central Regional Ethics Committee Administrator

Email: jiska_van_bruggen@moh.govt.nz
4. CONTRAST ENHANCED CT SCANNING FOR RADIATION THERAPY PLANNING

CONTRAST ENHANCED CT SCANNING FOR RADIATION THERAPY PLANNING

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WORKING DOCUMENT COPY – LAST UPDATED 16 APRIL 2008

1. PURPOSE

To provide a guideline for the administration of contrast agents for the purposes of radiation therapy planning.

2. SCOPE

Radiation Oncologists (RO)
Radiation Oncology Registrars (ROR)
Radiation Therapists (RT)
Radiation Oncology Nurses (RON)
Radiation Oncology Booking Clerk

3. PROTOCOL INDEX

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| A | Administration of Contrast – clinical guideline |
| B | Contra-indications for IV contrast media in radiation oncology |
| C | Reactions to Contrast media, treatment and DOCUMENTATION |
| D | Treatment for extravasation of contrast media |
| E | Storage and warming of contrast media in radiation oncology |
A. Administration of Contrast – clinical guideline

A.1 ROLES & RESPONSIBILITIES

Radiation Oncologists
- The RO will append the QCL to alert the Booking Clerk that the patient will require contrast at CT.
- The RO will give the patient a blood test request form to check the serum creatine levels and instruct the patient that once they have been informed of the appointment time for the CT they are to have the blood test done 2 days prior to the appointment.
- A RO or ROR prescribes the contrast to be administered.

Radiation Oncology Registrars (ROR)
- A ROR must be present in the CT/Planning area and aware that the contrast is to be given before intravenous contrast is administered.
- A RO or ROR prescribes the contrast to be administered.
- The RORs complete and maintain the level 7 CORE training.
- The ROR is responsible for Patient consent process.

Radiation Therapists (RT)
- Complete Fundamental IV Therapy training and injector training.
- Fundamental IV Therapy training & Use of the AED+ defibrillator will be part of CORE skills, a bi-annual requirement for all Radiation oncology staff. Injector training will be given initially to all staff then the CT supervisor will be responsible to provide continuing education for current and new staff to the area.
- The RT ensures that the consent form for contrast injection is complete and signed prior to commencing the contrast scan.

Radiation Oncology Nurses (RON)
- Commence Intravenous Fluids prior to contrast to ensure the IV peripheral cannula remains patent until the patient leave nursing clinic area.

Booking Clerk
- The booking clerk will send the “Consent form for X-Ray Contrast Injections” and “Information sheet for patients receiving contrast media” to the patient with their appointment time.
- The booking clerk will book the CT scan on Wednesday afternoons only.
- Patients requiring a mask will have their mask made prior to the nurse’s appointment. It is possible that this may be in the morning if necessary to allow for more bookings Wednesday afternoons.

A.2 PREREQUISITES

- Consent form and drug chart have been completed and signed.
- The RON will retrieve the blood test results for patients receiving a contrast scan prior to the CT scan.
- The patients blood test results have been checked by the ROR as part of the initial patient assessment prior to the CT appointment and levels of Serum Creatinine are within limits (consider using Visipaque 270 if levels are high).
- Suitable Intravenous access.
Contrast is warmed in the incubator to a temperature of 37°C.
Emergency resuscitation trolley and AED (automatic external defibrillator) is present in room.

A.3 CLINICAL GUIDELINE

STAFF HEALTH AND SAFETY

- All Staff involved have the appropriate level of training.
- Resuscitation equipment and emergency trolley are present throughout the procedure.
- Infection control standards are maintained.
- No persons remain in the CT room, other than the patient, during the scan.

Assessment Prior to CT
- Prior to the CT appointment, in a clinic room, the ROR will go over the consent form for x-ray contrast injections, and if contrast is recommended, it will be signed by the patient and the ROR (as a witness).
- If the patient is requiring a mask the mask can be made prior to the insertion of the cannula. Once the mask is made the patient can be sent around to the nurses for the cannulation and pre contrast interview with the ROR.

Preparation Prior to CT
- Take a gown to the nurses clinic so the patient can change before the line is inserted.
- The ROR will fill out the Drug chart to prescribe the contrast and IV fluids as well as establish suitable IV access.
- The RON will commence a 0.9% Sodium Chloride infusion (250ml bag) to ensure IV Cannula is patent and fluids are running freely.
- The patient will then be transferred to the CT room, and the procedure explained to them.
- RT liaises with ROR re the size of the cannula inserted. If a 20 gauge is used flow rate 3ml/sec and if a 24 gauge cannula is used reduce flow rate to 1ml/sec.
- The RT takes the pre warmed (37°C) contrast out of the incubator and checks the expiry date and type/strength of contrast with another RT.
- The two RTs who checked the contrast will sign the drug chart under ‘nurse’s signature’ and attach the contrast batch label to the patients drug chart.
- The required contrast will be drawn up/loaded in to injector by the RT and checked by the ROR prior to aseptically disconnecting the IV 0.9% Sodium Chloride infusion, attaching a combi lock to the IV administration set and connecting the automatic injector to the patient.
- The appropriate scan protocol will be selected; this will include a topogram, a scan with out contrast, followed by the administration of the contrast, a time delay (if necessary) and a second scan of the same area.
- After the first, non-contrast CT scan the CT mark will be placed and then marked on to the patient with gentian pen. Remind the patient to remain very still through out this procedure. With-out re-zeroing the couch move the patient back to the start position.
Contrast Administration
- The contrast will then be administered while the appropriately trained staff member observes the injection site, watching for signs of extravasation (see appendix D). The site needs to be observed for 10-15 seconds then the staff member will leave the room and start the second CT scan after the appropriate time delay.
- Consider using a slower flow rate of 1ml/sec for elderly or frail patients.

<table>
<thead>
<tr>
<th>SITE</th>
<th>Recommended contrast agent</th>
<th>Recommended amount of contrast</th>
<th>Recommended flow rate</th>
<th>Recommended time delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radical Brain</td>
<td>Omnipaque 350</td>
<td>50 ml</td>
<td>Hand pushed</td>
<td>None (up to 5 minutes is acceptable)</td>
</tr>
<tr>
<td>Radical Chest, Head &amp; Neck, Seminoma, Pelvis</td>
<td>Omnipaque 350</td>
<td>100 ml</td>
<td>2ml/sec (in back of hand, if using cannula in ante cubital fossa use 3ml/sec)</td>
<td>30-40 seconds</td>
</tr>
</tbody>
</table>

Completion of CT
- Once the final CT scan is complete and all final marking/photographs and measurements are done the injector can be disconnected and patient assisted off the couch.
- The IV 0.9% Sodium Chloride infusion can be restarted: wash hands, scrub the hub with an alcohol wipe and allow to air dry, remove the combi lock and re-connect the IV administration tubing and commence the infusion by opening the roller clamp.
- The patient should then remain in their gown and pre treatment patient education can be given.
- The patient should be observed for 30 minutes after the administration of the contrast, once the 30 minutes is up the IV cannula can be removed by the RT.
- The patient should be advised of possible late side effects of the contrast and, to drink plenty of water over the next 24 hours.
B. **Contra-indications for IV contrast media in radiation oncology**

B.1 **ROLES & RESPONSIBILITIES**

The RO / ROR is responsible for the decision to use contrast media and which contrast media to be used.

B.2 **PREREQUISITES**

Patient to complete the pre- contrast consent form and be interviewed prior to administration of contrast.

B.3 **GUIDELINE**

At the initial consultation patients who may be requiring a contrast scan are to be given a blood test request form for serum creatine levels and instructed that they are to have the blood test done two days before they come for the radiation therapy planning CT.

The booking clerk will remind the patient about having the blood test two days before the CT appointment when the patient is given their appointment time.

A ‘contrast information and consent’ form is sent out with their initial appointment time.

The day prior to the CT appointment, the RON will obtain the patient’s blood test results for serum creatinine levels and inform the ROR.

The ROR will go over the consent form at the pre CT appointment in the clinic rooms.

The ROR will assess the patient’s suitability for IV contrast and decide if Omnipaque 350 or Visipaque 270 will be used.

Any patient taking Metformin will not have IV contrast.

The Patient, if happy to proceed with the scan, the ROR or RO will complete the consent process.

**Conditions which MUST be brought to the attention and assessed by the Radiation Oncologist or Registrar prior to administration of IV contrast media**

- History of previous reaction to any contrast media
- Asthma
- Allergies
- Multiple Myeloma
- Diabetes (especially if taking Metformin)
- Renal Dysfunction
- Cardiac disease
- Pulmonary hypertension
- Epilepsy or history of seizures
- High serum creatinine levels (see Table 1)
- Pregnancy/breast feeding
- Pheochromocytoma
- Hyperthyroidism
- Waldenstrom’s macroglobulinemia
The RO or ROR will decide which contrast media to use and whether to go ahead with the contrast injection or not.

### Table 1  Serum Creatinine levels:

<table>
<thead>
<tr>
<th>Serum Creatinine level:</th>
<th>Result:</th>
<th>Contrast:</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;130</td>
<td>normal</td>
<td>Omnipaque 350</td>
</tr>
<tr>
<td>130-180</td>
<td>Abnormal</td>
<td>Review need for contrast. If necessary use Visipaque 270. Patient may also require additional fluids prior and after administration of contrast.</td>
</tr>
<tr>
<td>&gt;180</td>
<td>Very High</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

#### Reactions to Contrast media, treatment and documentation

**C.1 ROLES & RESPONSIBILITIES**

**Reaction & Treatment**
- Observation of patients given contrast.
- Informing the Radiation Oncologist/Registrar of any adverse reactions.
- Resuscitation, emergency first aid.
- Dialling 777 in an emergency to call Arrest team.
- Patient monitoring.

**Radiation Oncology Nurses**
- Maintenance of Arrest trolley.
- Resuscitation, emergency first aid.
- Patient monitoring.

**Radiation Registrar**
- Deciding on treatment options.
- Resuscitation, emergency first aid.
- Administration of IV medication.
- Referral to E.D. if necessary.

**Documentation**
- Radiation Registrar: Fills in required MCH documentation (adverse reaction to Medicine)
- Radiation therapists: Ensure reaction is recorded in LANTIS in the Patient notes and in “Allergy and Alerts”

**C.2 PREREQUISITES**

- Patient with adverse reaction to Intravenous or other contrast
- Emergency drugs and equipment available
- Oxygen supply
- IV access
C.3 CLINICAL GUIDELINE

Health and Safety

Standard precautions for IV Injections and care with bodily fluids
Ensure a Radiation Oncologist/Registrar is available and aware of the injection before administering contrast

REACTION & TREATMENT

Minor Reactions
Flushing, nausea, arm pain, pruritis, vomiting, headache, mild urticaria.
These are usually mild and self-limiting and require no specific treatment other than reassurance.

Oral Claratyne (Loratadine) 10mg may be given
or Phenergan (Promethazine) 25mg im or IV(diluted in 10ml saline)

Bronchospasm
Mild to moderate bronchospasm can be treated with Salbutamol inhalation
Hydrocortisone 100mg iv
For more severe bronchospasm add Adrenaline (5ml of 1/10,000 im) until response achieved.

Reassurance of the patient and Oxygen via high concentration mask administration are also important

Severe or life-threatening reactions
Severe degrees of the above, convulsions, hypotension, unconsciousness, laryngeal oedema, pulmonary oedema, severe cardiac arrhythmias or cardiac arrest.

If there is felt to be any risk to the airway or cardiac output then the Cardiac Arrest team 777 should be called immediately.

The following may be required:
Adrenaline 1/10,000 im boluses IV or 5ml IM
Secure the airway with oral airway or ET tube
Oxygen
Artificial ventilation with Ambubag
External Cardiac Massage
Escalating doses of adrenaline if cardiac arrest
Intravenous 0.9% Sodium Chloride 250ml, or 1000ml bags for infusion
Frusemide (40-80mg IV) for pulmonary oedema
Diazepam 10mg IV for convulsions
Hydrocortisone 100mg iv for allergic or anaphylactic symptom
Phenergan (Promethazine) 25mg im or IV(diluted in 10ml saline)
C.4 DOCUMENTATION

RT and RO or ROR ensures LANTIS records are updated to include “ALLERGY and ALERT”

collects 4 forms for Radiation Registrar to fill in
sends forms to appropriate areas as indicated on forms
1. forms to Pharmacy
2. form to Medical records for patient notes
3. places “ALLERGIC” stickers in patients notes
4. Inform radiology of reaction

ROR - fills out 4 forms, gives forms to RT

C.5 REFERENCES

Blackwell Science

Treatment for extravasation of contrast media

D.1 ROLES & RESPONSIBILITIES

RTs involved in administration of intravenous contrast media are responsible for observation of IV site during injection of contrast media.
RO/ROR/RT recognises signs and symptoms of extravasation and discontinues infusion or injection immediately.
Radiation therapy staff provides immediate first aid.
Radiation therapy staff document incident in the patient notes in LANTIS and inform nurses in ward if an inpatient.

D.2 PREREQUISITES

Appropriate consent form for CT scan which requires administration of intravenous contrast media.
Insertion of intravenous cannula into identified and prepared patient.
RT’s who are qualified to administer intravenous contrast medium.

D.3 PROCEDURE
Health and Safety
Extravasation will be avoided by careful attention to technique. If an incident of extravasation occurs it will be treated promptly in accordance with procedure.

- Infusion is discontinued immediately and I.V. cannula removed.
- Apply ice pack to affected area.
- Elevate affected limb.
- Explain what has occurred to the patient and reassure as necessary.
- Inform RO in charge of patient.
- Inform ward staff when patient is an inpatient.
- Document incident in patient notes on LANTIS.
- The Radiation Oncologist will decide if the scan is to be continued, or the patient rebooked.
- Arrange follow-up if required.

D.4 DEFINITION

Extravasation is defined as escape of vesicant fluid from its proper vessel into the surrounding tissues (Dorland).

Signs and Symptoms
Erythema
Swelling usually subside without further untoward side effects
Burning or stinging sensation

Patients at Risk
Elderly (fragile veins)
Unconscious patients
Past radiation to I.V. site
Peripheral vascular disease
Diabetes Mellitus
Raynauds disease

D.5 REFERENCES
Storage and warming of contrast media in radiation oncology

E.1 ROLES & RESPONSIBILITIES

Radiation therapy staff working in CT will ensure that the bottles of contrast stored in the incubator are not kept for longer than 3 months at 37°C or past their expiry date.

RTs administering the IV contrast will ensure the contrast is warmed to 37°C prior to injecting.

The Specialist/supervisor working in CT will ensure that daily QA of the incubator is performed by all staff.

E.2 PREREQUISITES

Contrast media
Light tight Incubator set to 37°C

E.3 CLINICAL GUIDELINE

**STAFF HEALTH AND SAFETY**

Check setting on the incubator – must be 37°C (body temperature)

Glass bottles of contrast media may be stored for up to 3 months at 37°C

Contrast media should be protected from light and secondary x-rays

Staff in CT can collect the required contrast media (Omnipaque 350) from the cupboard in clean utility, where it is ordered on Imprest. (Visipaque 270 can be borrowed if needed from Radiology)

The contrast is placed in the incubator with the date which is it was placed in the incubator written on a sticker and placed on the top of the bottle.

Up to 6 bottles of contrast media are to be kept in the incubator at all times, when selecting a bottle for use ensure you take the bottle with the oldest date (not older than 3 months).

Always check the contrast media’s expiry date prior to use.

QA of contrast media warming incubator:

The incubator is stored in the store room in the CT room. It is important that this be NOT stored in the actual CT room so to protect the contrast from secondary X-rays.

Each day as part of the normal CT QA process the internal temperature of the incubator must be checked. To do this, place a thermometer in the incubator
for 5 minutes (with the door closed). Read the temperature and record this in LANTIS under patient: CT QA, Assessments, daily RT QA. Tolerance for the temperature is ±2°C of 37°C. Report any out of tolerance readings to CT supervisor/specialist.

E.4 REFERENCES

Omnipaque information sheet
Radiology storage of contrast media documentation

5. DEFINITION

AED+ – Automatic external defibrillator
RO – Radiation Oncologist
RT - Radiation therapist
IV – Intravenous

6. FURTHER INFORMATION / ASSISTANCE

Resuscitation officer
ICU staff
Radiation Oncologist
Radiation Oncology Staff Nurse
Pharmacist

7. RELATED MDHB DOCUMENTS

MDHB-3726 Information & Consent Form for X-ray Contrast Injections [Form]
MDHB-1002 Adult peripheral intravenous cannulation [Procedure]

Intravenous Contrast for Radiation Therapy Planning CT Scanning – Patient information sheet

8. KEYWORDS

Contrast media, Radiation therapy, CT scanning, Extravasation, Incubator QA