Improving high dose rate and pulsed dose rate prostate brachytherapy – alternative prostate definition and treatment delivery verification methods.

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**Declaration**

Except where acknowledgements are made in the text, all work described in this thesis is that of the author. This thesis has not previously been submitted in whole or in part for any academic award to any Institute or University. The content of this thesis is the result of work carried out since the official commencement date of the approved research program. Ethics procedures and guidelines have been followed.

Andrew Gordon Howie
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Summary
Brachytherapy is a form of radiotherapy in which radioactive sources are placed at short distances from, or even inside the target volume. The use of high dose rate brachytherapy is a widely accepted and clinically proven treatment for some stages of prostate cancer.

The aim of this project was to investigate potential improvements on two of the most important aspects of high dose rate (HDR) and pulsed dose rate (PDR) prostate brachytherapy – prostate definition and treatment delivery verification.

The use of magnetic resonance (MR) imaging in addition to the conventional computed tomography (CT) imaging methods currently used routinely for brachytherapy planning may provide some benefit in accurately defining the prostate and surrounding critical structures. The methods used in this project involved analysis of data sets provided by two Radiation Oncologists at St George Hospital. With only two Oncologists providing the data, the results presented were assessed for trends and were not expected to provide statistically rigorous conclusions. The study presented here would require a larger cohort of participating Oncologists to be able to draw such conclusions.

The results presented showed inter-observer and intra-observer variations in the size and shape of the prostate, as well as analysis of the dosimetric differences that may be reported due to the differences in prostate size and shape. The results also included analysis of critical structure dosimetry – dose to the surrounding radio-sensitive rectum and urethra.

In summary, the results showed that the prostate was defined to be smaller using MR imaging than CT, however the consistency between Oncologists was not significantly improved using MR imaging. Assuming MR imaging is more accurate than CT in defining the prostate as reported in publications such as Menard, Susil et al. (2004), it may be useful in reducing the dose to normal tissue surrounding the prostate and in obtaining better coverage of the smaller target volume, without compromising the critical structures.
The use of LiF:Mg,Ti thermoluminescent dosimeters (TLDs) is a potential avenue for \textit{in vivo} dose verification of an HDR or PDR prostate brachytherapy treatment plan. This project included a phantom study of these TLDs with the aim to determine their feasibility for clinical use. Cylindrical TLD rods (6 mm length x 1 mm diameter) were used, as these fit inside the brachytherapy needles implanted into the prostate, and therefore had potential to be used clinically to verify the dose delivered in the prostate.

This study was extended to include determination of a correction factor to allow an independent radiation source (6 MV photon beam from a linear accelerator) to be used to obtain control readings for this relative dosimetric method.

The results showed these TLDs to be a promising \textit{in vivo} dosimeter for prostate brachytherapy with potential errors in the order of 4%. Their potential lies in the fact that they could detect and flag significant calculation errors in treatment plans, and they utilise equipment used routinely for external beam radiotherapy dosimetry in many treatment facilities, reducing the cost of implementing such a procedure.

Incorporation of these potential improvements into clinical use requires further work. As MR imaging involves a greater cost than CT imaging, it is important to be able to justify the potential benefit to the patient. To commence using MR imaging routinely would require further analysis of data from a larger cohort of Oncologists to obtain a more statistically rigorous set of results than those presented in this thesis. A trial use of LiF:Mg,Ti TLDs for \textit{in vivo} dosimetry of prostate brachytherapy at St George Hospital is supported based on the results of this investigation along with data that has been published by Anagnostopoulos, Baltas, \textit{et al} (2003) and Toye, Das \textit{et al} (2008). If the results of such a trial are successful, it may be feasible to include this as a routine procedure for all prostate HDR brachytherapy patients.
Chapter 1: General Introduction

The aim of this thesis was to investigate potential improvements on the two most important aspects of high dose rate (HDR) and pulsed dose rate (PDR) prostate brachytherapy – prostate definition and treatment delivery verification. By investigating the use of magnetic resonance imaging of the prostate post-implant and analysing the results of TLD measurements in a phantom study, this thesis provides an assessment of the benefits of incorporating these techniques into the current clinical environment, with a focus on the brachytherapy program at St George Hospital in Sydney, Australia.

1.1 Prostate Cancer

Prostate cancer is the most prevalent form of malignancy in the male population. The American Cancer Society estimated over 30,000 deaths from the disease in the United States of America in 2005, and over 230,000 new diagnoses (Butler and Merrick 2005). Australian data suggests that prostate cancer accounted for 23% of all new cases of cancer in men in 2001 (McDermid 2005) and over 29% in 2005 (AIHW and AACR 2008). Prostate cancer made up 13.8% of all male deaths from cancer in 2005 (AIHW and AACR 2008). The incidence of prostate cancer was stable in the 1980s, however there was a sharp rise in the number of cases diagnosed in the early 1990s as shown in Figure 1.1 (Tracey, Chen et al. 2006). This upward trend is due to the availability of prostate-specific antigen (PSA) testing and therefore reflects a rise in diagnosis rather than incidence. The incidence of prostate cancer in Australia is rising at a rate of 3.1% per year, however mortality from the disease is decreasing at a rate of 0.4% per year (AIHW and AACR 2008).
1.2 Treatment Options

There are various treatment options available for prostate cancer. The decision of which option to choose is ultimately made by the patient, with recommendations from their urologist. These recommendations will be made based upon various factors including stage and grade of the disease, as well as the general health and circumstances of the patient such as residential proximity to treatment facilities and work commitments.

Surgery (radical prostatectomy) and radiotherapy are the two main curative treatment techniques (Chin, Bullard et al. 2006). There are various treatment regimes within radiotherapy including external beam monotherapy, external beam treatment with a High Dose Rate (HDR) brachytherapy boost, HDR monotherapy and Low Dose Rate (LDR) permanent seed implant. Other treatment options for clinically localised prostate cancer include active surveillance and cryotherapy (Cox and Amling 2008).

There is no well-defined optimal treatment for localised prostate cancer; however disease control rates for intermediate- to high-risk disease are suboptimal when standard doses of external beam radiotherapy are delivered (Chin, Bullard et al.
Increasing the dose with standard external beam radiotherapy increases the side effects. **Brachytherapy** provides one option to escalate the dose whilst minimising toxicity (Chin, Bullard et al. 2006).

### 1.3 External Beam Radiotherapy for Prostate Cancer

External Beam Radiotherapy is an effective treatment option for men with early stage prostate cancer. It can be used as a definitive treatment on its own, it may be used after radical prostatectomy to ensure that any tumour cells remaining are incapable of reproducing, or it may be used in combination with brachytherapy. Treatments are generally given on a daily basis for a period of up to 6 or 7 weeks, and external beam therapy can be delivered as an outpatient treatment.

A **linear accelerator** produces a high-energy photon beam, which is directed to the tumour site. Sophisticated three-dimensional planning systems are used to plan the treatments. The major disadvantage of external beam radiotherapy is that all the normal tissue between the skin surface and the tumour site receives a large dose of radiation.

This form of radiotherapy treatment is well documented in literature (Perez, Brady et al. 2004), and will not be considered in any further detail within this thesis.

### 1.4 Brachytherapy

Brachytherapy is a special form of radiotherapy in which radioactive sources are placed at short distances from the target volume. The sources may be placed within the target (interstitial), in a cavity close to the target (intracavitary) or on the surface of the patient (surface plaques - basal cell skin layer treatment or eye moulds).

The major advantage of brachytherapy over external beam radiotherapy is its ability to deliver a high dose of radiation to a confined region. Brachytherapy sources have a rapid dose fall-off with distance from the source, as shown in Figure 1.2 below (Laub 2002) allowing sparing of surrounding tissues. This makes it ideal for the treatment of prostate tumours due to the proximity of radiosensitive organs such as the rectum and bladder.
Brachytherapy is a more invasive procedure than external beam radiotherapy, however it avoids high doses of radiation passing through normal healthy tissue to reach the target volume.

1.5 Brachytherapy for Prostate Cancer

There are two major forms of brachytherapy currently in use for the treatment of prostate cancer. These are LDR permanent seed implants and HDR afterloading.

Permanent LDR seed implants are becoming a more popular treatment option for low risk patients. A high radiation dose can be delivered to the prostate with only a short hospital visit. Accurate seed deployment within the prostate to match the pre-planned positions is difficult. An HDR treatment plan is based on the actual positions of the needles rather than on a best case scenario as in the case of LDR planning, making it a more pliable technique. HDR also has the advantage of being temporary. The treatment is delivered quickly and no radioactive material is left in the patient.
Permanent seed prostate implants are well documented in the literature (Bice 2005; Butler and Merrick 2005; Lief 2005).

HDR brachytherapy is commonly used as a boost to external beam radiotherapy. This thesis will focus on the HDR technique. It involves the insertion of needles through the perineum into the prostate using transrectal ultrasound guidance. An iridium-192 source contained in a remote afterloading device is then programmed to dwell at various positions within each needle for a pre-determined time to create a three-dimensional dose distribution throughout the prostate. The blue isodose cloud in Figure 1.3 below is a typical dose distribution for a prostate treatment. The prostate is shown in red under the translucent 100% isodose cloud, and the rectum is shown as the pink wireframe. This image was created in the PLATO brachytherapy planning system – a commercially available planning software package from Nucletron Pty Ltd (Australia).

![Figure 1.3 Three-dimensional view of a typical HDR prostate dose cloud – PLATO brachytherapy planning system (Nucletron Australia Pty Ltd).](image)

Remote afterloading was introduced with HDR in the late 1980s. The Ir-192 source is located in a shielded afterloader, which is operated from outside the room. This technique has replaced manual loading, and it minimises the radiation dose received
by staff and provides significantly better control of where the radiation dose is delivered (Ouhib 2005). This technique also provides increased flexibility to optimise where the radiation is delivered. Afterloading has removed the constraint of using a source with fixed activity and location, allowing for the reduction of occurrence of regions of excessive or insufficient dose. This leads to a reduction in normal tissue toxicity (Hoskin 2001).

Prostate cancer differs from other types of cancer in that the prostate cancer cells reproduce slowly. The rate of reproduction is comparable to healthy tissue cells (Pickett and Pouliot 2005). Successful treatment can therefore only be achieved if a higher dose of radiation is delivered to the prostate than to the surrounding normal tissue. HDR brachytherapy can deliver a highly conformal dose distribution in a small number of fractions, making it ideal for the treatment of prostate cancer (Pickett and Pouliot 2005).

The total dose prescribed to the prostate and the fractionation (amount of dose delivered per session) varies between centres. Table 1.1 (Vicini, Kini et al. 1999; Ouhib 2005) lists various fractionation schedules from various treatment centres around the world. All centres included in this list perform HDR prostate brachytherapy as a boost to external beam radiotherapy.

HDR brachytherapy is frequently used in conjunction with hormone (androgen deprivation) therapy. The hormones reduce the prostate in size and make the prostate cancer cells more sensitive to radiation, thereby making the treatment more effective (Butler and Merrick 2005).

For HDR brachytherapy to be most effective, it requires accurate dose planning, followed by accurate and verifiable delivery (Williamson, Ezzell et al. 1994). These issues will be discussed below and will be the main focus of this thesis.
Table 1.1. External beam in combination with brachytherapy - treatment regimes used in published studies. This data is collated from Vicini, Kini et al. (1999) and Ouhib (2005) based on references therein.

<table>
<thead>
<tr>
<th>External Beam Dose</th>
<th>Brachytherapy Regime</th>
<th>Total Brachytherapy Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>36 Gy</td>
<td>6.0 Gy x 3 fractions (2 insertions)</td>
<td>36 Gy</td>
</tr>
<tr>
<td>39.6 Gy</td>
<td>6.0 Gy x 4 fractions</td>
<td>24 Gy</td>
</tr>
<tr>
<td>45 Gy</td>
<td>5.5 Gy x 3 fractions</td>
<td>16.5 Gy</td>
</tr>
<tr>
<td>45 Gy</td>
<td>35 Gy</td>
<td>35 Gy</td>
</tr>
<tr>
<td>45.6 Gy</td>
<td>5.5 – 6.5 Gy x 3 fractions</td>
<td>16.5 Gy – 19.5 Gy</td>
</tr>
<tr>
<td>46 Gy</td>
<td>5.5 Gy x 3 insertions</td>
<td>16.5 Gy</td>
</tr>
<tr>
<td></td>
<td>6.0 Gy x 3 insertions</td>
<td>18 Gy</td>
</tr>
<tr>
<td></td>
<td>6.5 Gy x 3 insertions</td>
<td>19.5 Gy*</td>
</tr>
<tr>
<td>50 Gy</td>
<td>4.0 Gy x 4 fractions</td>
<td>16 Gy</td>
</tr>
<tr>
<td>50 Gy</td>
<td>10 Gy x 2 fractions</td>
<td>20 Gy</td>
</tr>
<tr>
<td>50 Gy</td>
<td>10.2 Gy x 2 insertions</td>
<td>20.4 Gy</td>
</tr>
<tr>
<td>50 Gy</td>
<td>15 Gy x 2 insertions</td>
<td>30 Gy</td>
</tr>
<tr>
<td>50.4 Gy</td>
<td>3.0 – 4.0 Gy x 4 fractions</td>
<td>12 Gy – 16 Gy</td>
</tr>
</tbody>
</table>

* This was the fractionation scheme used at St George Hospital at the time the patients used in this study were treated.

1.6 HDR Prostate Brachytherapy Planning

Accurate treatment of the prostate using HDR brachytherapy requires accurate definition of the target followed by a method to accurately expose the target to the prescribed dose of radiation whilst avoiding other surrounding structures (Williamson, Ezzell et al. 1994; Hoffelt, Marshall et al. 2003).

Cladwell and Mah (2005) said that “precise and accurate definition of the target volume for radiation treatment is essential to maximise the probability of both tumor coverage and normal tissue sparing.” This is a statement that provides the focus for the imaging component of this thesis.
Most modern brachytherapy software allows the user to view Computed Tomography (CT) or Magnetic Resonance (MR) images on the screen, and mark the target volume and critical structures (such as rectum, urethra, bladder and seminal vesicles) as well as the implanted needles. The software utilises detailed information on the radioactive source structure, design and activity in its algorithm to calculate dose.

Unlike planning systems used for external beam treatments, most brachytherapy planning systems do not utilise density information from the CT scans to calculate radiation dose. They assume that the tissues in and around the implant are water-equivalent (Rivard, Coursey et al. 2004). The brachytherapy systems are based on geometry. Further corrections are applied such as source anisotropy corrections and radial dose functions. These corrections are defined in detail in the AAPM Radiation Therapy Committee Task Group No. 43 and its subsequent update (Nath, Anderson et al. 1995; Rivard, Coursey et al. 2004).

The brachytherapy planning system is used to represent the prescribed dose to the prostate and there are various methods available to optimise the three-dimensional distribution of this dose (Ezzell 2005; Pouliot, Lessard et al. 2005). By optimising, the planner can achieve an accurate conformal plan, without over-radiating the critical structures. There are a variety of systems commercially available for the planning of HDR prostate brachytherapy treatments.

It has been documented that an accurate representation of the prostate volume is crucial for successful treatment (Hoffelt, Marshall et al. 2003). Citrin, Ning et al. (2005) indicate that MRI provides superior visualisation of the prostate and surrounding tissues in comparison to other imaging modalities, improving the accuracy of defining the target volume for a prostate treatment. Whereas CT images provide a map of electron density as measured by photon attenuation, MR images provide information on proton density as well as the freedom of hydrogen-containing molecules to rotate. They also give information on the proportion of water contained in different body-fluid compartments (Leach 1988). These properties make MR imaging better for soft-tissue differentiation than CT imaging (Cladwell and Mah 2005).
Despite this, CT imaging remains the modality of choice for most radiotherapy techniques (Carey, 2005). This is largely due to its wider availability and lower cost compared with MR imaging (Sistrom and McKay 2005).

1.7 Toxicity in Prostate Brachytherapy
Exposing normal tissue to radiation can be detrimental to normal function of that tissue due to the damage imparted to the DNA (Kunkler 2003). There are several critical structures in close proximity to the prostate, to which the radiation dose must be limited. The urethra and rectum are two of the most important structures in this regard.

The urethra runs from the base of the bladder, through the middle of the prostate and out via the penis. Typically, HDR treatments of the prostate are designed to treat the entire prostate, so the prostatic urethra inevitably receives a high dose of radiation – often higher than the prescribed dose to the prostate. **Urethral strictures** are a common form of urethral toxicity in this form of treatment (Butler and Merrick 2005).

The rectum runs posterior to the prostate and frequently approaches to within 1 cm of the prostate. **Proctitis** is a common late effect of over-exposure of the rectum to radiation (Butler and Merrick 2005).

It is important to ensure the dose to the critical structures is kept as low as possible. Verification of the location, size and shape of the target region is necessary for successful treatment. In addition, the regions where radiation delivery is not desirable must also be clearly defined. Verification of accurate delivery is the next step to ensure the best possible outcome for the patient.

1.8 *In vivo* Dosimetry
It is common practice in external beam radiotherapy to use a form of *in vivo* dosimetry to verify the radiation dose received by critical structures. The European Society for Therapeutic Radiology and Oncology (ESTRO) show the importance of verification of the absorbed dose delivered during a radiation treatment (Van Dam and Marinello 2006). They indicate that *in vivo* dosimetry is useful to detect errors in individual patients, errors in core procedures, to evaluate the quality of specific
treatment techniques and to evaluate the dose delivered in situations where the dose
calculation is inaccurate or not possible (Van Dam and Marinello 2006). In vivo
dosimetry is not common practice in brachytherapy as it is in external beam
radiotherapy, and few centres currently utilise any form of in vivo dosimetry for
brachytherapy. Often in brachytherapy treatments, higher doses of radiation are
delivered per fraction than in external beam treatments. A method to verify the
radiation dose is therefore justified, and various detectors have been proposed for this
purpose, however none are currently in routine use.

Thermoluminescent dosimeters (TLDs) come in various materials, shapes and sizes.
This project will consider lithium fluoride TLDs doped with magnesium and titanium
(LiF:Mg,Ti) for use in prostate brachytherapy. This material has well-established
characteristics and has been in use for external beam radiotherapy in vivo dosimetry
measurements for many years.

Other dosimeters currently under investigation by other research groups for use in
brachytherapy in vivo dosimetry include Metal Oxide Semiconductor – Field Effect
Transistors (MOS-FETs) (Cygler, Saoudi et al. 2006), lithium fluoride TLDs doped
with magnesium, copper and phosphorus (LiF:Mg,Cu,P) (Duggan 2002) and optical
fibre dosimeters (Lambert, McKenzie et al. 2006). Further detail on these dosimeters
is presented in Section 2.3.2.

1.9 Aims and Outline of the Thesis
The aim of this thesis as stated in the opening paragraph was to investigate potential
improvements on the two most important aspects of prostate HDR and PDR
brachytherapy – prostate definition and treatment delivery verification.

The issue of prostate definition was addressed via the introduction of the use of MR
imaging into prostate brachytherapy planning. This included a study of the ability to
delineate the prostate and critical structures consistently, and the ability to accurately
define the needle positions. It also included a study of the effect of the alternative
prostate and critical structure dimensions as determined by the different imaging
modalities on the dosimetric outcomes for the patients.
The issue of accurate treatment delivery verification was addressed by adapting an existing method for in vivo dosimetry in external beam radiotherapy to verify the dose delivered in prostate HDR brachytherapy. This was carried out as a phantom study using a standard thermoluminescent material and was aimed at determining the suitability of this material for routine verification of patient dose, with particular focus on establishing a consistent conversion factor to allow the use of an independent control dose to TLDs exposed to radiation from a 6 MV linear accelerator.

Chapter 2 is a literature review discussing the imaging techniques examined within this thesis, as well as a review of the information available on the thermoluminescent dosimeters (TLDs) used in this project. It also includes a summary of recent findings reported in the literature relevant to imaging of the prostate and in vivo dosimetry for brachytherapy.

Chapter 3 is a study investigating the use of MRI in prostate HDR brachytherapy. This chapter contains detail on the materials and methods used in this project. It contains the results and a discussion of this study involving the comparison of the use of CT and MRI in prostate HDR brachytherapy planning.

Chapter 4 is a study developing and investigating the use of a standard thermoluminescent material for in vivo dosimetry of prostate HDR brachytherapy. This chapter contains detail on the materials and methods used in this project. It also contains the results and a discussion of the phantom study investigating the use of LiF:Mg,Ti TLDs for verifying patient dose in prostate HDR and PDR brachytherapy, including the measurement of a conversion factor to account for measurement of control doses on a linear accelerator.

Chapter 5 provides conclusions and recommendations based on the results presented in Chapters 3 and 4.

Items highlighted throughout the thesis in bold type are defined in Appendix A – Glossary.
Chapter 2: Literature Review

2.1 HDR Prostate Brachytherapy

Adenocarcinoma of the prostate is currently the most common cancer diagnosed in men (Nori and Moni 1997; D'Amico, Cormack et al. 1998; Menard, Susil et al. 2004; McDermid 2005). The advent of prostate-specific antigen (PSA) testing has led to earlier diagnosis of prostate adenocarcinoma in younger men (Nori and Moni 1997). Late complications of the treatment technique used must be considered carefully as this cohort of early-diagnosed men have a much longer survival rate (Nori and Moni 1997). Quality of life is also more important for these younger men, including issues such as urinary and rectal function as well as erectile function (Butler and Merrick 2005).

External beam radiotherapy is regarded as the gold standard treatment modality for patients with locally advanced prostate cancer. The recurrence rates after this form of treatment are quite high. Some reports indicate recurrence rates of up to 60% (Martinez, A., Gonzalez et al. 1995). Standard external beam treatments for prostate cancer deliver a total of around 70 Gy in fractions of 2 Gy per day, 5 days per week or 9 days per fortnight (TROG 2003). This treatment fractionation schedule raises concerns with internal organ motion from day to day, as well as setup inaccuracies over 35 separate treatments. To overcome this, a margin is usually added around the prostate. This results in the delivery of large doses to non-cancerous tissues around the prostate (Martinez, A., Gonzalez et al. 1995). Doses in excess of 70 Gy delivered as external beam radiotherapy can result in an increase in genitourinary and gastrointestinal side effects (Chin, Bullard et al. 2006). Currently available options to increase the total dose while minimising toxicity include intensity-modulated radiation therapy (IMRT) and brachytherapy (Chin, Bullard et al. 2006).

For early-stage prostate cancer, the best method of obtaining a conformal treatment is to insert radioactive sources directly into the prostate in the form of temporary placement of a radioactive source in implanted needles (HDR brachytherapy), or permanent seeds (Grimm, Blasko et al. 1996), however these forms of treatment are not appropriate for all forms of the disease.
HDR brachytherapy has the advantages of being able to deliver conformal high doses of radiation to a precisely localised target, rapid dose fall-off and minimal target movement during the treatment. Both the position and the dwell time along the implanted catheters can be altered to obtain a very conformal dose distribution, and this also allows greater sparing of nearby organs at risk, particularly the urethra and rectum (Chin, Bullard et al. 2006).

The use of remote afterloading with Ir-192 HDR for prostate treatment was introduced in the late 1980s. HDR has been used for more than 40 years to treat other anatomical sites. The technique for HDR and Pulsed Dose Rate (PDR) treatment of the prostate is identical. Needles are inserted in the operating theatre under transrectal ultrasound and fluoroscopic guidance. A template is usually fixed to the perineum, through which the needles are inserted through the prostate. Most centres use CT-based planning, so the patient must be taken to the CT scanner after the implant procedure. CT markers are commercially available for plastic needles, and these allow visualisation of the first possible dwell position of each needle. The Radiation Oncologist defines the target volume as well as the critical structures or organs at risk. The urethra, rectum and bladder are commonly defined as critical structures in the planning system. The afterloader is programmed to move the Ir-192 source in specified steps within each needle (Ouhib 2005).

Various different fractionation regimes have been used with HDR brachytherapy at many treatment centres around the world. Generally, it is used as a boost to external beam radiotherapy treatments (Vicini, Kini et al. 1999), but has also been used as a monotherapy technique (Martinez, A. A., Pataki et al. 2001; Martin, Baltas et al. 2004). However, brachytherapy as a monotherapy technique is usually reserved for lower risk disease, and is still considered investigational (Chin, Bullard et al. 2006).

At St George Hospital in Sydney, Australia, at the time of the measurements presented in this thesis, standard combined brachytherapy and external beam treatment delivered 19.5 Gy in three fractions of brachytherapy (each fraction separated by a minimum of six hours – total treatment completed within 36 hours), followed by 46 Gy of external beam radiotherapy in 2 Gy fractions over 23 days. This external beam component of the treatment commenced three weeks after the
brachytherapy implant. The brachytherapy component was delivered using a PDR Iridium-192 (Ir-192) source.

A non-exhaustive list of other treatment regimes using Ir-192 in various studies around the world was given in Table 1.1. (Vicini, Kini et al. 1999; Ouhib 2005).

The minimum time between fractions is usually 6 hours. This is due to the radiobiological effects of the radiation, to allow sufficient repair and re-oxygenation of late-responding normal tissues which have been damaged by the radiation exposure (Brenner, Dale et al. 2001). Unless specified as separate insertions, the fractions given in Table 1.1 are all delivered during one insertion (implant).

2.2 Imaging of the Prostate

Imaging of the prostate began with the introduction of the trans-rectal ultrasound in the early 1970s. In the subsequent decades, technological developments have introduced various other imaging modalities including CT and MRI (Carey 2005). These modalities are discussed in this section with particular focus on their use in brachytherapy.

2.2.1 Issues in prostate imaging

Improvements in radiotherapy techniques have led to the requirement for more accurate delineation of the location and extent of prostate cancer (Carey 2005). The main imaging modalities currently available for imaging the prostate are transrectal ultrasound, CT and MR. (Carey 2005).

Ultrasound is mostly used for needle placement. It can be used to define the peripheral zone of the prostate reliably, which is the location in which most prostate cancers originate (Carey 2005).

CT is the technique most widespread for planning radiation treatment. Despite this, CT does not show any tumour within the prostate gland, cannot define prostate margins with great accuracy, and overestimates the true gland volume (Carey 2005).
MR imaging of the prostate provides the most accurate information about the anatomy and location of tumour within the prostate gland (Menard, Susil *et al.* 2004). It also exhibits good correlation with both ultrasound and pathologic evaluation of the prostate (Dubois, Prestidge *et al.* 1998). The high incidence of prostate cancer and the high cost of MRI combine to make this imaging technique less economically viable for healthcare facilities (Carey 2005).

### 2.2.2 Computed Tomography

#### 2.2.2.1 History and Theory

Computed Tomography (CT) scanners produce thin cross-sectional images of the human body. CT is considered a non-invasive radiographic technique, and the scanner collects a large number of x-ray attenuation measurements, which are then used to reconstruct the cross-sectional image (Van Dyk and Taylor 1999).

CT scanners first became available in the early 1970s. Since that time, the technology has advanced significantly. Van Dyk and Taylor (1999) provide an overview of the historical development of CT scanners, and Cladwell and Mah (2005) provide an update of more recent developments.

CT images provide electron density information, however for brachytherapy applications, this information is not utilised for dosimetry calculations – only in the generation of the images.

#### 2.2.2.2 CT in Brachytherapy

The first study using CT for prostate brachytherapy was published in the early 1990s. This was for seed post-implant dosimetry carried out at Memorial Sloan-Kettering Cancer Centre. Today, CT is still the most utilised imaging tool for post-implant dosimetry due to its relatively low expense and good visualisation of the seeds (Bice 2005).

It was not until the late 1990s that CT was first used for HDR brachytherapy planning. Prior to this, the common planning procedure was based on ultrasound images of the prostate before and after the implantation. Martin, Kolotas *et al.* (1999) were one of the first groups to utilise CT based planning for HDR prostate brachytherapy. They
found that the significant advantages in using CT imaging to plan the treatment were the ability to reconstruct non-parallel needles, define an individual planning target volume, optimise the dose distribution and evaluate the quality of the implant.

Also in 1999, Kolotas, Baltas et al. (1999) published their study on the use of CT for interstitial brachytherapy. They report the advantage of CT-based brachytherapy planning as allowing anatomy-based planning as opposed to applicator-based planning traditionally used in brachytherapy treatments. This study examined various anatomical regions including the brain, pelvis and lymph nodes in the neck. Results were compared to reconstruction using radiographs, and the CT reconstruction was found to give equivalent accuracy in a much shorter time.

Pouliot, Lessard et al. (2005) also report on this shift to anatomy based planning due to the introduction of 3 dimensional imaging techniques. It was previously assumed that if the dose distribution covered the catheters, then it should also cover the anatomy. This resulted in the treatment typically of a cylindrical-shaped prostate, causing significant overdosage of normal tissues surrounding the prostate.

2.2.3 Magnetic Resonance Imaging (MRI)

2.2.3.1 History and Theory

Nuclear magnetic resonance (NMR) was proposed as a method for detecting tumours around 1971, many years before it became the 3-dimensional imaging tool in use today. MRI was developed and arrived on the scene approximately 6 to 10 years after CT, which had already been established as the primary imaging modality for radiotherapy treatments (Peters, Slomka et al. 1999).

Peters, Slomka et al. (1999) provide a thorough outline of magnetic resonance imaging.

Despite the advantages of MR over CT in some areas, it is not commonly used as a replacement for CT in radiotherapy planning. Reasons for this include the lack of electron density information, susceptibility to distortion and the lack of software availability to integrate and manipulate MR images within planning systems (Peters, Slomka et al. 1999).
2.2.3.2 MRI in Brachytherapy

Various studies have been published on the use of MRI for brachytherapy planning of the prostate. These studies contain information on both permanent seed implantation and HDR prostate brachytherapy procedures.

Menard, Susil et al. (2004) published an investigation concerning MRI-guided HDR prostate brachytherapy. They reported that MRI provided “superior visualisation of the prostate and surrounding anatomy, making it the modality of choice for imaging the prostate gland”.

D'Amico, Cormack et al. (1998) used MRI to perform real-time MR-guided seed implantation of the prostate. This was studied as an alternative technique to the standard 2-dimensional transrectal ultrasound guided technique. The advantage of this technique was that the imaging did not interfere with the prostate shape. A transrectal ultrasound probe may distort the prostate and therefore cause a change in the geometric distribution of seeds when removed, resulting in a different dose distribution to that planned. This study reported that this technique provided the ability to achieve the MR-planned, optimised dose-volume histogram profiles to the clinical target volume and other structures with minimal acute morbidity. No discussion of the accuracy of the MR imaging was included.

McLaughlin, Narayana et al. (2002) conducted a comparison of MRI pulse sequences in defining prostate volume after permanent seed implantation. They compared $T_1$-weighted, $T_1$-weighted fat saturation and $T_2$-weighted axial MRI studies on a total of 45 patients. This study reported that the $T_2$-weighted MR images gave a consistently smaller prostate size than the other methods. It was suggested that this was due to the superior prostate definition provided by the $T_2$-weighted technique, particularly with interfaces between the prostate and other structures including the membranous urethra, apex, and anterior base/bladder and posterior base/seminal vesicle interfaces.

Susil, Camphausen et al. (2004) proposed a system for the use of a 1.5 Tesla MRI scanner for prostate HDR brachytherapy. They reported placement of 14 or 15 HDR brachytherapy catheters under MR guidance, taking 2 hours for each of the first two patients, then 1.5 hours on subsequent patients. The patient was placed on his side in
the scanner, in the left lateral decubitus position. The MR images could then be used to create an optimised treatment plan. This technique would involve having an MRI scanner in the operating theatre, and is therefore not an option for many treatment centres in Australia.

Some investigations have also been carried out on the use of magnetic resonance spectroscopy imaging (MRSI) for planning prostate brachytherapy treatments. Zaider, Zelefsky et al. (2000) proposed the use of MRSI to distinguish between regions of cancerous and non-cancerous prostatic tissue. This information could then be used to escalate the dose to intraprostatic tumour deposits using radioactive seed brachytherapy. The proposed system, which included an integer-programming technique to optimise the seed distribution, achieved a minimum dose of 120% of the prescribed dose to MRS positive voxels, with relative sparing of surrounding normal tissue. Only one patient was used in this study.

A similar study was published two years later (DiBiase, Hosseinzadeh et al. 2002). Fifteen patients were recruited in this study and the data was used for fourteen of these patients’ treatment plans. The reason for the one patient whose MRSI data could not be used was the presence of multifocal disease, making focal boosts impractical. This study reports boosts of 130% of the prescribed dose in the focal regions, with urethral and rectal doses within normal limits. MRSI is a potential method of improving the therapeutic ratio in prostate seed brachytherapy and similarly in HDR brachytherapy. These MRSI studies demonstrate a further advantage of using MR for the planning of prostate brachytherapy treatments. Mizowaki, Cohen et al. (2002) also suggested the use of MRSI as a further advantage of MR imaging for prostate brachytherapy. They similarly report that functional imaging may be utilised to assist in determining the location of the cancer cells within the prostate. This could allow for dose escalation in certain regions of the prostate where the cancer cells are most prolific, however they report that MRSI involves the use of an endorectal balloon receiver coil that distorts the prostate. Further work would be required to establish this procedure as routine for prostate brachytherapy planning.
Citrin, Ning et al. (2005) reported on the use of MRI alone for HDR prostate brachytherapy treatment planning. The issues they addressed included correction and verification of spatial distortion (caused by non-uniform magnetic fields, and correctable using commercially available software), correction of the DICOM (Digital Imaging and Communications in Medicine) header to allow MR image transfer into the planning system, and determination of the first dwell position based on visualisation of the void created by the needle. Their results showed that it was possible to complete a prostate HDR treatment plan on MRI images alone.

No literature was found discussing the results of the use of MRI in radiotherapy or brachytherapy planning in terms of improved survival.

**2.2.4 Comparison Studies**

Various comparison studies between CT and MR imaging of the prostate for brachytherapy procedures have been reported in the literature. No specific comparison studies were found for HDR brachytherapy imaging of the prostate. The publications refer to permanent seed brachytherapy imaging of the prostate. The same general conclusions can be made for imaging of the prostate for HDR brachytherapy.

Dubois, Prestidge et al. (1998) reported on intraobserver and interobserver variability of MR and CT derived prostate volumes for 41 permanent brachytherapy seed implants of the prostate. They reported that transrectal ultrasound could adequately visualise the prostate gland, however the seeds caused significant artefact and the position of the ultrasound probe may have prevented accurate source localisation. CT and MR imaging had the advantage of being non-invasive. CT was excellent for visualising the seeds, and equally the needles used for HDR brachytherapy when a CT marker was used (refer to Section 3.1.1.7), however the prostate was not clearly delineated. It was reported that MR imaging correlated closely with the volume of the prostate both with ultrasound imaging and pathologic evaluation.

This paper reported a significantly higher variation in prostate volume between observers for CT imaging (8.5 cm$^3 \pm 9.74$) compared with MR imaging (1.9 cm$^3 \pm 11.7$) at a similar expense. The volumes delineated on the MR images were also more consistent from an intraobserver’s perspective. Observer 1 CT variability was 2.9% ±
29.4, and MR variability was 3.2% ± 8.4. Observer 2 CT variability was 6.4% ± 15.5, and MR variability was 1.2% ± 1.2.

Crook, Milosevic et al. (2002) also reported on interobserver variability in prostate volume for permanent seed brachytherapy. They used MRI-CT fusion as the gold standard for prostate-edge identification. Prostate volumes on CT images alone were generally 25 – 40% larger than on ultrasound or MRI in this study. This was reportedly due to the difficulty in distinguishing the prostate from the surrounding muscles and venous plexus. The rationale for this particular study stemmed from the fact that if the prostate volume was inaccurate, then dosimetry of the brachytherapy implant would be imprecise and any dose-response relationships would be less apparent. Brachytherapy dose calculations are based on geometry of the implant and anatomical structures. The steep dose gradient makes dosimetry around this fall-off difficult to achieve with great accuracy, so if the volume is imprecise, there may be a significant difference in dose delivered. This Group found that CT/MRI fusion was the ideal imaging tool for determining the correct spatial relationship between the seeds and target contours, as the accuracy of the seed location was best determined on the CT images, whereas the prostate was delineated more clearly and reproducibly on the MR images (based on interobserver differences).

Various other publications including Polo, Cattani et al. (2004); Solhjem, Davis et al. (2004); Carey (2005); Miquel, Rhode et al. (2006) all report the same findings that CT is inadequate for accurately defining the prostate volume and indicate that MRI is a better method for accurate prostate definition. These authors all focus on seed brachytherapy implant imaging except for Carey (2005), who examines the imaging of prostate cancer in general.

2.2.5 Image Fusion

Polo, Cattani et al. (2004) reported on the fusion of MR and CT images for permanent seed dosimetric analysis, comparing the dosimetric results with those generated on a CT alone. They noted significant differences in the dose level to the prostate with each method of imaging, and the volume of the prostate was on average 36% greater using CT alone compared with CT-MRI fusion. This result was dependent on the person defining the volume on the images and applies equally to HDR brachytherapy as well as permanent seed implants.
Miquel, Rhode *et al.* (2006) reported on a combined x-ray and MR imaging technique under development, using MRI fused with x-ray images. This technique may become more useful with further development for permanent seed post-implant dosimetry purposes, however its use in HDR brachytherapy is further limited by the time it would take to reconstruct the position of the needles.

No specific studies related to fusion of images for HDR brachytherapy were found.
2.3 **In vivo Dosimetry**

2.3.1 **Thermoluminescence Dosimetry**

2.3.1.1 **History and Theory**

Kron (1995) provides a thorough history of thermoluminescence dosimetry in medicine. A brief outline will be reported here.

The phenomenon of thermoluminescence has been known for hundreds of years. Shortly after the discovery of ionising radiation, Marie Curie noted the thermoluminescence of calcium fluoride after exposure to radium. Further work was undertaken in 1925 by F. Wick to study the effect of X-rays on thermoluminescent materials (Kron 1995).

It was a further 20 years before J. Randall and M. Wilkins formulated a theory of TLD, based on the interpretation of glow curves. This is still the basis for the current understanding of TLD (Kron 1995). An article in 1953 by F. Daniels *et al* reports on the use of lithium fluoride (LiF) TLDs for clinical measurements. Daniels was also the first to establish the annealing of LiF at 400°C, a method still in use today (Kron 1995).

Towards the end of the 1950s, the purity of the LiF was increased, resulting in a decline in the ability of the material to measure radiation dose. J. Cameron demonstrated the importance of the impurities – particularly the magnesium. His work led to the development of the TLD material used in this project – LiF:Mg,Ti (TLD100 – lithium fluoride doped with magnesium and titanium) (Kron 1995).

In the following years, research was carried out to test different forms of the TLD material. By incorporating LiF powder into a Teflon coating, the dosimeters could be made to any shape or form. Research also continued to improve the tissue-equivalence of the TLD material (Kron 1995).

TLD is still one of the most important techniques for assessing ionising radiation doses, both for evaluation of new diagnostic techniques as well as for *in vivo* dosimetry on real patients. Its uses extend into radiation protection and environmental monitoring (Kron 1995).
A detailed theory of thermoluminescence is complex, and beyond the scope of this project. Duggan (2002) lists various publications such as McKinlay (1981) and McKeever (1995) that are dedicated to this complex theory. Kron (1994) published a simplified theory, which will be discussed here only to provide sufficient information for an understanding of the use of TLDs in brachytherapy.

A thermoluminescent (TL) crystal is usually a non-conducting crystal. At room temperature, all electrons reside in the valence band. By exposing the crystal to ionising radiation, some electrons gain enough energy to be promoted into the conduction band. In a perfect crystalline structure, after exposure to radiation, the electrons in the conduction band would drop back down to the valence band, emitting energy in the process. TL crystals have imperfections that trap a small percentage of the electrons in an energy state between the conduction and valence band. The energy gap between conduction band and the trap is only a few electron volts. The number of electrons trapped is a function of the intensity of the radiation (Kron 1994).

The probability of the electrons gaining enough energy to escape from the trap depends on the depth of the trap as well as the temperature. If the temperature is sufficiently high, the trapped electron may gain enough energy to move back up to the conduction band. It will then spontaneously fall back to the valence band, recombining with a hole and emitting visible light in the process (Kron 1994). The basic process involved can be seen in Figure 2.1 below (Kron 1999).

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**Figure 2.1:** Schematic diagram of thermoluminescence process.
Reproduced with permission. (Kron 1999).
Most TL materials have various trap types, with differing energy gaps to the conduction band. They will therefore empty at different temperatures. This can lead to a complicated function of light intensity vs temperature, known as a glow curve (Kron 1994). Figure 2.2 is a typical glow curve for LiF:Mg,Ti, the material used in this project (Kron 1999). LiF:Mg,Ti has at least eight different energy traps, and therefore eight distinct peaks in the glow curve (only six are shown in Figure 2.2 – the other peaks occur at higher temperatures) (Kron 1994).

The intensity of the visible light emitted is related to the intensity of ionising radiation the TL material was exposed to. It is also influenced by various factors including the geometry of the material, the thermal and radiation history of the material, the time between irradiation and readout, total radiation dose, dose rate and radiation quality. TLD is therefore most suitable for relative dosimetry and not absolute dosimetry (Kron 1994).

To read the amount of light emitted by the TLD, a photo multiplier tube is used. The TLD is exposed to a constant heating rate. The light recorded by the photo multiplier tube is associated with the temperature at which it was emitted by the TLD and this information is combined to create a glow curve (Section 2.3.1.2.1) (Kron 1994).

### 2.3.1.2 Properties of LiF:Mg,Ti
Kron (1994) describes the properties of the most commonly used clinical TL material, LiF:Mg,Ti. A brief summary of this is included here to provide sufficient information for an understanding of the use of LiF:Mg,Ti in brachytherapy.

#### 2.3.1.2.1 Glow Curves
A typical glow curve for LiF:Mg,Ti is shown in Figure 2.2 (Kron 1999). Seven distinct glow peaks can be observed for LiF:Mg,Ti when read up to 300°C. Each of these is associated with different traps. Peaks IV and V are typically used for evaluation of dose. The higher peaks generally only occur when high doses are delivered, and are usually not evaluated (Kron 1994).
Most TLD readers in use for clinical measurements heat up the TLDs at a relatively fast rate. This keeps the readout time short, but results in the merging of two or more peaks into one (Kron 1994).

Following radiation exposure, the TLD can be annealed at a low temperature (100°C) for a short time to reduce the effect of the lower temperature peaks on the reading (Kron 1994).

2.3.1.2.2 Fading
There is a possibility that some electrons can gain enough energy at room temperature to escape from their traps. The smaller the energy gap between the trap and the conduction band, the more probable it is that this spontaneous emission of light will occur. This will reduce the TL signal and is therefore known as fading (Kron 1994). The half life for the various traps in LiF:Mg,Ti at room temperature vary from a few minutes to several years. Peaks IV and V have half lives of approximately 10 years and 80 years respectively. This equates to fading of the order of 5% over 12 weeks. Exposure of the crystals to light, particularly UV components, can increase the amount of fading (Kron 1994).
2.3.1.2.3 **Linearity**

At very low doses, LiF:Mg,Ti overestimates the dose. The response has been reported to be linear above approximately $10^{-5}$ Gy, which is around the detection limit of the material (Kron 1994). The response is linear up to doses of around 1 – 3 Gy. Beyond this level, the sensitivity of the dosimeters increases. This phenomenon is known as supralinearity. There is approximately 5% supralinearity at 3 Gy, resulting in a higher dose being reported. At very high doses (100-1000 Gy), the sensitivity decreases again due to irreversible radiation damage (Kron 1994). This trend can be seen in Figure 2.3 (Kron 1999).

![Figure 2.3: Dose response of LiF:Mg,Ti. Reproduced with permission. (Kron 1999).](image)

The effect of supralinearity can be reduced by irradiating a control set of TLDs to a known dose of the same magnitude as the dose to be measured, at the radiation quality in question (Kron 1994).

2.3.1.2.4 **Annealing Cycles**

A full anneal cycle must be carried out after each readout, prior to using the TLDs again. This restores the sensitivity of the TL material by removing any residual electrons from their traps (Kron 1994). Various anneal cycles have been proposed for
LiF:Mg,Ti. These include annealing to 400°C for 1 hour only, 1 hour at 300°C followed by 16 hours at 80°C, 1 hour at 400°C followed by 24 hours at 80°C, 1 hour at 400°C followed by 2 hours at 100°C (Horowitz 1990). The pre-irradiation anneal cycle suggested by the manufacturer (Thermo Electron Corporation, Canada) is 1 hour at 400°C followed by 2 hours at 100°C. It has been noted that there is a significant increase in sensitivity at high doses of radiation (>1 Gy) if significantly lower temperatures (for example 300ºC) are used for the high-temperature anneal (Horowitz 1990). However, no change in sensitivity was found when the anneal temperature was between 360ºC and 440ºC (Horowitz 1990). For high precision measurements, Horowitz (1990) recommends that the annealing temperature accuracy should be within ±5%.

2.3.1.2.5 Dose Rate Dependence
LiF:Mg,Ti show no dose rate dependence at dose rates used for clinical treatment, however this has only been documented to within a level of accuracy of 5% (Kron 1994).

2.3.1.2.6 Variation with Radiation Quality
The energy response of TL materials to X-rays depends on various factors including the effective atomic number, dopants and impurities, supralinearity differences between radiation qualities, attenuation within the material itself (particularly low energy X-rays can be absorbed within a large crystal), the read-out process, the size of the detector and the thermal history of the material (Kron 1994).

2.3.1.2.7 Accuracy and Precision
The accuracy of the readings depends ultimately on the reproducibility (precision) of the dosimeter and the standard dosimeter used to define its sensitivity. Some groups have reported precision to below 0.5% for a single standard deviation, however a reasonable effort will allow a precision of around ±2% or better, as long as a correction is made for the individual dosimeter (Kron 1994).
2.3.1.3 LiF:Mg,Ti Thermoluminescence Dosimetry in Brachytherapy

In 1995, Kirov, Williamson et al. (1995) used LiF:Mg,Ti TLDs along with diodes to measure dose-rate profiles and anisotropy function values of an Ir-192 HDR brachytherapy source. The results were compared to Monte Carlo simulations and agreement was established to within 5% on average.

Anagnostopoulos, Baltas et al. (2003) reported on the use of LiF:Mg,Ti for dose verification of Ir-192 HDR prostate brachytherapy. Their measurements were undertaken for five patients either receiving HDR monotherapy (four fractions of 9.5 Gy each) or HDR as a boost to external beam radiotherapy (three fractions of 7 Gy each).

A batch of 50 LiF TLD type-100 cylindrical rods – 6 mm long and 1 mm in diameter were used. The pre-irradiation annealing cycle of one hour at 400°C followed by two hours at 100°C was used, and the Harshaw Model 5500 Automated TLD Reader was used with a maximum acquisition temperature of 270°C and a constant heating rate of 15°C s\(^{-1}\).

The TLDs were calibrated under a 6MV photon beam and each TLD was given an individual sensitivity factor.

For the \textit{in vivo} measurements, the TLDs were inserted into a thin plastic needle which was then placed inside a plastic brachytherapy needle that had been inserted into the patient’s prostate.

The mean differences between the measured dose and the dose calculated by the treatment planning system (PLATO BPS v. 14.2.2 (Nucletron B.V. The Netherlands), which incorporates a full TG-43 dose calculation algorithm) varied up to approximately 7%. In view of the uncertainties discussed in the report, the authors were satisfied that the differences were acceptable, and the dose was reproducible over all the fractions administered to each patient.

Another study using LiF:Mg,Ti TLDs was conducted by Brezovich, Duan et al. (2000). This group packaged the same TLD type-100 rods into a linear array.
configuration of typically 20 rods inserted into a closed-ended brachytherapy catheter. The TLD-loaded catheter was sterilised using ethylene oxide gas (no effect was noted with sterile/non-sterile measurements). This catheter was then inserted to the tip of the urinary catheter for the duration of an HDR prostate treatment, and the measured doses were compared to the treatment plan.

The results of this study showed good agreement between measured and computed urethral doses. The measured doses were typically lower than computed doses, and all measurements fell within the range of experimental error.

The authors noted some areas of the study that could be improved if the method was to be used on a regular basis. These areas include improvement of positioning and localisation of the TLD rods, improvement of spatial resolution, and the potential for the TLDs to be available commercially precalibrated and sterilised, saving significant time in the process.

Williamson and Rivard (2005) discuss energy response for TLD-100 based on the literature. They show that the relative energy response of TLD-100 at mean Ir-192 energies of 375 keV (Khan, 2003) is approximately 1.04 at distances around one cm from a point source compared to higher energy photon beams (Cs-137, mean energy 662 keV (Khan, 2003)). This response is reported to be closer to 1.00 at 10 cm from the point source (Williamson and Rivard, 2005). The same authors suggest that LiF TLDs (TLD-100) have become the detector offering the best compromise between small size, sensitivity, energy response and ease of positioning for brachytherapy, and is currently accepted as the experimental gold-standard for measurement of absolute dose rates in brachytherapy.

The in-phantom response of LiF:Mg,Ti (TLD-100) using an Ir-192 source was assessed by Pradhan and Quast (2000). Using 1 mm x 1 mm x 6 mm TLD rods and standard annealing and processing procedures, the authors found that the expected uncertainty amounted to less than 3% when compared to a PTW 0.3 cm$^3$ ionisation chamber.
More recently, Das, Toye et al. (2007) used LiF:Mg,Ti TLDs on 48 patients to verify dose delivered in the urethra and rectum during HDR brachytherapy. The TLDs used were 1 mm diameter and 6 mm length. The TL detectors were individually calibrated under a 6 MV beam from a linear accelerator to a dose of 0.5 Gy. This group found that the TLD results matched well with the planning data, with the average difference being 0.1 Gy to the urethra and 0.17 Gy to the rectum. In their discussion, the authors state that “it is unlikely that the calibration using a 6 MV X-ray beam from a linear accelerator is introducing an error exceeding 3%”. However, they report a significant supralinearity effect, suggesting that future studies would require control TLDs to be irradiated to high doses simultaneously with the patient dosimetry.

The same group, Toye, Das et al. (2008) in an accepted manuscript (in press at the time of writing) extended the work reported in their previous publication (Das, Toye et al. 2007) by analysing rectal doses. By incorporating a shift correction, the results improved compared with those previously reported. This study adds to the evidence that LiF:Mg,Ti is suitable for in vivo dosimetry in prostate HDR brachytherapy.

2.3.2 Other In vivo Dosimetry Options for Brachytherapy

Various studies involving materials other than LiF:Mg,Ti TLDs have been published.

Hood, Duggan et al. (2002) investigated the use of LiF;Mg,Cu,P TLDs for brachytherapy dosimetry. This was only a relative study, but the TLDs showed good relative agreement with the treatment planning system (ADAC Pinnacle), however limitations in the TLD energy correction did not allow for absolute dose comparisons.

Duggan, Bucci et al. (2004) also suggested the use of LiF:Mg,Cu,P TLD material for prostate HDR brachytherapy in vivo dosimetry measurements. The reasons for using this material are listed as the more uniform response to different photon energies compared with LiF:Mg,Ti, improved sensitivity allowing for better precision and improved spatial accuracy using miniature TLDs. No studies have been published showing results using this material in brachytherapy.

Pai, Reinstein et al. (1998) used radiochromic film with a vaginal cylinder brachytherapy treatment geometry. The film was placed on the outside of the
cylinder, and covered with a rubber sleeve prior to insertion. The variation between calculated and measured dose was ±10% and the dose could not be read until the applicator was removed. This makes it less accurate than other reported methods and feasibility for use with prostate brachytherapy is limited.

Alecu and Alecu (1999) used silicon diode detectors to measure the in vivo rectal dose during cervical HDR treatments. The same concept is applicable to prostate treatments as the diode was inserted into a hollow rectal marker. Phantom measurements gave measurement values within 5% of calculated values. For in vivo measurements, the results were not as satisfying, with differences up to 15% between measured and calculated doses.

Kipouros, Papagiannis et al. (2003) published a study using a radiosensitive polymer gel and MRI to obtain a 3D dose verification for HDR prostate monotherapy. This study was not done in vivo, but was done in a phantom where a plan was used to treat the homogeneous gel. This provided a simulation of a patient’s treatment, and was a good comparison between the planning system and real dose measurements; however it is not feasible to use this as a quality assurance procedure for every patient due to the time involved in reproducing the individual patient setup in the gel.

Cygler, Saoudi et al. (2006) performed a feasibility study using micro-MOSFETs (Metal Oxide Semiconductor Field Effect Transistors) for in vivo dosimetry of permanent brachytherapy seed implants. These were used to measure dose rate in the urethra in real time. The major advantage of this for permanent seed brachytherapy is that extra seeds may be added if it is deemed that the urethral dose is lower than expected and therefore prostate coverage compromised.

Lambert, McKenzie et al. (2006) developed a scintillation dosimeter thin enough to be inserted into the urethral catheter to measure the dose to the urethra in an HDR prostate brachytherapy treatment. The scintillation detector was attached to an optical fibre and this design was aimed to allow real-time dosimetry in brachytherapy. It was designed with a small detector volume, allowing high spatial resolution required for measurement in the steep dose gradients involved in HDR brachytherapy. Readings from this dosimeter were achieved to within 3% of predicted values.
Lambert, Nakano et al. (2007) – the same Group that developed the scintillation dosimeter above (Lambert, McKenzie et al. 2006), published a comparison of various \textit{in vivo} dosimeters for HDR brachytherapy. They included a diamond detector, MOSFET, TLD and scintillation detector (BrachyFOD). The TLDs used in this study were LiF:Mg,Ti with dimensions $3 \times 3 \times 0.9 \text{ mm}^{3}$. They reported that these TLDs provided limited use in brachytherapy due to their potential for large errors. This was attributed partly to the depth dependent sensitivity of the LiF chips, as well as small differences in absorbed dose in solid water compared with liquid water for low energy photons.

2.4 Summary

Little work has been published on prostate imaging specifically for HDR purposes where both prostate delineation and needle location are important. These requirements lend themselves to establishing a hybrid of different imaging techniques to utilise the best properties of multiple imaging techniques.

The current procedure used at St George Hospital (CT imaging only) may benefit from the introduction of MR imaging into the planning process, particularly with regard to dosimetry implications. The literature overwhelmingly indicates that CT imaging over-estimates the prostate volume and that MR imaging gives a more accurate representation of the prostate location and size. Dosimetrically, this would indicate that a larger volume than necessary receives a high dose of radiation and therefore, surrounding critical structures may be receiving more dose than is necessary for tumour control.

\textit{In vivo} dosimetry in HDR brachytherapy using LiF:Mg,Ti TLDs has been established through the work of a range of investigators as outlined in the literature review. All of these published investigations used \textit{in vivo} measurements to determine suitability. The aim of this work is to utilise this suitability to improve the HDR process at St George Hospital and to take the work of others back a step in an attempt to make the implementation of the TLD system more accurate.

This involved the use of a phantom under strict conditions to determine the accuracy and precision of the TLDs and to determine if sufficient accuracy can be achieved by
using a linear accelerator to expose control TLDs. This would simplify the in vivo measurements by introducing a conversion factor to account for the differences in the radiation qualities used for the patient measurements and the controls, and provide greater confidence in the treatment delivery.

The main advantage of LiF:Mg,Ti TLD rods and the reason for choosing these over other available in vivo dosimeters was the cost and their well-established properties. LiF:Mg,Ti TLDs are also used at St George Hospital for external beam in vivo dose measurements in their chip form, as they are in many radiotherapy treatment centres. The annealing and readout process for this material is well documented and in regular use. If these TLDs were to be suitable, it would allow a smooth integration into clinical use without the introduction of more expensive equipment.
Chapter 3: A comparison of computed tomography (CT) and magnetic resonance imaging (MRI) for high dose rate (HDR) and pulsed dose rate (PDR) prostate brachytherapy.

Due to the advantages of MR over CT for prostate imaging as outlined in Chapter 2, it may be expected that planning on MR images would improve brachytherapy treatment in terms of both accuracy and consistency. The aim of this study was to determine whether this benefit could be confirmed quantitatively by an analysis of doses to the target volume and surrounding critical structures. The potential for improved consistency of target volume delineation was considered by evaluating intra- and inter-observer variation.

3.1 Materials
This section will outline the materials and equipment used to obtain data for the comparison. It will include details on the items used for the implant and imaging relevant to this project. Anaesthetic equipment and general surgical equipment will not be discussed.

3.1.1 Implant Equipment
Various specialised items were used for each HDR brachytherapy implant. These items were:

3.1.1.1 Ultrasound unit
A Falcon Ultrasound Scanner Type 2101 (B-K Medical, Denmark) as shown in Figure 3.1 was used in the operating theatre with a Bi-plane Transducer Type 8658 (B-K Medical, Denmark) for trans-rectal visualisation of the prostate during the implant procedure.
3.1.1.2 Stepper/Stabiliser

A Barzell Microtouch system with stabiliser and brachystepper (Barzell-Whitmore Maroon Bells Inc, Florida) was used to step the ultrasound transducer through the rectum to obtain accurate prostate dimensions and images. It is shown assembled with the ultrasound probe in Figure 3.2 below.
3.1.1.3 Brachytherapy Grid
A Perspex grid was developed in-house to allow MRI scans to be taken, avoiding the risk of ferromagnetic materials being taken into the MRI suite. The grid is shown in Figure 3.3 below. The grid was sterilised with Ethylene Oxide between patients. Autoclaving caused the Perspex to expand, closing up the holes such that the needles were unable to pass through. The grid was modelled on the standard grid used for St George Hospital HDR prostate brachytherapy patients – the HDR Contour Template from Mick Radio-Nuclear Instruments, Inc (New York).

![Perspex prostate brachytherapy template, manufactured at St George Hospital based on HDR Contour Template (Mick Radio-Nuclear Instruments Inc, New York).](image)

3.1.1.4 Marker Seeds
ACCULOC® soft tissue gold marker seeds (CMS alphatech, Sydney Australia) were used in all patients for this study. Two seeds were placed at the base of the prostate, and one at the apex under ultrasound guidance.

3.1.1.5 Pathfinder Needles
Pathfinder needles from Mick Radio-Nuclear Instruments Inc (New York) were used to pierce the skin and create the tracks through the prostate prior to the insertion of the brachytherapy needles.
3.1.1.6 Brachytherapy Needles
Six French (French catheter scale – equivalent to 2 mm outer diameter), 240 mm length Oncosmart Proguide sharp needles supplied by Nucletron Pty Ltd (Australia) were used for all patients in this study. They are shown in Figure 3.4. A minimum of 18 needles and a maximum of 22 needles were used in each patient as determined necessary by the Radiation Oncologist to obtain adequate treatment options for coverage of the prostate.

3.1.1.7 CT Markers
Specialised CT markers (Nucletron Pty Ltd, Australia) were used for the simulation and CT scans. These markers are made of copper and have a radio-lucent section between the tip and the remainder of the marker as shown in Figure 3.4. This design allows easy determination of the first dwell position possible within each needle on the CT scan.

![Figure 3.4 Oncosmart Proguide sharp needles and CT markers (Nucletron, Australia).](image)

3.1.1.8 Rectal Marker
All patients had a Shadowform® 10 cm rectal marker with T-bar handle (IZI Medical Products Inc, Baltimore) inserted into the rectum to assist with visualisation on the CT images. The rectal marker is shown in Figure 3.5.
3.1.2 Simulator
All patients had an x-ray film of their implant taken on a Ximatron Simulator (Varian Medical Systems, Australia), pictured in Figure 3.6.

Figure 3.5 Shadowform® rectal marker (IZI Medical Products Inc, Baltimore).

Figure 3.6 Ximatron Simulator (Varian Medical Systems, Australia)
3.1.3 CT Scanner
All patients for this study were scanned using a single slice Toshiba Xpress SX Computed Tomography Scanner (Toshiba Australia Pty Ltd, Australia). Helical scans were taken as per the protocols developed for brachytherapy at St George Hospital. The parameters used are listed in Table 3.1 below.

Table 3.1 CT Scanning Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Field of View</td>
<td>240 mm²</td>
</tr>
<tr>
<td>Slice Thickness</td>
<td>5 mm</td>
</tr>
<tr>
<td>Slice Spacing</td>
<td>5 mm</td>
</tr>
<tr>
<td>Gantry Tilt</td>
<td>0°</td>
</tr>
<tr>
<td>kVp</td>
<td>120</td>
</tr>
<tr>
<td>mA</td>
<td>300</td>
</tr>
</tbody>
</table>

3.1.4 MRI Scanner
All patients for this study were scanned using a Philips Intera 1.5 Magnetic Resonance Imaging unit. Software version 11.1.4.3 was used. Axial T1 and T2 scans were taken with parameters listed in Table 3.2 below.

Table 3.2 MRI Scanning Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Axial T1</th>
<th>Axial T2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Field of View</td>
<td>240 mm²</td>
<td>240 mm²</td>
</tr>
<tr>
<td>Number of slices</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Slice Thickness</td>
<td>5 mm</td>
<td>5 mm</td>
</tr>
<tr>
<td>Slice Spacing</td>
<td>0 mm*</td>
<td>0 mm*</td>
</tr>
<tr>
<td>TR (Repetition Time)</td>
<td>530</td>
<td>3302</td>
</tr>
<tr>
<td>TE (Echo Time)</td>
<td>10</td>
<td>80</td>
</tr>
<tr>
<td>Matrix size</td>
<td>256 x 320</td>
<td>256 x 512</td>
</tr>
<tr>
<td>NSA (Number of Signal Averages)</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>
* Slice spacing of 0 mm in Table 3.2 is equivalent to slice spacing of 5 mm listed in Table 3.1 for the CT scans. This means that the slices are contiguous (one slice commences immediately after the previous slice).

3.1.5 Planning Systems

3.1.5.1 Anatomy Modelling

The planning system used for fusion of CT and MR images as well as for the delineation of the organs of interest was the Oncentra Masterplan system (Nucletron Pty Ltd, Australia). Version 1.5 Service Pack 1 was used (Software v1.5.1.11, Documentation v1.5.1.5). The anatomy modelling component of the software was used. A Wacom tablet monitor and stylus supplied by Nucletron Pty Ltd Australia was used for the voluming of all structures.

3.1.5.2 Brachytherapy Planning

The planning system used for the brachytherapy treatment including implant reconstruction and dose calculations was the Plato Brachytherapy Planning System (BPS) Version 14.3.5.
3.2 Methods

3.2.1 Patient details
A total of nine HDR prostate brachytherapy patients were scanned with both CT and MRI. One patient (Patient 7) had a hip replacement, creating severe artefact in the CT images and making the MR images less sharp. One patient’s data was difficult to fuse in Oncentra Masterplan as it appears that the rectal marker was displaced between the two separate scans, causing some distortion in the anatomy (Patient 6). Patient data was anonymised prior to any delineation of organs taking place.

3.2.2 Implant procedure
The implant procedure was complex and required a multi-disciplinary team including Anaesthetists, theatre staff, a Radiation Oncologist, a Urologist and a Radiation Therapist or Physicist. A brief summary of the procedure will be provided here.

The patients were required to perform a bowel preparation involving the use of Fleet Enemas prior to the procedure. The patient was placed under a general anaesthetic in the operating theatre and placed into the lithotomy position.

The procedure commenced with the insertion of the rectal ultrasound probe. The probe was attached to the stepper unit, allowing accurate visualisation of superior/inferior distances through the rectum. The prostate size and position was assessed to ensure the procedure was going to be possible. The main reason for abortion of the procedure is pubic arch interference – where the pubic bone is in the path of the brachytherapy needles and coverage of the disease would not be possible. The brachytherapy template was stitched onto the perineum.

Three gold marker seeds were inserted via ultrasound guidance through the brachytherapy template and into the prostate. Two seeds were placed at the base of the prostate and one seed at the apex. These seeds were used for localisation of the prostate and quality assurance purposes.

Pathfinder needles were used initially to pierce the skin through the brachytherapy template and to create a track through the prostate as viewed on the ultrasound unit. Brachytherapy needles were inserted through these tracks into the prostate. The grid
locations of each needle were noted. Care was taken to avoid piercing the urethra and the rectal wall. The needles were all pushed beyond the end of the prostate to ensure complete coverage. For this project, 18 to 22 needles were inserted in each patient, as decided by the Radiation Oncologist to ensure adequate coverage of the entire prostate. Fluoroscopy was also used in conjunction with the ultrasound to ensure the needles were placed in adequate locations. The length of each needle protruding from the end of the grid was measured and adjusted so that all needles were at an equivalent depth.

At the end of the procedure, a cystoscopy was performed to ensure the urethra had not been damaged by the needles, and the anterior rectal wall was palpated to ensure there were no needles passing through it.

A 3-way Foley catheter was inserted to allow for irrigation of the bladder (the needles often pass all the way into the bladder causing bleeding and therefore irrigation is necessary to avoid blood clots) and a rectal marker was inserted for improved visualisation of the rectum on the CT scans. The patients were given a PCA (Patient Controlled Analgesia) allowing self-administration of morphine as required. A Perspex protective cone was placed over the needles and attached to the brachytherapy grid. The purpose of this cone was to prevent the needles digging into the patient’s bed.

The patients were sent to Recovery to be roused from the general anaesthetic.

3.2.3 Imaging procedures
There were three components to the imaging for these patients. They will be presented here in the order in which they were completed.

3.2.3.1 Simulation
The patients were taken to the Radiotherapy Simulator where a reference x-ray film was taken. The film was taken with CT markers placed in two lateral needles in a mid-prostate plane, as well as a 10 cm magnification marker in another needle in the same plane. The film was taken in the anterior to posterior direction. Adjustments to the needle positions were made if there was inadequate coverage of the prostate based
on the CT marker position compared with the gold marker seed location, both clearly visible on the film. Usually this involved inserting the needles further through the prostate. Again, all needles were adjusted so that equal lengths protruded from the brachytherapy grid. The final film taken at the Simulator was then the reference film, to which all subsequent films would be compared. Mobile X-ray films were taken prior to each fraction and the position of the implant with respect to the gold marker seeds was compared to the reference film and adjusted if necessary.

3.2.3.2 CT Scan Procedure
Helical scans were taken for this project. The CT gantry was set to 0.0°, slice thickness set to 5 mm and slice spacing also set to 5 mm to give contiguous images. This thickness and spacing was selected to correspond with the brachytherapy source stepping positions of 5 mm as defined in Plato BPS. The afterloader has the ability to step the source in 2.5 mm increments, and a smaller slice thickness and spacing would give more accuracy in defining the extent of the prostate in the superior to inferior direction and the precise location of the first dwell position, however it would increase the time involved in organ delineation and planning the patient’s treatment. The decisions on the settings used were based on a balance between accuracy and time for organ delineation and planning.

Due to the movement of the patient from simulator couch to bed, and from bed to CT couch, the needle positions were verified prior to scanning to ensure they had not shifted with respect to the brachytherapy grid. The patient was set up on the CT couch as closely as possible to the proposed treatment position.

CT markers were placed into all the needles prior to scanning. A scout image was taken and the region of interest selected, ensuring the CT scan covered the region from the brachytherapy grid to several slices above the tips of the needles. A field of view of 240 mm² was used to zoom in on the prostate, as Plato BPS is limited in its ability to zoom in on the images.
3.2.3.3 MRI Scan Procedure
The MRI settings were selected to match the CT settings used as a part of the brachytherapy imaging protocols at St George Hospital. Two series of images were taken as outlined in Table 3.2 above. The patient position was matched as closely as possible to the CT position. Needle positions were verified to within the tolerance level of ±1 mm by measuring the length of needle protruding from the brachytherapy grid as for the CT scan procedure. The time period between CT and MRI scans ranged between approximately thirty and ninety minutes.

3.2.4 Planning procedure
As this was a retrospective study on the imaging of prostate brachytherapy cases, the planning procedure described here was that used in this study only and differs from current clinical treatments.

3.2.4.1 Image Fusion
All CT and MR images were imported into Oncentra Masterplan and anonymised. Fusion of the CT images with the Axial T1 MR images was performed using the Landmark Fusion method. Various points along each needle around the region of the prostate (based on the implanted marker seeds) were correlated between the two image sets providing a good match between the images of needle position. This automatically created a fusion between the CT and Axial T2 MR images. This method was chosen due to the lack of external body contour on the images, as well as the movement of the implant with respect to other anatomical landmarks in moving the patient from the CT couch to MRI. It was assumed that the prostate did not move with respect to the needles piercing it. If there was swelling of the prostate between the scanning procedures, the needles would have shifted with the prostate, so any error in fusion caused by swelling would be minimised. If the prostate shifted parallel to the needles piercing it, the fusion using this method could be in error. To account for this, the gold marker seeds were also used as Landmark fusion points.

3.2.4.2 Organ Delineation
Organ volumes were delineated by two Radiation Oncologists on two sets of images for each patient. The first was the CT alone, with a hard copy of the ultrasound printouts from theatre available for reference (CT plan 1 and CT plan 2 for Oncologist
1 and 2 respectively), and the second was the CT/MR fused image set (MR plan 1 and MR plan 2 for Oncologist 1 and 2 respectively). It was found that the prostate was more clearly defined on the Axial T2 fusion than the Axial T1 fusion for all patients, so this was the MRI set used for delineating the organs.

As only two Oncologists delineated the organs on all data sets, the data presented here is expected to potentially show some trends, however a larger cohort of Oncologists would be necessary to improve statistical rigour of the results and provide conclusive evidence regarding the benefit of MRI in prostate brachytherapy.

A rectangular body contour was placed around each of the images as required for the Plato BPS dose calculations. The marker seeds were delineated to assist in defining the base and apex of the prostate. The anatomical structures delineated by the Oncologists were the prostate (target), urethra and rectum. A peripheral zone was also added, following the shape of the target, but curving in a horseshoe shape around the urethra. This technique is used routinely at St George Hospital to assist in obtaining a good initial plan using the IPSA (Inverse Planning Simulated Annealing) optimisation algorithm.

3.2.4.3 Treatment Planning
After the organ delineation was completed by the Oncologists, the images and structure sets were transferred to Plato BPS via a network connection. Once imported into Plato BPS, the catheters (needles) used for the patient’s treatment were marked. A total of 18 catheters were marked for each patient. Some patients had more than 18 catheters implanted, however the Nucletron PDR afterloader available at St George Hospital only had capacity for 18 channels. The additional needles were placed to allow greater choice as to which needles to use for treatment. The decision on which needles to leave out of the plan was based on various factors including proximity to the urethra, proximity to other needles and location within the prostate based on the delineated organs on CT plan 1. All plans generated for each individual patient used the same 18 needles.

Patient points were placed along the centre of the urethra, or the expected region of highest urethral dose on slices where the urethra was not within the prostate volume.
Patient points were also placed in the rectum at a distance of 5 mm from the anterior rectal wall as per the St George Hospital protocol.

The viewing axes were rotated to match the axes of the needles through the prostate, however the centre of the co-ordinate system was not adjusted from the default position allocated as the centre of the target volume by Plato.

IPSA was used to generate an initial reference plan on CT plan 1. This data set was chosen as it represented the clinical situation at the time these patients were treated. A total dose of 650 cGy was prescribed and the class solution is listed below in Table 3.3. The same class solution was used for each patient.

<table>
<thead>
<tr>
<th>Volume of interest</th>
<th>Margin (mm) dose control</th>
<th>Margin (mm) catheter activation</th>
<th>Organ type</th>
<th>Minimum surface dose (cGy)</th>
<th>Minimum surface dose weight</th>
<th>Maximum surface dose (cGy)</th>
<th>Maximum surface dose weight</th>
<th>Minimum volume dose (cGy)</th>
<th>Minimum volume dose weight</th>
<th>Maximum volume dose (cGy)</th>
<th>Maximum volume dose weight</th>
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<tbody>
<tr>
<td>Peripheral zone</td>
<td>0.0</td>
<td></td>
<td>Target</td>
<td>120</td>
<td>650.0</td>
<td>975.0</td>
<td>120</td>
<td>650.0</td>
<td>975.0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Rectum</td>
<td>0.0</td>
<td>0.0</td>
<td>Organ at risk</td>
<td>0</td>
<td>0.0</td>
<td>455.0</td>
<td>50</td>
<td>0</td>
<td>0</td>
<td>455.0</td>
<td>50</td>
</tr>
<tr>
<td>Target</td>
<td>1.0</td>
<td>5.0</td>
<td>Reference target</td>
<td>100</td>
<td>650.0</td>
<td>975.0</td>
<td>100</td>
<td>650.0</td>
<td>975.0</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Urethra</td>
<td>0.0</td>
<td>0.0</td>
<td>Organ at risk</td>
<td>100</td>
<td>650.0</td>
<td>715.0</td>
<td>120</td>
<td>650.0</td>
<td>715.0</td>
<td>120</td>
<td>120</td>
</tr>
</tbody>
</table>

After running the IPSA algorithm, the graphical optimisation method was used to obtain a plan appropriate for patient treatment with constraints as per the St George protocol shown in Table 3.4 below:

<table>
<thead>
<tr>
<th>Dosimetric Parameter</th>
<th>Constraint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose to urethra</td>
<td>&lt; 120% of prescribed target dose</td>
</tr>
<tr>
<td>Dose to rectum</td>
<td>&lt; 70% of prescribed target dose</td>
</tr>
<tr>
<td>D_{90} (Target)</td>
<td>&gt; 100% of prescribed target dose</td>
</tr>
<tr>
<td>V_{100} (Target)</td>
<td>&gt; 95%</td>
</tr>
<tr>
<td>V_{150} (Target)</td>
<td>&lt; 50%</td>
</tr>
<tr>
<td>V_{200} (Target)</td>
<td>&lt; 15%</td>
</tr>
</tbody>
</table>
D$_{90}$ represents the dose to 90% of the target volume and should be at least 100%. $V_{100}$ represents the percentage of the target volume receiving 100% of the prescribed dose. This should ideally be greater than 95%, however it may be reduced if the rectum is too close to the prostate to avoid rectal complications. $V_{150}$ and $V_{200}$ represent the target volume receiving 150% and 200% of the prescribed dose respectively. This is an indication of hot spots. Hot spots are expected around each source; however large regions of high dose are not desirable.

As a comparison, the dwell times planned on the reference data set (CT plan 1) were copied across to the other three data sets (CT plan 2, MR plan 1 and MR plan 2) generating a total of four plans per patient. As the patients were treated using the reference image set, the non-reference plans represent the dose delivered to the prostate and critical structures if these organs were incorrectly represented on the reference CT plan and the alternative volume sets were correct. The same prescription dose and treatment time were entered to place the same isodose pattern on all data sets.

Dose volume histograms (DVHs) were calculated for all plans and analysed to determine target volumes and differences in various dosimetric parameters as detailed in Section 3.2.5.

3.2.5 Analysis procedure

3.2.5.1 Defining needle position
Defining the first dwell position within each needle is important for correct positioning and therefore accurate delivery of the brachytherapy treatment. The CT images and MR images were visually inspected to determine the modality in which the needle tips were clearly defined.

3.2.5.2 Inter-observer variation
The variation in total volume, length, height and width of the prostate contours across the central planes was determined and the difference between image sets and Oncologists was analysed. This variation was assessed for CT alone as well as for the CT/MR fused images to observe any benefit in terms of consistency when using MR images in addition to CT. The gold-standard which all data was compared to was
chosen to be the average dimensions of the prostate from all four data sets (as outlined in section 3.2.4.2) for each patient.

To obtain the volume of the target, a DVH table was generated in Plato BPS for the target. The DVH table was then used to determine the volume in cubic centimetres of the prostate.

The DVH data was obtained from Plato BPS using a sample size of 60000 points. Lower dose limit was set to 0 and upper dose limit to 4. These dose limits are multiples of the prescribed dose, so the upper dose limit of 4 means that the DVH data extended to 4 times the prescribed dose of 650 cGy = 2600 cGy.

The length, height and width were determined using the “Ruler” function in Plato BPS on the two-dimensional reconstructed images, along the axes of the target volume (Figure 3.7). The error in measurement using this method was estimated to be ±0.2 mm for the height and width, however the error in the length was greater due to the 5 mm slice thickness and spacing, and was therefore estimated as ±2.5 mm. Length was measured as the superior to inferior length (from apex to base), height was measured as the anterior to posterior distance and width was measured as the lateral (left to right) distance of the target volume.

Figure 3.7 Prostate dimensions
The location of the base and apex was assessed for each case and compared to the gold standard (average location from all four data sets). This was to determine if one imaging modality showed greater consistency than the other in defining these superior and inferior levels of the prostate.

3.2.5.3 Intra-observer variation

For each individual Oncologist, the variation between CT alone and CT/MR fused images was analysed for the same parameters as listed above in Section 3.2.5.2 using the same methods. The purpose of this was to determine the extent of difference in volumes by each individual Oncologist using the two different imaging modalities.

3.2.5.4 Target Dosimetry Analysis

The dwell times from the optimal treatment plan created on CT plan 1 were copied into each of the other data sets so that the same treatment plan was applied to all four organ volume sets for each patient. The parameters analysed for comparison between each modality based on CT plan 1 were: $D_{80}$, $D_{90}$, $D_{100}$, $V_{80}$, $V_{90}$, $V_{100}$, $V_{150}$ and $V_{200}$, where $D_x$ is the dose received by $x\%$ of the target volume, and $V_y$ is the target volume receiving $y\%$ of the prescribed dose. The complexity of creating an “average” set of volumes based on all Oncologists’ volumes was beyond the scope of this project.

An analysis of 200% regions outside of the target was completed to determine how much normal tissue was exposed to very high doses of radiation based on the contours from the different imaging modalities. The extent of these regions was calculated from DVH data by determining the volume in cubic centimetres of the 200% dose regions inside the target, subtracted from the 200% regions inside the Body contour. The procedure was repeated for the 150% regions.

3.2.5.5 Critical Structure Dosimetry (Toxicity)

Maximum urethral and rectal doses at the patient points described in Section 3.2.4.3 were compared for each of the four plans. A further analysis of the doses to the urethra and rectum was considered by looking at the maximum dose to 2 cc, 1 cc and the maximum point dose to the organs (dose to 0.01 cc), all based on DVH data. These parameters were not used in the analysis of these patients’ treatment plans, however they have become more commonly used parameters at St George Hospital.
recently. They were obtained from DVH data. The upper dose limit was set to 2 (1300 cGy) for the rectum and 3 (1950 cGy) for the urethra (refer to Section 3.2.5.2 for the definition of upper dose limit).

Standard deviations were used throughout the analysis procedure to define the errors involved in the comparison of the four data sets analysed. All standard deviations in this project were calculated using equation 3.1 (Kirkup 1994):

\[ \sqrt{\frac{\sum (x-x)^2}{(n-1)}} \quad \text{Equation 3.1} \]

Where \( x \) is the individual result, \( \bar{x} \) is the mean result, and \( n \) is the sample number.
3.3 Results and Discussion

3.3.1 Defining needle position

The needles used in this study were made of a plastic material, however a copper CT marker (Section 3.1.1.7) was inserted into each needle for the CT scan. This marker clearly showed the needle positions on the CT scan, including the location of the first possible dwell position for the Ir-192 source near the tip of the needle. No markers were placed in the needles for the MR scan as there are no MRI markers commercially available, and the needles appeared as dark spots on the image. There is no clear method to distinguish between the needle and an empty needle track. Examples of each image are shown below in Figure 3.8. The CT image on the left clearly defines the CT markers (white spots). The prostate is much clearer on the MR image on the right, however there is no difference in the MR image between needles and empty needle tracks making it difficult to locate the tips of the needles accurately.

Therefore, for accuracy, it is important to include the CT data in the planning process. If using MR data to define the prostate, it should be fused with the CT data to ensure the needle locations are accurately defined in the brachytherapy planning system.

Figure 3.8 CT (left) and MR (right) images of the prostate brachytherapy implant.
3.3.2 Target volume and dimension variations

Figure 3.9 shows the average target volume, length, width and height for all four data sets, averaged for all nine patients. This graph demonstrates both inter- and intra-observer variation in the target volume and dimensions. CT plans are indicated by the pale colours and MR plans are indicated by the dotted darker colours. The error bars here represent one standard deviation from the average value over nine patients, and as such represent the variation in prostate sizes between the nine patients. The sizes of the error bars in this plot do not indicate clearly that one data set consistently gave smaller volumes or dimensions than another; however there were notable trends in the average data. On average, the MR data sets gave smaller target volumes than CT data sets, and particularly the length and width of the target were on average smaller on the MR data sets.

![Figure 3.9 Average target dimensions for nine patients.](image)

From the data in Figure 3.9, the trend on the average data showed that the average volume of the prostate when delineated with MR imaging was smaller than when delineated with CT imaging. However, the consistency between Oncologists was slightly worse with MR imaging. This may be due to a learning curve effect as the Oncologists were not familiar with defining the prostate for brachytherapy using MR
imaging. As Figure 3.9 is an average of all the data, figures 3.10 – 3.13 have been presented below to show the results for each patient.

**Figure 3.10 Target volume for each patient**

**Figure 3.11 Target length (sup/inf) for each patient**
From Figure 3.10 it can be seen that there was no significant effect of prostate size on the variability of results. The spread of the data was reasonably consistent for all
patients, with the greatest variability observed in Patient 3. There were no obvious irregularities in Patient 3 that would cause this variability compared with other patients.

The scales of the Y-axis in figures 3.11 – 3.13 are equivalent. Therefore it can be seen that the length (superior to inferior length) of the prostate showed the most variability of the three dimensions examined, and was therefore the largest area of uncertainty in defining the target volume.

As discussed in Section 3.2.1, Patient 7 had a hip replacement, and the CT data set had significant artefacts that may have interfered with accurate target delineation. However, as can be seen in Figures 3.10 to 3.13, the intra-observer and inter-observer differences were not significantly different to the other cases. The MR imaging in this case did not provide a clear benefit to defining the target volume.

MR imaging did not consistently determine the length of the prostate to be shorter than it had been defined in the CT imaging, however Figure 3.14 and 3.15 show the variation in the definition of the base and apex position for each patient.

These results do not show any significant improvement in defining the base or the apex of the prostate using MR imaging. The deviations between the Oncologists are similar when the prostate is delineated with CT as when it is delineated with CT/MR fused images.
Figure 3.14 Deviation of Base from Gold Standard

Figure 3.15 Deviation of Apex from Gold Standard
3.3.2.1 Inter-observer variation

Table 3.5 shows the results of the prostate volumes and dimensions for each Oncologist for CT alone (CT plan 1 and CT plan 2) for all patients. Table 3.6 shows the results of the prostate volumes and dimensions for each Oncologist for the CT/MR fused data sets (MR plan 1 and MR plan 2) for all patients.

Table 3.5 CT Prostate Volumes and Dimensions

<table>
<thead>
<tr>
<th>Patient</th>
<th>Oncologist 1</th>
<th></th>
<th>Oncologist 2</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Volume (cm³)</td>
<td>Length (mm)</td>
<td>Height (mm)</td>
<td>Width (mm)</td>
<td>Volume (cm³)</td>
</tr>
<tr>
<td>1</td>
<td>40.67</td>
<td>46.1</td>
<td>37.3</td>
<td>40.4</td>
<td>54.42</td>
</tr>
<tr>
<td>2</td>
<td>44.52</td>
<td>50.7</td>
<td>34.0</td>
<td>43.4</td>
<td>57.67</td>
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<tr>
<td>4</td>
<td>39.42</td>
<td>53.0</td>
<td>31.6</td>
<td>37.2</td>
<td>33.12</td>
</tr>
<tr>
<td>5</td>
<td>47.9</td>
<td>51.1</td>
<td>33.5</td>
<td>45.1</td>
<td>49.98</td>
</tr>
<tr>
<td>6</td>
<td>33.76</td>
<td>39.6</td>
<td>29.0</td>
<td>39.3</td>
<td>23.77</td>
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<tr>
<td>7</td>
<td>34.03</td>
<td>51.1</td>
<td>28.5</td>
<td>35.0</td>
<td>24.22</td>
</tr>
<tr>
<td>8</td>
<td>39.21</td>
<td>45.9</td>
<td>30.6</td>
<td>44.4</td>
<td>28.8</td>
</tr>
<tr>
<td>9</td>
<td>79.94</td>
<td>60.7</td>
<td>40.1</td>
<td>51.1</td>
<td>74.1</td>
</tr>
</tbody>
</table>

Table 3.6 CT/MR Prostate Volumes and Dimensions

<table>
<thead>
<tr>
<th>Patient</th>
<th>Oncologist 1</th>
<th></th>
<th>Oncologist 2</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Volume (cm³)</td>
<td>Length (mm)</td>
<td>Height (mm)</td>
<td>Width (mm)</td>
<td>Volume (cm³)</td>
</tr>
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<td>37.88</td>
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<td>35.6</td>
<td>49.94</td>
</tr>
<tr>
<td>2</td>
<td>38.45</td>
<td>40.6</td>
<td>33.0</td>
<td>37.9</td>
<td>37.86</td>
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<td>32.84</td>
<td>26.4</td>
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<td>31.6</td>
<td>32.3</td>
<td>31.71</td>
</tr>
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<td>25.22</td>
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<td>28.5</td>
<td>33.2</td>
<td>19.03</td>
</tr>
<tr>
<td>7</td>
<td>28.94</td>
<td>40.9</td>
<td>31.8</td>
<td>30.5</td>
<td>25.5</td>
</tr>
<tr>
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<td>37.35</td>
<td>51.7</td>
<td>31.4</td>
<td>34.5</td>
<td>28.85</td>
</tr>
<tr>
<td>9</td>
<td>85.62</td>
<td>61.2</td>
<td>48.4</td>
<td>55.4</td>
<td>70.46</td>
</tr>
</tbody>
</table>
The average and maximum deviations between the Oncologists is shown in Table 3.7 for both CT alone and CT/MR fused image sets. This is directly based on the data in Table 3.5 and 3.6 above.

Table 3.7 Inter-observer Deviations between two Oncologists in Target Volume and Dimensions

<table>
<thead>
<tr>
<th>Image Set</th>
<th>Average deviation over nine patients</th>
<th>Maximum deviation on a single patient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Volume (cm$^3$) Length (mm) Height (mm) Width (mm)</td>
<td>Volume (cm$^3$) Length (mm) Height (mm) Width (mm)</td>
</tr>
<tr>
<td>CT only</td>
<td>0.3 3.9 0.2 1.6</td>
<td>15.7 16.1 4.0 7.3</td>
</tr>
<tr>
<td>CT/MR Fusion</td>
<td>2.6 1.3 2.4 0.8</td>
<td>15.2 10.8 9.2 5.9</td>
</tr>
</tbody>
</table>

3.3.2.2 Intra-observer variation

Table 3.8 shows for each Oncologist, the difference between prostate volumes and dimensions, comparing the CT only image set to the CT/MR fused image sets. A positive number indicates that the dimension of the prostate delineated on the CT images was larger than the prostate delineated on the MR images, a negative number the reverse.

Table 3.8 Intra-observer Variation in Target Volume and Dimensions – Difference between CT and fused CT/MRI

<table>
<thead>
<tr>
<th></th>
<th>Oncologist 1</th>
<th>Oncologist 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Volume (cm$^3$) Length (mm) Height (mm) Width (mm)</td>
<td>Volume (cm$^3$) Length (mm) Height (mm) Width (mm)</td>
</tr>
<tr>
<td>Average Deviation</td>
<td>5.7 4.8 -1.9 4.4</td>
<td>8.5 2.2 0.3 3.6</td>
</tr>
<tr>
<td>Maximum Deviation</td>
<td>18.7 19.8 8.3 9.9</td>
<td>41.07 10.9 9.0 11.9</td>
</tr>
</tbody>
</table>
For both Oncologists, the maximum deviation in overall prostate volume occurred in the same patient (Patient 3). The MR volume was smaller than the CT volume in all except three out of 18 data sets (one patient for Oncologist 1 and two patients for Oncologist 2 – all on different patients).

3.3.3 Target Dosimetry
The dose volume histograms created in Plato BPS were analysed and the results are presented below. Figure 3.16 is a sample DVH plot for Patient 1. The prescription dose was 650 cGy. The reference plan (CT plan 1) is represented as the pale blue curve, which shows the best target coverage of the four plans. This is expected as the plan was optimised for this target shape and critical structure positions.

![Figure 3.16 Normalised Target Dose Volume Histogram for Patient 1.](image_url)

The typical target dosimetric parameters analysed at St George Hospital prior to patient treatment as discussed in Section 3.2.5.4 are presented in their average forms in Figures 3.17 and 3.18 below. Error bars represent the maximum range of the data for the nine patients, and not the standard deviations.
Figure 3.17 Target dosimetry data – D$_{80}$, D$_{90}$ and D$_{100}$ (average over all nine patients). Error bars represent maximum range of the data.

Figure 3.18 Target dosimetry data – V$_{80}$, V$_{90}$, V$_{100}$, V$_{150}$ and V$_{200}$ (average over all nine patients). Error bars represent maximum range of the data.
As the treatment plan for each patient was created based on the structures defined by Oncologist 1 on the CT data set (CT plan 1), the parameters were optimised for these organ delineations.

If it was assumed that MR gave better target definition than CT based on the evidence presented in Sections 2.2.3.2 and 2.2.4, it could be concluded that the target volume was not being covered with as much radiation as intended. Some parts of the target were receiving significantly less than 100% of the prescribed dose as seen from the $V_{100}$ parameter in Figure 3.18 (dotted bars representing the CT/MR fused data sets).

Dosimetry parameters $D_{90}$, $V_{100}$, $V_{150}$ and $V_{200}$ used for determining plan suitability prior to treatment are separated out for each patient in Figures 3.19 – 3.22 below.

![Figure 3.19 D_90 (Dose received by 90% of the target volume)](image)

The largest variation in $D_{90}$ occurs in most patients between the plans placed on CT images (pale blue and pale orange squares). According to the Oncologist 2 CT data, patients 1 – 4 are all receiving insufficient dose ($D_{90} < 100\%$). Five out of the nine patients are receiving insufficient dose according to the Oncologist 2 CT/MR fused data, and two of the patients are receiving insufficient dose according to the Oncologist 1 CT/MR fused data.
Figure 3.20 $V_{100}$ (Target volume receiving 100% of the prescribed dose)

Figure 3.21 $V_{150}$ (Target volume receiving 150% of the prescribed dose)
From Figures 3.21 and 3.22, it can be seen that there were generally less hotspots within the target volume when it was delineated using CT/MR fusion. Overall, the entire radiation dose to the prostate appeared to be less according to this DVH data. As the total dwell times are the same in all cases, there must be significant dose outside the target volumes. Some dose is expected outside the target volume as the photon spectrum of Ir-192 drops off exponentially. As the needles are spaced apart, there will be curves in the isodose distribution so it is inevitable that some regions outside the target will receive 100% or more of the dose to ensure as much coverage of the target with 100% as possible.

As the regions outside the target are considered normal tissue, hot spots in these regions should be avoided. Figure 3.23 represents the extent of the 200% hotspots (regions receiving at least 200% of the prescribed dose) outside of the target volume. Figure 3.24 is the same plot for the 150% regions. In most cases, there are more 200% hotspots outside the target for the CT/MR fused data sets than for the CT only data sets, which correlates with the result that MR imaging gives a smaller target volume than CT imaging. In terms of clinical effects, this means that more normal tissue is being exposed to high doses of radiation than is expected. A similar trend is observed with the $V_{150}$. 

Figure 3.22 $V_{200}$ (Target volume receiving 200% of the prescribed dose)
Figure 3.23 $V_{200}$ (tissue volume receiving 200% of the prescribed dose) outside the target volume

Figure 3.24 $V_{150}$ (tissue volume receiving 150% of the prescribed dose) outside the target volume

It has been reported that CT typically overestimates the prostate volume (Dubois, Prestidge et al. 1998; Crook, Milosevic et al. 2002; Polo, Cattani et al. 2004; Solbjem,
Davis et al. 2004; Carey 2005; Miquel, Rhode et al. 2006), however this project shows that this extra margin inherent in CT delineation does not always encompass the entire prostate as determined by MR. There were some regions outside the prostate as defined by MR imaging that received extra dose, however there were regions inside the prostate that did not receive the full treatment dose. This initial investigation would suggest that CT does not always overestimate the prostate dimensions in all regions, thus the need to move to MR imaging may be greater than anticipated.

3.3.4 Critical Structure Dosimetry (Toxicity)

The maximum doses to the patient points described in Section 3.2.4.3 are displayed in Figure 3.25 below for each patient. All points above the 100% line are urethral dose points and the points below the 100% line are rectal dose points.

From this plot there is no clear indication that the dose to the critical structures is less when defined with one imaging modality over the other. However it does show that there is very little variation in the maximum dose to the urethra from both intra-observer and inter-observer comparisons. If the reference clinical plan was generated based on the CT/MR fused images, the doses to the critical structures would be
different. The major limitation of this analysis is that the reference plan (CT plan 1) was applied directly to the other data sets, and not optimised for each data set individually.

There is more deviation in the rectal position with respect to the implant when compared with the urethral deviation. In most cases, the MR images show the anterior wall of the rectum to be further away from the prostate than in the CT scan. This may be affected by rectal movement between the time of the CT scan and the MR scan. This does not affect the urethra to the same extent as the urethra passes through the prostate and will tend to shift with the prostate and hence with the implant.

As the point doses are not fully representative of the dose received by the organs, DVH data was also analysed. Figure 3.26 shows the average dose received by 2 cc, 1 cc and a single point in the rectum and urethra based on the plan generated on the Oncologist 1 CT data sets. The dose received was on average, lower when the critical structures were delineated with the assistance of MR imaging. The error bars represent one standard deviation from the mean.

Figure 3.26 Critical structure DVH data (average for nine patients)
This result would allow for an increase in target dose whilst maintaining critical structure doses at acceptable levels, assuming that the MR imaging gave a more accurate depiction of the structure locations at the time of treatment. The results for the individual patients for the rectum are displayed in Figures 3.27 – 3.29. The same trend can be observed as in Figure 3.25 with the fused images in most cases showing less dose to the rectum than that from the CT imaging alone.

![Figure 3.27 Dose to 2 cc of the rectum](image-url)
Figure 3.28 Dose to 1 cc of the rectum

Figure 3.29 Maximum dose to the rectum (dose to 0.01 cc)
3.4 Conclusions
The results show that the volume of the prostate is significantly smaller when delineated on MR images compared with CT images. Therefore, if it were assumed that MR imaging still provided a more accurate, if not more consistent prostate delineation than CT imaging (Dubois, Prestidge et al. 1998), it may have a place in prostate brachytherapy to reduce the dose to normal tissue surrounding the prostate and obtaining better coverage of the smaller target volume, without compromising the critical structures.

The move to incorporating MR imaging would eliminate not only the overestimation of prostate volumes, but also any incorrect definition of prostatic tissue (areas of prostatic tissue not encompassed by the CT volumes).

Based on this study, there is no clear benefit in the use of MR for imaging the prostate in HDR or PDR brachytherapy in terms of achieving more consistent organ delineation between Oncologists. Data for this study has only been collected from two Radiation Oncologists. Therefore the data presented here is limited and a larger cohort of Oncologists would provide more conclusive results. Due to time constraints, it was not possible to obtain data from more than two Oncologists. This is a potential area for further work.
Chapter 4: The use of LiF:Mg,Ti TLDs for *in vivo* prostate brachytherapy dosimetry – a phantom study.

The aim of this chapter was to confirm the feasibility of using LiF:Mg,Ti TLDs for *in vivo* prostate brachytherapy dosimetry at St George Hospital. This was to address the lack of dosimeters currently in use for verification of dose delivery in prostate brachytherapy. The investigation was carried out as a phantom study with a view to extending toward studies in patients if the TLDs were deemed suitable. The investigation was aimed at determining a consistent correction factor to allow the use of an independent control dose to TLDs exposed to radiation from a 6 MV linear accelerator for accurately determining the dose delivered to the TLDs using an Ir-192 source.

4.1 Materials
This section will outline the materials and equipment used for the *in vivo* dosimetry phantom measurements taken as a part of this project.

4.1.1 Thermoluminescent Dosimeters (TLDs)
Harshaw TLDs (Thermo Electron Corporation, Australia) made of lithium fluoride doped with magnesium and titanium (LiF:Mg,Ti) were used in this study. These TLDs are also known as TLD-100 material. They are available in various physical forms, however for use inside the brachytherapy needles, cylindrical rods were selected. The dimensions of the TLD rods were 1 mm diameter, 6 mm length, as shown in Figure 4.1. TLDs with a shorter length would provide better spatial resolution, however they would be more difficult to manage as the readout carousel (as shown in Figure 4.3) is designed for up to 6 mm length rods. Smaller rods do not slot symmetrically into the carousel and can fall through small holes in the bottom of the carousel.
Figure 4.1 LiF:Mg,Ti TLD rods 1mm diameter, 6mm length (Thermo Electron Corporation, Australia) stored in an aluminium annealing tray.

4.1.2 TLD Oven
Annealing of the TLDs was performed in a PTW-TLDO oven (PTW Freiburg) as shown in Figure 4.2. The TLDs were stored and annealed in aluminium annealing trays, as shown above in Figure 4.1.

Figure 4.2 TLD oven (PTW Freiburg)
4.1.3 TLD Reader
The TLD rods were placed into the rod carousel as shown in Figure 4.3. They were then read in a Harshaw Model 5500 Automatic TLD Reader (Thermo Scientific, Australia).

![Figure 4.3 TLD reader and carousel (Thermo Scientific, Australia)]

4.1.4 Tweezers
The TLD rods were handled using vacuum tweezers. The vacuum was produced using a Dymax 30 pump (Charles Austen Pumps Ltd, Surrey, UK) as shown in Figure 4.4. This helped to avoid damaging the sensitive TLD material or allowing body oils (from the fingers) to come in contact with the rods.

![Figure 4.4 Vacuum tweezers (Charles Austen Pumps Ltd, Surrey UK)]
4.1.5  $^{90}$Sr TLD Irradiator
A strontium-90/yttrium-90 TLD irradiator (Thermo Electron Corporation, Australia – Model 2210) was used to establish sensitivity factors for the TLDs. The irradiator is shown in Figure 4.5. As the sensitivity factors are relative readings, the difference in energy between $^{90}$Sr (average energy ~970 keV) and $^{192}$Ir (average energy ~375 keV) (Khan, 2003) was expected to have minimal effect on the determination of these factors. The source had a nominal activity of 33 MBq on 4th November 2004 traceable to international standards (Germany). The documentation states that the dose delivered is 40 µGy per revolution of cobalt-60 equivalent radiation at an activity of 33 MBq.

![Figure 4.5 TLD irradiator (Thermo Electron Corporation, Australia)](image)

4.1.6 Solid Water Phantom
A custom-made solid water phantom was drilled from a 1 cm thick slab of water-equivalent material – Goettingen White Water (PTW, Freiburg). This material is specified as water-equivalent in the energy ranges from Cobalt-60 to 25 MV photons, however the work described in Section 4.2.5 and the results shown in Figure 4.12 aim to verify that the solid water was sufficiently accurate at the lower energies emitted by Ir-192 for the purposes of this project.

A space was drilled for a 6F ProGuide sharp needle (Figure 3.4) in the centre of the slab, and holes were drilled surrounding the needle in a grid, each hole large enough for the 6 mm TLD rods as described in Section 4.1.1. The centre of the middle row of TLD holes was aligned with the centre of the radioactive source inside the needle as
defined by the CT marker. Figure 4.6 shows this phantom with the space for the ProGuide needle. The holes are spaced 4 mm apart (centre to centre) perpendicular to the direction of the needle, and 1 cm (centre to centre) parallel with the axis of the needle.

Figure 4.6 Solid water TLD phantom slab with spaces for the ProGuide needle and 6 mm length TLD rods

4.1.7 Linear Accelerator
A Varian Clinac iX linear accelerator (Varian Medical Systems, Australia) was used for initial testing of the TLDs as well as regular exposures for control measurements (Figure 4.7). 6 MV nominal photon energy was used for all linear accelerator measurements for this project.

4.1.8 Pulsed Dose Rate Afterloader
A Pulsed Dose Rate (PDR) remote afterloading device (Nucletron, Australia) containing an Ir-192 source (Mallinkrodt B.V. Netherlands) was used for all Ir-192 measurements in this project (Figure 4.8). The source was changed approximately every 3 months throughout the duration of this project, and each source had an initial activity of approximately 2 Ci. The source design was a version 1 (classic) PDR source which consists of two 0.5 mm diameter, 0.5 mm length pellets of solid Iridium encapsulated in stainless steel. A PDR remote afterloading device is essentially the same as a high dose rate (HDR) remote afterloading device. The only difference being the activity of the radioactive source. Typical HDR activities for Ir-192 are around 10 Ci. The PDR unit is currently used at St George Hospital for prostate
brachytherapy in addition to other sites such as oesophagus, bronchus and cervix. For prostate treatments, brachytherapy is delivered using HDR fractionation schemes as described in Section 2.1.

Figure 4.7 Varian iX Linear Accelerator (Silhouette Edition) (Varian Medical Systems, Australia)

Figure 4.8 PDR Afterloader (Nucletron Pty Ltd, Australia)
4.2 Methods

Standard deviations were used throughout the analysis procedure to define the errors involved. All standard deviations in this project were calculated using Equation 4.1 (Kirkup 1994):

$$\sqrt{\frac{\sum (x - \bar{x})^2}{(n - 1)}}$$  \textbf{Equation 4.1}

Where \(x\) is the individual relative response, \(\bar{x}\) is the mean relative response of one TLD rod, and \(n\) is the sample number.

4.2.1 TLD Oven Readings

The accuracy of the oven temperature was verified to determine if the temperature matched the expected temperature. As outlined in Section 2.3.1.2.4, a lower temperature anneal may not clear all electrons from their traps (Kron 1994). A temperature too high may result in a reduced sensitivity of the chips (Horowitz 1990).

This verification was undertaken using a Fluke 52 K/J Thermometer. Two probes were used. One was placed near the oven’s thermostat and the other in the body of the oven (where the TLDs would be placed when annealing). The position of the probes was swapped to rule out any differences in the probes. Three separate readings were taken at 100°C and two at 400°C. The results were plotted and compared to the ideal case where the temperature reported by the oven’s thermostat matched the independently measured temperature inside the oven.

4.2.2 Initial TLD Preparation

Prior to measurements being taken, three cycles of readouts were undertaken. The TLDs were annealed using the pre-irradiation annealing procedure suggested by the manufacturer (1 hour at 400°C and 2 hours at 100°C), and exposed to 2 Gy of 6 MV photon radiation on the linear accelerator. This dose was delivered in the solid water phantom described in Section 4.1.6 using a 10x10 cm field, TLDs at 100 cm source to detector distance, 9 cm solid water backscatter material below the phantom slab, and 1.5 cm additional solid water buildup. This setup represents the absolute calibration settings for this linear accelerator, translated to a solid phantom setting as opposed to the liquid water measurements used for absolute calibration as based on the
International Atomic Energy Agency’s protocol detailed in their Technical Report Series (TRS) 398 (Andreo, Burns et al., 2000). 200 monitor units (MU) was equivalent to 2 Gy delivered to the TLDs on this linear accelerator. The TLDs were then annealed at 100ºC for 10 minutes prior to readout.

The readout of the TLDs was completed automatically using the TLD Shell software supplied with the TLD reader. The time-temperature profile (TTP) selected heated the TLD at 15ºC/second to a temperature of 335ºC. The temperature was then kept steady until the readout was complete (total time = 23.3 seconds).

The TLDs were divided up randomly into 2 sets of 50 rods, named hereafter as Set 1 and Set 2.

4.2.3 Reproducibility
Set 1 was used to establish reproducibility of this batch of TLDs. All TLDs were annealed, exposed and read under the same conditions as outlined in Section 4.2.2, however only 1 Gy (100MU) was delivered. Reproducibility was determined by dividing the raw reading of each rod by the average reading of all 50 rods over a total of 12 cycles to give the mean relative response. The reproducibility of each individual rod within the set was evaluated using the standard deviation of the relative response.

4.2.4 Sensitivity Factors
Set 2 was used to establish sensitivity factors using the strontium-90 irradiator. The rods were annealed using the same procedure as outlined in Section 4.2.2. Each TLD rod was exposed in the irradiator to 25000 revolutions. The dose delivered to the TLDs was approximately 0.925 Gy, based on the activity of the $^{90}$Sr source at the time of irradiation and the number of revolutions.

After this exposure, the post-irradiation anneal of 100ºC for 10 minutes was applied, and the rods were read using the same procedure as outlined in Section 4.2.2. Sensitivity factors for each rod were calculated by dividing the reading from each individual rod by the average reading of all 50 rods in Set 2. The rods were sorted in
order of decreasing sensitivity and the process was repeated three more times. The average of the final three sets of sensitivity factors was used for future measurements.

4.2.5 Iridium-192 Exposures (Initial Testing)

The solid water phantom was used to accurately deliver dose from the PDR unit to known distances from the source. Four 1 cm thick slabs of 30 cm$^2$ solid water backscatter material were placed below the phantom slab, and five 1 cm thick slabs of solid water placed on top. Distances approximating the dimensions of a prostate were used and Set 2 TLDs were placed at equal distances on both sides of the source and in line with the dwell position of the source to obtain an average reading from 2 rods. The distances from the source selected for these measurements were: 1.2 cm, 2.0 cm, 3.2 cm and 4.0 cm. The TLDs were exposed using the PDR afterloader for 120 seconds.

The expected dose to the TLDs was calculated using the TG43 formalism in Equation 4.2 (Nath, Anderson et al. 1995):

$$D(r,\theta) = S_k \times t \times Delta \times G(r,\theta) \times g(r) \times F(r,\theta) \quad \text{Equation 4.2}$$

$D(r,\theta)$ is the dose at the distance $r$ from the source at angle $\theta$ from the source (90$^\circ$ for all measurements in this project).

$S_k$ is the air kerma strength of the source at the time of exposure, measured in units cGy cm$^2$ h$^{-1}$.

$t$ is the exposure time in hours.

$Delta$, $G(r,\theta)$, $g(r)$, $F(r,\theta)$ are source-specific parameters taken from Karaiskos, Angelopoulos et al. (2003).

The calculated dose was compared with the dose reported by Plato under the same conditions using a CT scan of the phantom setup and a single dwell position calculation at the date and time of the exposure.

Plato BPS is in full compliance with the TG43 protocol in its dose calculations, therefore, this procedure was designed to verify via a spot check that the source data had been entered into the planning system correctly for the source and detector orientations used in this project. The TG43 protocol has a high level of accuracy for
the sources used in PDR and HDR brachytherapy. The most uncertainty occurs close to the source where there may be significant contribution of dose from electrons from the core and source capsule. Tissue heterogeneities are also not covered by the TG43 protocol (Meigooni & Wallace, 2005). These uncertainties were irrelevant to this project as all measurements were done in a homogeneous medium (solid water) and at distances from the source beyond the level of electron contamination.

Control measurements were taken on the linear accelerator (photon energy = 6 MV) using the setup outlined in Section 4.2.2. Four rods were exposed to each of the following doses: 0.2 Gy, 0.5 Gy, 1.0 Gy and 2.0 Gy. The reading from each of these linear accelerator-exposed TLDs was divided by its individual sensitivity factor, and the average of the four rods taken to obtain a control reading for each of those doses.

The readings from the Ir-192 exposed TLDs were divided by their individual sensitivity factors, and then divided by the control reading closest to their expected dose according to the TG43 calculations as per Equation 4.3. This gave a measured dose result, however did not include any correction for the different energy of the Ir-192 source used for the distance measurements compared with the 6 MV photon beam from the linear accelerator used for the control measurements.

\[
Dose = \frac{R}{SF \times Control}
\]

\textbf{Equation 4.3}

Where R = raw TLD reading, SF = Sensitivity Factor, and Control = reading from linac exposure divided by the known dose delivered on the linac.

To determine if there was any significant energy change with depth as the radiation passed through the solid water, a power fit to the measured data was completed, and an inverse square law fit was placed on the data corrected only for individual chip sensitivity. This was normalised to 4 cm depth as the gradient of the depth dose curve at this depth is small. The difference between the curves at the smallest measured depth was analysed using the equations of the trend line curves as derived in Microsoft Excel.
4.2.6 Iridium-192 Exposures (Doses similar to those delivered in prostate treatments)

On confirmation that the TG43 dose calculation matched the Plato reported dose, and therefore confidence that the parameters used in the manual calculation were correct, TG43 was again used to calculate the time required to deliver a dose expected in a prostate treatment.

For the in vivo dosimetry measurements, the spare needles where the TLDs may be placed are typically within the prostate volume. Therefore the dose expected would be around 100% to 200% of the prescribed dose. At St George Hospital, the standard prescribed dose for a single brachytherapy fraction at the time the patients involved in the imaging component of this project were treated was 6.5 Gy, therefore the time to deliver 13 Gy (200% of the prescribed dose) to a TLD placed at 1.2 cm from the source was calculated using TG43 formalism by rearrangement of Equation 4.2. The doses delivered to TLD positions at 1.6 cm and 2.0 cm, 2.4 cm and 2.8 cm in the time calculated above were also calculated by using Equation 4.2. The same treatment and measurement procedure as outlined in Section 4.2.5 was used, however the doses delivered to the control TLDs were different to account for the increased dose overall. The doses delivered to the control TLDs were 2.4 Gy, 3.3 Gy, 4.7 Gy, 7.3 Gy and 13 Gy to match closely with the doses expected on the TLDs from the Ir-192 exposure (based on TG43 calculations). The first Ir-192 measurement was only undertaken at three positions (1.2, 1.6 and 2.0 cm). All subsequent measurements were undertaken at all five positions listed above. A total of nine sets of measurements were taken.

The first two sets of TLDs exposed to these high doses of Ir-192 radiation were re-read twice following the initial reading to ensure the total charge received on the first readout was representing the full dose delivered. The re-read doses were analysed as a percentage of the dose reported in the first readout.

4.2.7 Energy conversion factor (ECF)

The ECF was derived to account for the differences between the radiation spectrum of a 6 MV beam from a linear accelerator used for control measurements, and the spectrum of the radiation emitted by the Ir-192 source. It cannot be assumed that the response of the TLDs to both spectra will be equivalent.
The method for determining an ECF was based on the LiF:Mg,Ti TLDs having well defined properties when exposed under a 6 MV photon beam from a linear accelerator (Kron 1994). This implies that a known dose delivered to these TLDs using a 6 MV linear accelerator will be measured accurately and reliably.

Calculating the expected dose from an Ir-192 source at a point using the TG43 formalism has also been shown to give accurate dosimetric results (Nath, Anderson et al. 1995; Rivard, Coursey et al. 2004).

The calculated doses using the TG43 formalism were divided by the measured doses from the TLDs exposed to Ir-192 in Section 4.2.6 to obtain the ECF. This procedure was carried out for all nine sets of results and the reproducibility of this factor calculated to determine if this was an appropriate method for converting the TLD reading to dose. The results were analysed by plotting the calculated ECFs with errors based on standard deviations.

Investigations were also undertaken to determine if the ECFs were dependent on the quantity of dose delivered and the annealing process. To determine if the ECF was dependent on the quantity of dose delivered, the average results for each TLD location were plotted. To determine if the ECF was dependent on the annealing process, the last three of the nine sets of results were all annealed at the same time and plotted against the average data from all nine sets, giving an assessment of the effect of variations in the oven temperature as a potential source of error.

4.2.8 Method to determine Ir-192 doses - theoretical

If these TLDs were deemed accurate and reproducible for *in vivo* dosimetry using the methods described, the combination of the factors derived in Sections 4.2.4 and 4.2.7 could be used to determine the dose read from TLDs exposed to Ir-192 sources. Equation 4.4 summarises the method to determine the measured dose:

\[
Dose = \frac{R \times ECF}{SF \times Control} \quad \text{Equation 4.4}
\]

Where \( R \) = raw TLD reading, \( ECF \) = Energy Correction Factor, \( SF \) = Sensitivity Factor, and \( Control \) = reading from linac exposure divided by the known dose delivered on the linac.
4.2.9 *In vivo measurements - theoretical*

In order to use these TLDs for *in vivo* dose measurements, the rods would be placed inside a four French (1.33 mm outer diameter) round ended OncoSmart ProGuide needle. The 1 mm diameter TLD rod slides into this size needle smoothly but would need to be held in place with a form of plunger to prevent TLD movement within the needle. The four French needle fits snugly inside the six French needle implanted into the patient. This would allow for dose measurement in the spare needles that would be implanted as described in Section 3.2.4.3. This method is theoretical only and will not be attempted as a part of this project. However it may be applied as a follow-up to this project based on the phantom study results presented.
4.3 Results and Discussion

4.3.1 TLD Oven Readings

The accuracy of the temperature of the annealing oven (Section 4.1.2) was investigated. The results showed that the oven was consistently hotter than the oven’s thermostat was reporting. The temperature in the body of the oven was also significantly hotter than the temperature at the thermostat location. Figure 4.9 displays the results of these measurements in the body of the oven and at a position near the thermostat location. The error bars represent ± one standard deviation from the mean result.

![Figure 4.9: TLD annealing oven temperature checks: temperature in the body of the oven (green) and temperature near the thermostat (blue).](image)

This shows that the oven thermostat is reading up to almost 85°C below the actual temperature in the body of the oven at the maximum pre-exposure anneal temperature (defined as 400°C). The oven temperature is not reported accurately by the oven’s thermostat. Reproducibility was found to be within ±15°C at 100°C, and ±5°C at 400°C. These results would not be expected to affect the readings from TLDs annealed at different times significantly; however this may cause some of the error noted in the following results, as outlined in Section 2.3.1.2.4.
4.3.2 Reproducibility

The mean and standard deviation of the relative response for each chip in Set 1 over 12 readings are shown in Figure 4.10 below.

![Figure 4.10 Relative reproducibility (Set 1). Error bars represent one standard deviation from the mean of 12 measurements.](image)

The maximum standard deviation for any one rod was 0.014. It was assumed that Set 2 has similar characteristics to Set 1 as all of the TLDs came from the same batch.

The error bars in Figure 4.10 represent ± one standard deviation from the mean based on 12 readings for each TLD rod. The TLDs display promising relative reproducibility under a 6 MV photon beam from a linear accelerator, comparable to results presented by Kirby, Hanson et al. (1992) who found that with a reproducibility of 1.5% (1 SD), an overall dose uncertainty of 2% (1 SD) could be achieved.

As this data is for twelve separate measurements, the results show that reproducibility is not significantly compromised by the annealing temperature being higher than expected, and therefore is not expected to have a significant effect on the measurements presented in this thesis.

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4.3.3 Sensitivity Factors

Figure 4.11 below is a plot of the average sensitivity factors of Set 2 and the error bars represent ± one standard deviation from the mean. The downward trend of the data is due to the initial sorting of the TLD rods based on their sensitivity factors from the first set of measurements. The results presented here do not include these first results but the average of three sets of results taken subsequently.

![Figure 4.11](image)

**Figure 4.11 Average Sensitivity Factors (Set 2). Error bars represent one standard deviation from the mean of three measurements.**

These results show that the sensitivity factors are reproducible for each TLD rod. By using the average of the three readings in subsequent applications of this correction factor, we are further minimising the error caused by the variability in the sensitivity of each rod.

This Sr-90 source could be used to expose control TLDs in a similar method to that used with the 6 MV exposed TLDs in this project; however exposure of the control TLDs to doses expected within the prostate would take several weeks. Exposing control TLDs to lower doses would introduce supralinearity effects, therefore it was
deemed more appropriate to investigate control exposure on a 6 MV linear accelerator.

4.3.4 Ir-192 Exposures (Initial Tests)
The results of the initial Ir-192 exposures and comparison with TG43 calculations and Plato BPS doses are listed in Table 4.1. The equation used in the TG43 formalism is shown in Section 4.2.5 (Equation 4.2). The doses calculated by Plato BPS match closely with those calculated using TG43 as expected. The slight differences are most likely due to the inherent error in placing the points accurately in Plato BPS. This verifies that the TG43 calculations have been applied correctly and also that Plato BPS can be relied upon to provide accurate dosimetric results based on the latest literature available on brachytherapy dosimetry, particularly for simple cases.

Table 4.1 Comparison of TG43 and Plato BPS dose calculations at fixed distances from the Ir-192 source.

<table>
<thead>
<tr>
<th>Distance from Source (cm)</th>
<th>Calculated Dose (TG43) (Gy)</th>
<th>Calculated Dose (Plato BPS) (Gy)</th>
<th>Difference (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2</td>
<td>1.5039</td>
<td>1.4919</td>
<td>0.0120</td>
</tr>
<tr>
<td>2.0</td>
<td>0.5435</td>
<td>0.5454</td>
<td>0.0019</td>
</tr>
<tr>
<td>3.2</td>
<td>0.2140</td>
<td>0.2136</td>
<td>0.0004</td>
</tr>
<tr>
<td>4.0</td>
<td>0.1361</td>
<td>0.1365</td>
<td>-0.0004</td>
</tr>
</tbody>
</table>

Figure 4.12 is an average plot of the corrected TLD results (raw reading corrected for sensitivity) from the exposures outlined in Section 4.2.5. The error bars are displayed as ±5% which is a typical expected maximum error for LiF:Mg,Ti readings (Kron 1994). The blue curve is a fit to the data, showing almost an inverse square dependence. The orange curve is an inverse square trendline normalised to the measured data at 4 cm depth where the gradient of the depth dose curve is small and positional accuracy will not play a significant role in dose accuracy. The discrepancy between the two curves at the measurement position closest to the Ir-192 source is 0.5 mm, which is smaller than the diameter of the TLD rod. This is not entirely unexpected as the dose gradient close to the source is very steep and slight errors in positioning of the TLDs may result in large differences in the dose. This plot
indicates that there is no significant effect on measured dose other than the inverse square law in the plane perpendicular to the source over distances similar to those expected in prostate treatments. The air gaps in the solid water phantom also do not appear to produce any significant differences in dose to the TLDs. Therefore this phantom appears to be viable for relative dosimetry measurements using an Ir-192 source.

Figure 4.12 Inverse square fit of TLD data measured in solid water phantom. Blue line is a fit to the measured data. Orange line is an inverse square fit normalised to depth 4 cm. Equations for each trendline are presented on the graph.

4.3.5 Ir-192 Exposures (Doses similar to those delivered in prostate treatments)
The methods for this part of the project are outlined in Section 4.2.6. A sample representation of the detailed results of the measurements is presented in Table 4.2. This is a sample only for one set of data. The other calculations were completed identically, with the necessary corrections for source decay based on the time of exposure.
Table 4.2 Calculation of energy conversion factors (ECF) – sample calculation

<table>
<thead>
<tr>
<th>Linear Accelerator Control Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose (cGy)</td>
</tr>
<tr>
<td>------------</td>
</tr>
<tr>
<td>1300</td>
</tr>
<tr>
<td>730</td>
</tr>
<tr>
<td>470</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ir-192 Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance from Source (cm)</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>1.2</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1.6</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>2.0</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Figure 4.13 is a plot of the average conversion factors for the individual measurement dates. The error bars represent ± one standard deviation from the mean. The results range from 0.863 to 0.917 with an average of 0.891 (with one standard deviation of 0.02). This represents acceptable reproducibility of the conversion factor.

There appears to be minimal dependence of the conversion factor on the dose as shown in Table 4.3 and Figure 4.14. Table 4.3 is a summary of the results and shows the average conversion factor from all nine measurements separated into their dose groups (or distance from the source).
Figure 4.13 Average energy conversion factors for each separate Ir-192 exposure

Figure 4.14 is a plot of the average conversion factors for each distance from the source. The standard deviation of the nine results is small, indicating that the reproducibility of results using the TLDs for Ir-192 dose measurements under these conditions is suitable for \textit{in vivo} dosimetry. The error bars on this plot represent \(\pm\) one standard deviation from the mean. At the position closest to the Ir-192 source, the factor was calculated to be higher than at other positions. This is likely to be due to the steep dose gradient at this proximity to the source, resulting in a difference between the measured and calculated doses.

Figure 4.14 Average conversion factors for using 6MV linear accelerator control TLDs with Ir-192 measurement TLDs
Table 4.3 Conversion factors for using 6MV linear accelerator control TLDs with Ir-192 measurement TLDs

<table>
<thead>
<tr>
<th>Distance from Source (cm)</th>
<th>Control Dose (cGy)</th>
<th>21-Jan</th>
<th>11-Feb</th>
<th>11-Feb</th>
<th>3-Mar</th>
<th>3-Mar</th>
<th>10-Mar</th>
<th>31-Mar</th>
<th>31-Mar</th>
<th>31-Mar</th>
<th>Average Conversion Factor</th>
<th>SD</th>
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<td>0.951</td>
<td>0.969</td>
<td>0.886</td>
<td>0.908</td>
<td>0.929</td>
<td>0.876</td>
<td>0.871</td>
<td>0.882</td>
<td>0.921</td>
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<td></td>
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<td>1.6</td>
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<td>0.862</td>
<td>0.831</td>
<td>0.861</td>
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<td>0.886</td>
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<td>0.851</td>
<td>0.832</td>
<td>0.861</td>
<td>0.872</td>
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<td>0.884</td>
<td>0.923</td>
<td>0.876</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The first re-read of the Ir-192 exposed TLDs gave an average of 0.18% of the dose in the first readout. The second re-read gave an average of 0.07%. This showed that almost all of the electrons trapped in the impurities of the crystal were released from the traps and included in the first readout. The extra dose obtained from the re-read is insignificant compared to the expected errors from these measurements. It is therefore not necessary to repeat the readout.

As a further investigation, the last three of the nine results were all completed with the entire tray of TLDs placed into the annealing oven at the same time. The TLDs therefore received exactly the same pre-exposure and pre-read anneal temperatures, and the three Ir-192 exposures were analysed using the same set of linear accelerator exposed control TLDs. The results are displayed below in Figure 4.15.

![Figure 4.15 Conversion factors for entire TLD set annealed together (3 readings – yellow series) and overall results for all nine readings (blue series).](image)

The results for the single anneal process for all three exposures follows the same pattern on average as the overall data. There is no significant benefit in annealing the control and measurement TLDs at the same time as slight variations in the oven’s temperature control do not appear to have a significant effect on the results.
From these results, the average ECF was calculated to be 0.891. This average was calculated including the measurement point closest to the Ir-192 source, as clinical measurement situations may result in the TLD being placed this close to a source position. This factor could be applied to the raw doses measured from the Ir-192 exposures to give \textit{in vivo} dosimetry results. This corresponds to an over-response of the TLDs at Ir-192 energies of approximately 11% - a significantly greater difference than that reported by Williamson and Rivard (2005) of approximately 4%. The additional error introduced into the \textit{in vivo} measurement by using this factor is ±2% (for one standard deviation). As current techniques for external beam TLD measurements can give results in the therapeutic range with accuracies up to ±2% (Kron 1994), the expected error in HDR TLD measurements would be in the order of ±4%.

Further investigations to pursue the use of LiF:Mg,Ti TLDs for HDR and PDR prostate brachytherapy \textit{in vivo} dosimetry could involve the use of the Ir-192 source as the control measurements. The main disadvantage of this method is that it uses the same source for calibration as is used for the \textit{in vivo} dose measurements. Although this method of using the same radiation source for control measurement and dose delivery is used for external beam \textit{in vivo} dose measurements, the LiF:Mg,Ti TLDs are well established in this area, whereas their properties are less certain at Ir-192 energies. This method could be useful for detection of deviation in dose delivered compared with planned dose, however it does not provide an independent check that the source calibration is correctly entered into the planning system.
Chapter 5: Conclusions

The aim of this thesis was to investigate potential improvements on two areas in HDR and PDR prostate brachytherapy - the definition of the prostate and treatment delivery verification.

The results of the study into the use of MRI for improving the definition of the prostate showed similar trends to the literature in that the CT volume was larger than the MR volume of the prostate. The results did not give conclusive evidence that the use of MR imaging improved the consistency between Oncologists in defining the prostate.

Since the MR images define the prostate to be smaller than that defined with CT images, MRI may have a place in prostate brachytherapy to reduce the dose to normal tissue surrounding the prostate. This statement assumes that the prostate volume delineated using the MR images is more accurate than that generated using CT images. The use of MR could therefore result in more conformal coverage of the target volume without compromising the surrounding critical structures.

Extension of the study to a much larger study incorporating more patients and in particular more Oncologists to delineate the structures on the different modalities would give a more statistically rigorous set of results. At the time of publication of this thesis, plans for this extended study have begun at St George and Liverpool Hospitals.

LiF:Mg,Ti TLDs have been shown in this thesis to have acceptable accuracy when measuring radiation dose from an Ir-192 source. An energy conversion factor to allow the use of control TLDs exposed to 6 MV radiation from a linear accelerator has been derived empirically and shown to be effective. This could in principle be applied to in vivo dose measurements to verify the dose delivered to the patient. Phantom results indicate the accuracy of such measurements is achievable to within ±4% using existing systems at St George Hospital.
Further investigation is required to verify if this technique gives accurate results under the less structured setup inherent with *in vivo* measurements. It is also recommended that the conversion factor be verified for individual centres based on the linear accelerator calibration beam that the control TLDs are exposed to.

The recommended *in vivo* trial is under consideration for 2009 following local ethics committee approval at St George Hospital.
Appendix A: Glossary

All terms in the glossary, unless otherwise stated, were defined with the assistance of Wikipedia (http://www.wikipedia.org).

Anisotropy – describes the directional dependence of the source. Simple dose models assume point-source geometry, however the design of the source is such that it does not emit a spherical radiation distribution, but is influenced by the length of the source and the positioning of the cable to which the source is attached. The anisotropy function describes the variation in dose as a function of the polar angle relative to the transverse plane of the source (Rivard, Coursey et al. 2004).

Brachytherapy – a form of radiotherapy where a radioactive source is placed inside or next to the area requiring treatment. From the Greek brachy meaning “short”.

Intensity-modulated radiation therapy (IMRT) – an advanced type of radiotherapy using dynamic multi-leaf collimators on a linear accelerator to optimise the dose delivery to the target tissue, minimising dose to the surrounding normal tissue and critical structures.

High Dose Rate (HDR) – defined in brachytherapy as a dose rate of 12 Gy per hour or greater (Nath 2005).

Linear Accelerator – an electrical device for the acceleration of subatomic particles. Used in a hospital environment to accelerate electrons to produce high energy photon or electron beams for external beam radiotherapy.

Lithotomy – a common position for surgical procedures involving the pelvis and lower abdomen. The patient is lain on the back with knees bent, positioned above the hips and spread apart through the use of stirrups.

Low Dose Rate (LDR) – defined in brachytherapy as a dose rate from 0.4 to 2 Gy per hour (Nath 2005).
**Patient Points** – points placed on the treatment plan. The planning system reports the dose delivered to each of these points. They can also be used as prescription points or dose optimisation points within the Plato Brachytherapy planning system.

**Peripheral Zone** – the region of the prostate to which the dose coverage should be optimal. It is typically a horseshoe shape following the outline of the prostate, but cutting in around the urethra. This is a slightly modified definition compared to the standard definition of peripheral zone, which is the sub-capsular portion of the posterior aspect of the prostate gland surrounding the distal urethra. It is from this region that 70% of prostatic cancers originate.

**Proctitis** – a potential side-effect of prostate brachytherapy if the dose to the rectum is excessive. It is an inflammation of the anus and lining of the rectum, causing diarrhoea and rectal bleeding amongst other symptoms.

**Pulsed Dose Rate (PDR)** – usually a medium dose rate source (medium dose rate is defined as 2 to 12 Gy per hour) (Nath 2005), used in a pulsed manner (for example one short pulse every hour) to achieve a similar treatment outcome to LDR brachytherapy.

**Toxicity** – the damage caused by ionising radiation to tissue.

**Radial Dose Function** – a parameter used to account for dose fall-off on the transverse plane of the source due to photon scattering and attenuation. It can also be influenced by filtration of photons by the encapsulation of the source and the source materials themselves (Nath, Anderson *et al.* 1995).

**Remote afterloading device** – a treatment machine containing a radioactive source that is inserted and retracted from the applicators in the patient by a computer-controlled mechanism. Remote afterloaders prevent high doses to staff as they are operated from outside of the treatment room, behind shielding.
**TE Echo time** – the time in milliseconds between the application of the 90º pulse and the peak of the echo signal in Spin Echo and Inversion Recovery pulses in MRI (FONAR 2003).

**TR Repetition time** – a parameter used in MRI to define the amount of time between successive pulse sequences applied to the same slice. Variations in this parameter control the image contrast characteristics (FONAR 2003).

**Urethral stricture** – a potential side effect of prostate brachytherapy if the dose to the urethra is excessive. It is a narrowing of the urethra causing side effects such as decreased force of urinary stream, incomplete bladder emptying, urinary terminal dribbling, increased frequency and acute or chronic retention of urine.
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