In-vivo real-time dosimetric verification in high dose rate prostate brachytherapy

Erin Redfearn

University of Wollongong

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IN-VIVO REAL-TIME DOSIMETRIC VERIFICATION IN HIGH DOSE RATE PROSTATE BRACHYTHERAPY

by

Erin Redfearn, BSc (Hons)

A thesis submitted in fulfilment of the requirements for the award of Master of Science – Research from the School of Engineering Physics at the University of Wollongong

2010
CERTIFICATION

I, Erin Redfearn, declare that this thesis, submitted in fulfilment for the award of Master of Science – Research, from the School of Engineering Physics, University of Wollongong, is wholly my own work unless otherwise referenced or acknowledged. The document has not been submitted for qualifications at any other academic institution.

Erin Redfearn

9th August 2010
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Without the support of the staff in the Oncology Department at the Mater Hospital, Crows Nest, this project would not have been possible, especially Oncologists Michael Izard and Gerald Fogarty, who provided the patients as well as valuable expertise. I would also like to give special mention to Jason Bonifacio who was the work horse of the Brachytherapy unit, always ensuring that procedures ran smoothly as well as assisting in patient data collection.

I would also like to thank Kym Nitschke for providing me with the time to write this thesis. Without his support my research would probably still only exist in messy excel sheets, with the final product far from completion.

Without the love and support of my family I would not be where I am today. Mum and Dad, thanks for always believing in me and allowing me to pursue any endeavour that I wished, no matter how foreign to you both. Lastly, I would like to thank my wonderful fiancé Dane, who has had to sit through years of disgusting theatre stories he probably wishes he hadn’t, but has always remained interested and supportive of my work. Thank you so much.
ABSTRACT

High Dose Rate Brachytherapy is a common modality used in the treatment of intermediate to high risk prostate cancers. Currently, no real-time quality assurance technique is widely used to accurately verify the doses delivered during treatment. In many centres more than one treatment is delivered over a 24 hour time interval with the implant in place. During the time between these fractions the prostate may swell due to the trauma from the needles and the needles may move relative to the prostate.

The main aims of this project are: to determine the characteristics of a commercially available semiconductor diode array and assess whether dose verification is possible on a routine basis; to assess whether prostate oedema significantly effects dose volume histogram statistics for subsequent fractions when the plan generated at the time of the initial procedure is used for subsequent fractions; and to determine whether oedema is the dominant cause of catheter movements required to reposition the implant with respect to the prostate for subsequent fractions.

The diodes’ dosimetric properties studied included linearity, reproducibility, directional dependence, dose rate dependence and temperature dependence. Linearity and reproducibility were compared to ion chamber measurements while the other characteristics were compared with published data.

The dosimetric study involved 28 patients who were treated at the Mater Hospital in Crows Nest during 2007 and 2008. The patients were all treated in the lithotomy position incorporating a plan developed on a real time planning system based upon ultrasound imaging. As they were treated in this position, a replica of the ultrasound probe, utilised for implantation and imaging, was developed in which the diode array could be placed for the duration of treatment. The position of the diodes inside the replica probe relative to the implant was determined using fluoroscopy so that dosimetric comparisons between the diodes and corresponding positions in the planning system could be made. Ultrasound images taken before each treatment fraction were used to determine the extent of oedema during the course of treatment.
Based upon the measurements examining the diode characteristics and physical set up uncertainty, the overall uncertainty in the patient dosimetric results was determined to be ±10%, which is comparable to published data. Of the patient data points compared, 72% showed agreement within this uncertainty. If this was extended to ±20%, assuming measurement uncertainty of ±10% and dose discrepancy of ±10%, then over 95% of the diode results exhibited agreement with the calculated data. A study of the 15 patients studied volumetrically indicated that the mobility of the prostate was patient specific and not dependent upon oedema present, and that the changes in volume that occur during the course of treatment do not significantly effect patient outcomes if the treatment used for the initial fraction is applied to subsequent fractions.

An in-vivo dosimetry program employing a commercial semiconductor diode array could be used to detect gross errors in the delivery of high dose rate prostate brachytherapy as long as the limitations of the device are well understood and the facility has the resources to incorporate such a program.
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Chapter 1 : Introduction and Literature Review

1.1 Project Research Questions

- Can semiconductor diodes be used to accurately verify point doses received to a phantom placed inside the rectum during High Dose Rate Brachytherapy (HDRB) treatment for prostate cancer?
- Does swelling of the prostate gland during the course of treatment, and therefore a possible change in needle positions relative to each other, significantly effect the dose volume histogram (DVH) statistics for subsequent fractions when the plan generated during the initial procedure at fraction one is used for fractions two and three?
- Are the catheter moves required for subsequent fractions linked to the degree of swelling in the prostate gland?

1.2 Project Aims

- Determine the characteristics of a commercially available diode array and assess whether dose verification for prostate HDRB procedures is possible on a routine basis.
- Undertake a study on a cohort of patients which incorporates rectal dosimetry and imaging for each of the three fractions delivered over a 24-30 hour period.
- Analyse needle positions using planning software and mathematical tools to determine oedema present in the base, mid and apex of the prostate gland and relate any changes to differences in implant DVH statistics.
- Assess whether oedema present is the dominant cause of catheter movements during patient treatments.
1.3 Introduction

1.3.1 Overview
Prostate cancer is one of the most prevalent forms of cancer for males in the western world. The Australian Institute of Health and Welfare (AIHW) has published Australian Cancer Incidence and Mortality (ACIM) workbooks, updated in 2009, with detailed information relating to cancer incidence rates from 1982 to 2006 and mortality rates from 1968 to 2006. In 2006, 17444 new cases of prostate cancer were diagnosed in Australian males, accounting for 29.5% of male cancers and 16.7% of cancer in the overall population, making it the most prevalent form of cancer affecting Australians.\(^1\)

The mean age of prostate cancer incidence is 68.9 years with males having a 1 in 7 risk up to the age of 75, increasing to a 1 in 5 risk by the time they are 85 years of age. Incidence rates have dramatically risen in the past 15 years, driven by more men having the Prostate Specific Androgen (PSA) test, which, at elevated levels, is an indicator of prostate cancer. In NSW, five year survival is 88% which is increased to 97% if the cancer is detected early and localised at diagnosis.\(^2\)

Treatment options depend upon the extent of disease and can include radical prostatectomy, conformal external beam radiotherapy (EBRT), intensity modulated radiotherapy, interstitial brachytherapy or a combination of the two. Brachytherapy treatments are best suited for patients with localised disease and can be applied in the form of a low dose rate (LDR) permanent seed implant or a high dose rate (HDR) temporary implant. LDR monotherapy is generally restricted to patients with initial PSA <10ng/mL, stage T1b – T2a and Gleason score < 6 but can be used in selected higher grade cases.\(^3\) HDR temporary implants can be utilised in conjunction with EBRT to treat patients with intermediate to high risk localised cancers that do not have any distant metastases.\(^4\)

Justification for dose escalation in prostate radiotherapy has been shown in numerous randomised studies.\(^5,6,7\) From 1993 to 1998 a total of 301 patients with stage T1b to T3 prostate cancer were accrued for a randomised radiotherapy dose escalation trial for prostate cancer at the University of Texas M. D. Anderson Cancer Centre. The long term results were published by Kuban \textit{et al}\(^5\) where all patients had follow up data ranging from 8-12 years. The trial was opened to test the hypothesis that 78Gy
compared with 70Gy would result in an absolute increase in freedom from failure (FFF), including biochemical failure, of 15% for patients treated with definitive external beam radiation for prostate cancer.

Patients were divided based on their pre-treatment PSA level: PSA <10 ng/mL; >10 to 20 ng/mL; and >20 ng/mL. Risk groups were defined as low risk, stage <T2a and Gleason score ≤6 and PSA ≤10 ng/mL; high risk, stage T3 or Gleason score ≥8 or PSA >20 ng/mL; and intermediate risk, all others. They determined that freedom from biochemical or clinical failure was significantly different for patients treated with 78Gy versus 70Gy with the difference between the two study arms increasing with time being 85% vs. 78% at 5 years, 78% vs. 59% at 8 years, and 73% vs. 50% at 10 years. It was also determined that patients with an initial PSA of >10 ng/mL experienced the greatest effect from dose escalation with 78% vs. 39% FFF at 8 years.

Late bladder and rectal toxicity were graded using the Radiation Therapy Oncology Group (RTOG) and Late Effects Normal Tissue Task Force scales with those receiving 78Gy experiencing significantly greater gastrointestinal toxicity of grade 2 or greater, 26% vs. 13%. They concluded with long term follow up that dose escalation in patients with localized prostate cancer is beneficial, with the greatest advantage shown to be in those patients with initial PSA >10ng/mL. Consequently, rectal complication rates also increase if an adjustment is not made to dose-volume constraints.

Similar differences in disease free survival results and complications with higher dose regimes were presented by Zietman et al. They presented a randomised study comparing 70.2Gy and 79.2Gy and recorded a 19% (61% vs. 80%) absolute difference in PSA disease free survival at 5 years using the ASTRO definition and a doubling (17% vs. 8%) of late grade 2 GI morbidity in patients treated to the higher dose level.

Dose escalation using conformal HDRB was presented by Martinez et al to test the hypothesis that local failure for patients with prostate cancer harbouring large volume disease is related to both large cell mass and radioresistant cell clones, which require biologically higher radiation doses than conventionally delivered with EBRT. A cohort of 207 patients with unfavourable and/or large volume prostatic adenocarcinoma were studied who had either an initial PSA level ≥10ng/mL, Gleason score ≥7, or a clinical
stage T2b or higher. The treatments consisted of 46 Gy in 23 fractions of EBRT using a four field technique in combination with either 2 or 3 brachytherapy boost doses of 5.5-11.5 Gy/fraction over 5 weeks. Patients were divided into 2 levels, those treated with a low biologically effective dose (BED) <93Gy (58 patients) and those taken to a higher BED >93Gy.

The 5 year biochemical control rates for the low and high dose groups were 52% and 87% respectively with an improvement also seen in cause specific survival. Based on multi-variate analysis they determined that a lower brachytherapy dose, higher Gleason score and higher PSA nadir value were associated with biochemical failure. Their toxicity study was based on RTOG specifications with 8% of patients experiencing Grade 3 urinary complications after 5 years, 0.5% of patients having Grade 3 and 0.5% with Grade 4 gastrointestinal complications. It was concluded that there is an incremental beneficial effect on biological control and cause specific survival with brachytherapy high dose escalation which is in agreement with the original hypothesis.

A comparison of HDRB and different regimes of IMRT as a boost to the prostate were determined for 10 patients by Hermesse et al. The patients were treated with 60Gy EBRT before receiving a single 10Gy HDRB boost. Four separate IMRT plans were determined retrospectively for each patient consisting of 32.85Gy and 26Gy with and without margins around the CTV. Dose normalisation to obtain 95% coverage of the PTV was used to compare treatment plans, and the DVH parameters were converted to 2Gy equivalent doses (EQD2). An alpha beta ratio of 1.5Gy was assumed for the prostate and 3Gy for the urethra, rectum and bladder. They determined that the HDRB plans delivered a higher mean dose to the PTV compared with the IMRT plans and a lower mean dose to critical structures even when no margins were placed. Quantitatively, mean rectal doses for HDRB and IMRT were 5.32 ± 0.65 Gy and 13.4 ± 1.49 Gy with 20% bladder volumes receiving 4.61 ± 1.24 Gy and 10.81 ± 4 Gy respectively. They determined that because of the better sparing of the organs at risk, dose escalation to the prostate is more easily achievable with HDRB as more conformal plans can be produced.

All external beam techniques deliver a significant amount of radiation dose to the critical structures that surround the prostate unless sophisticated techniques are used to
limit the volume of the critical tissues irradiated. A combination of EBRT and HDRB is a method which delivers a high dose radiation to the target, while simultaneously limiting the dose to surrounding normal structures. This treatment results in excellent 5 year biochemical control, cause specific survival and overall survival rates, especially in the intermediate and high risk groups and achieves these control rates with low morbidity.\(^9\)

Brenner et al\(^{10}\) has suggested that the \(\alpha/\beta\) ratio for the prostate is as low as 1.2Gy which is comparable to adjacent late responding normal tissues indicating that prostate cancers may be significantly more sensitive to larger fraction sizes than most other tumours. This is comparable with other published data\(^ {11, 12}\) and suggests that a HDR brachytherapy boost in conjunction with fractionated EBRT offers the potential for better local tumour control rates than conventional EBRT alone as larger fraction sizes will exploit this radiobiologic advantage and achieve biologic dose escalation for immediate and high risk groups.

The main advantage of brachytherapy over external beam radiotherapy is the ability to deliver a high amount of dose to a target by inserting a radioactive source directly into the target volume.\(^{13}\) The dominant dosimetric effect that occurs with brachytherapy sources is inverse square fall-off,\(^ {14}\) where, in clinical situations, a high dose is deposited close to the source inside the tumour volume, with the dose received by surrounding critical structures reduced due to the increased distance from the source. The theory behind the inverse square fall-off involves an isotropic emitting point source surrounded by a spherical surface in a vacuum and is shown schematically in Figure 1-1.\(^ {15}\) The intensity \((I)\) at the surface of the sphere is proportional to the inverse square of its distance, \(r\):

\[
I = \frac{\text{Source strength}}{\text{Area irradiated}} = \frac{S}{4\pi r^2}
\]  

\textbf{1-1}
The absorbed doses \((D_1)\) and \((D_2)\) at distances \(r\) and \(2r\) are related geometrically by:

\[
\frac{(D_1)}{(D_2)} = \left(\frac{2r}{r}\right)^2
\]

This theory applies to each radioactive point in a source and is purely a geometric representation that does not take into account any attenuation in a medium.

### 1.3.2 Brachytherapy for treatment of prostate cancer

In 2004 GEC/ESTRO-EAU released recommendations for template and transrectal ultrasound (TRUS) guided transperineal temporary interstitial prostate brachytherapy using a high dose rate iridium-192 stepping source and remote afterloading technique. They listed the advantages of the treatment as the ability to accurately position the source by first implanting non-active guide needles, the possibility to choose the source positions over the length of the needle, no movement of the target during irradiation, and stepping source technology which allows for dose and volume adaptation due to adjustment of source dwell locations and times according to 3D imaging based individual dose prescription before irradiation. The main disadvantage of temporary brachytherapy implants was stated as the fractionated schedule required which results in more workload per patient.

There is wide consensus that TRUS guided template implant techniques represent the standard of interstitial prostate brachytherapy, with accurate needle placement, as
excellent dose distributions and anatomy related dose optimisation has been seen in patients who fit the selection criteria.

The prognostic factors which have the highest impact on disease free survival are the initial PSA, Gleason score and stage. Reasons for exclusion from HDRB treatment include a prostate volume >60cm$^3$, extensive transurethral resection of the prostate (TURP) defect or TURP within 6 months, infiltration of the external sphincter of the bladder neck, significant urinary obstructive symptoms, pubic arch interference, rectum to prostate distance on TRUS <5mm, or if positioning the patient in the lithotomy position or anaesthesia is not possible. Patient selection is therefore crucial in determining whether a particular individual will benefit from this form of treatment. Once the individual is deemed suitable for treatment the radiotherapy department has to have a clinical team as well as equipment and facilities which comply with national regulations in radiation protection for performance of temporary brachytherapy as well as access to anaesthetic and sterilisation facilities. The techniques employed by the Mater Hospital Radiation Oncology department reflect these recommendations as well as the selection criteria for curative combined temporary brachytherapy and EBRT in the treatment of intermediate to high risk prostate cancer patients.

Treatment for HDR brachytherapy is delivered using a stepping source, usually Ir-192, which is automatically advanced along the catheters which have been placed in the target. One of the greatest advantages of this treatment is the ability to optimise the dose distribution by varying the length of time that the source stays at each dwell position along the catheters. This optimisation technique allows for greater sparing of the rectum, urethra and bladder than is achievable with conformal EBRT techniques allowing adequate coverage of the target volume without exceeding the critical organ tolerances. It also allows varying dose distributions across the target enabling, for example, selective dosing of the peripheral zone or boosting of an intraprostatic lesion. Fractionation schemes vary between departments with fraction sizes generally ranging from 4-15Gy delivered in 2-4 fractions. Imaging and planning techniques also vary between departments with radiographic film, CT, ultrasound or MRI modalities currently employed. A move has also been made from traditional imaging and planning a few hours post implant to real-time techniques where imaging, treatment planning and
delivery all occur during the initial insertion with the patient under anaesthetic.\textsuperscript{13,19} This technique is dependent upon the availability of a dedicated theatre and staff.

Dose constraints exist for the organs at risk surrounding the prostate so that side effects can be kept to a minimum. Complications that can result from brachytherapy include perineal pain, urinary retention, dysuria, proctitis and cystitis in the short term and urethral strictures, incontinence, changes in potency and different grades of proctitis and cystitis in the long term\textsuperscript{4}. The Radiation Therapy Oncology Group (RTOG) and the European Organisation for Research and Treatment of Cancer (EORTC) toxicity criteria\textsuperscript{20} are used to assess the grade of side effects which are shown in Table 1.1. To potentially avoid some dose related side effects and therefore provide improved patient outcomes, verification of dose from treatment plans is suggested through an in vivo dosimetry program which verifies that the computer generated dose distributions are actually being delivered to the patient.
<table>
<thead>
<tr>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lower G.I. including pelvis</strong></td>
<td>No change</td>
<td>Increased frequency or change in quality of bowel habits not requiring medication/rectal discomfort not requiring analgesics</td>
<td>Diarrhea requiring parasympatholytic drugs (e.g., Lomotil) mucous discharge not necessitating sanitary pads; rectal or abdominal pain requiring analgesics</td>
<td>Diarrhea requiring parenteral support; severe mucous or blood discharge necessitating sanitary pads; abdominal distension (flat plate radiograph demonstrates distended bowel loops)</td>
</tr>
<tr>
<td><strong>Genitourinary</strong></td>
<td>No change</td>
<td>Frequency of urination or nocturia twice pretreatment habit;</td>
<td>Frequency of urination or nocturia less frequent than every hour;</td>
<td>Frequency with urgency and nocturia hourly or more frequently;</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>dysuria, urgency not requiring medication</td>
<td>dysuria, urgency, bladder spasm requiring local anesthetic (e.g., Pyridium)</td>
<td>dysuria, pelvis pain, or bladder spasm requiring regular, frequent narcotic; gross hematuria with/without clot passage</td>
<td>passage, ulceration, or necrosis</td>
</tr>
<tr>
<td>Small/large intestine</td>
<td>None</td>
<td>Mild diarrhea; mild cramping; bowel movement 5 times daily; slight rectal discharge or bleeding</td>
<td>Moderate diarrhea and colic; bowel movement 5 times daily; excessive rectal mucosa or intermittent bleeding</td>
<td>Obstruction or bleeding, requiring surgery</td>
</tr>
</tbody>
</table>

Table 1-1b. Continued RTOG and EORTC toxicity criteria for assessing genitourinary and gastrointestinal complications.
1.3.3 Semiconductor Physics

Properties of Silicon

Silicon is the second most abundant element on earth and compromises 25% of the Earth’s crust.\(^1\) In its purist form silicon is an intrinsic semiconductor but its electrical properties can greatly increase with the introduction of small quantities of impurities. N-type silicon is produced by introducing impurities of a pentavalent element (e.g. phosphorus), which increases the number of free donor electrons as majority carriers in the lattice. P-type silicon is produced by doping with a trivalent element (e.g. boron) which increases the number of acceptors which acts as the majority charge carrier. Diodes are produced by taking n-type or p-type silicon and counter doping the surface to produce the opposite type material. For example, an n-type diode is formed by doping acceptor impurities into a region of the n-type silicon and a p-type diode is formed by doping donor impurities into a p-type substrate.\(^2\)

\(^{1}\) These dosimetric properties

The region where the n-type and p-type materials are in direct contact is called the p-n junction. In this region the majority carriers from both materials diffuse into the other creating an electric field due to positively charged ions being left on the n-side due to electron migration and negatively charged ions on the p-side due to diffusion of acceptor ions. This area is also called the depletion region as it is depleted of charged particles and poses a barrier for current. Ionising radiation generates electron-hole pairs throughout the body of the diode. If these minority carriers are within one diffusion length from the junction they may be able to reach it before recombining and be swept across the junction due to the intrinsic electric field, which is illustrated by Figure 1-2. If electrodes are connected to either side a current can be measured with an electrometer.

Important dosimetric properties

Diodes are known to experience dose rate dependence, temperature dependence, energy dependence and directional dependence which can differ for different types of dosimeters and must be investigated thoroughly before clinical use. Due to the higher atomic number of silicon relative to tissue an enhanced response to photoelectric
components is also prominent at low energies. The sensitivity of diodes is also known to vary with accumulated dose.

![Figure 1-2. Schematics of a Silicon p-n junction diode as a radiation detector.](image)

The excess minority carriers (electron—• and hole—○) generated by radiation within one diffusion length, $L_n$ on the n side and $L_p$ on the p side (lightly shaded region), are able to diffuse to the p-n junction (width $W$). They are then swept across the junction by the built-in potential $\Psi_0$ and are collected by the electrometer.

**Mechanism of operation**

The dominant process of charge recombination in a silicon diode is indirect recombination. This occurs when a minority carrier is captured by a recombination-generation centre and recombines with a majority carrier. Indirect recombination is responsible for variation in diode sensitivity related to instantaneous dose rate. As the instantaneous dose rate increases the rate of minority carrier generation also increases. If the population of recombination-generation centres remains approximately constant during an exposure then there will be a dose rate where any further increase will cause a saturation of the recombination centres and the excess minority carriers generated will be measured by the electrometer causing the sensitivity to increase. The instantaneous dose rate changes with source to detector distance, which is variable in brachytherapy procedures, and therefore needs to be investigated prior to use.

The current measured due to radiation may either increase or decrease with temperature resulting in variation of sensitivity with temperature. Commercial diodes used for in vivo dosimetry typically have a temperature coefficient of between +0.1 and
The positive coefficient may be due to the apparent increase in carrier lifetime with an increase in temperature due to the enhanced probability of carrier release from recombination-generation centres and traps in the lattice. As the diodes in this study were inserted into the rectum a temperature change was apparent and was therefore investigated.

Energy dependence of silicon diode systems is mainly related to the materials surrounding the diode including the electrode attachment, protective housing and cables. Due to their particular construction some diode systems will measure the current caused by ionisation from electrons scattered off surrounding equipment and build up material which will be energy dependent. As the diode array utilised for this investigation was only used with the Ir-192 photon spectrum, energy dependence was not investigated.

Directional dependence is caused by a combination of diode design, detector construction and scatter conditions. As anatomy dictates the position and angle of the diodes relative to the source in this study, the angular position of the array relative to the source could not remain consistent. Due to the flat rectangular construction of the diodes used directional dependence is expected to be apparent.

Radiation causes damage to the crystal lattice of the silicon diode which includes defects, such as the production of recombination-generation centres and carrier traps. These defects cause a decrease in sensitivity due to the capture of carriers and low probability of recombination. Sensitivity variation with accumulated dose therefore needs to be monitored with diode calibration occurring periodically to counteract any changes in sensitivity.

1.3.4 Dosimetric verification
Planned dose distributions for HDR brachytherapy can differ from the doses delivered clinically. Possible reasons for this include errors in reconstruction due to the imaging resolution and errors in digitizing, implant geometry changing between imaging and treatment due to oedema or anatomical changes that may be present, accuracy of planned source dwell position and times during delivery, source transit time, source
calibration uncertainty, the accuracy of the treatment planning system algorithm in dose calculations, and others.\textsuperscript{23}

\subsection{1.3.4.1 In-vivo dosimetry}

\textit{Previous studies- various detectors}

To verify that patients are receiving the doses displayed by the treatment planning system (TPS) an in vivo dosimetry program is necessary that can be easily incorporated into daily procedures. In-vivo dosimetry for prostate and gynaec brachytherapy in the past has been performed by placing dosimetry equipment in either a needle in the prostate, a catheter in the urethra or in the rectum. Dosimeters used previously have included thermoluminescent dosimeters (TLDs), radiophotoluminescent glass dosimeters (RPLGDs), diamond detectors, semiconductors, scintillators, and metal oxide semiconductor field effect transistors (MOSFETs).\textsuperscript{23, 24, 25, 26, 27} The advantages and disadvantages of various dosimeters used for brachytherapy are presented in tables 1.2a and b.

\textit{Studies employing TLDs}

TLD dosimeters were used to measure point doses to the urethra and rectum by Das \textit{et al}.\textsuperscript{24} for 50 patients receiving a high dose rate brachytherapy boost in their treatment for prostate cancer. The dosimeters employed were LiF:Mg, Ti TLD rods which were 6mm long, 1mm diameter and spaced 10mm apart in a train. The trains were placed inside catheters in the urethra and rectum before the two orthogonal films required for treatment planning were taken in which metal spacings between the TLD rods could be identified. The treatment planning software used to optimise the dose distribution was the Nucletron PLATO Vs 13.5 and 14.1 which provided points of interest to which the TLD measurements could be compared to.

Measurements were only taken for the patients’ first fraction with a Lorentzian fit applied to produce a comparison between the measured and theoretical data sets. They found that in general there was good agreement between the measured and predicted doses for the urethral data with the average difference between the measured and planned maximum dose being 0.1Gy. The rectal measurements were more difficult to interpret due to variability of TLD position between planning and treatment. An
improved method of identifying TLD position in the rectum immediately before treatment would have had to occur to account for the movement of the catheter in the time between the CT planning and treatment stages.
Table 1-2a. Advantages of various in vivo dosimetry systems used for brachytherapy.

<table>
<thead>
<tr>
<th>TLD</th>
<th>Semiconductor</th>
<th>MOSFET</th>
<th>Diamond Detector</th>
<th>Scintillation Detector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advantages</td>
<td>- Available in various forms (powder, chips, rods, ribbons)</td>
<td>- Small in size, able to be used in steep dose gradients and small fields</td>
<td>- Excellent spatial resolution</td>
<td>- Immediate dose readout</td>
</tr>
<tr>
<td></td>
<td>- Linear response over a wide range of doses</td>
<td>- Immediate dose readout</td>
<td>- little beam perturbation</td>
<td>- Tissue equivalent</td>
</tr>
<tr>
<td></td>
<td>- Simple to use</td>
<td>- High sensitivity</td>
<td>- Immediate dose</td>
<td>- Flat energy response</td>
</tr>
<tr>
<td></td>
<td>- Good mechanical stability</td>
<td>- Good mechanical stability</td>
<td>- Small sensitive volume and physical size</td>
<td>- Waterproof</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Radiation damage resistant</td>
<td>- High sensitivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Negligible directional variation in dose response</td>
<td>- Nearly energy independent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Small in size, high spatial resolution</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Good reproducibility and long term stability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Dose rate, temperature and directional independence</td>
</tr>
</tbody>
</table>
Table 1-2b. Disadvantages of various in vivo dosimetry systems used for brachytherapy.

<table>
<thead>
<tr>
<th>TLD</th>
<th>Semiconductor</th>
<th>MOSFET</th>
<th>Diamond Detector</th>
<th>Scintillation Detector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disadvantages</td>
<td>- Incapable of instantaneous readout</td>
<td>- Require periodic calibration</td>
<td>- Requires connection to bias voltage which must remain stable to sensitivity</td>
<td>- Optical fibre required for light transmission to detector which should be removed from primary beam to prevent background signal</td>
</tr>
<tr>
<td></td>
<td>- Require time consuming pre and post irradiation annealing</td>
<td>- Energy dependent</td>
<td>- Some dose rate dependence</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Have depth dependent sensitivity</td>
<td>- Non-linear dose response</td>
<td>- Large physical size</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Require calibration at each use</td>
<td>- Limited life span</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A series of TLD cylindrical rods that were 6mm long and 1mm diameter were used by Anagnostopoulos et al\textsuperscript{23} to measure effective point doses received in 18 fractions of HDR brachytherapy in 5 patients receiving treatment for prostate cancer. A set of 14 rods were placed in a 4F catheter which was positioned within either an extra needle inserted into the prostate after consultation with the patient or the last numeric treatment catheter before the CT planning scan.

Nucletron’s PLATO treatment planning system version 14.2.2 was utilised to construct the treatment plan and select the points of interest required for comparison with the measured results. In all cases the greatest deviation observed between the measured and calculated results was for readings that occurred outside the PTV and were therefore attributed to transit dose at these points. The maximum differences observed between the measured and planned dose points for a single treatment fraction was 8.6%. Over all fractions of a patient’s treatment this average reduced to 6.9%.

The systematic uncertainties cited included defining the TLD centre as well as treatment needle positioning due to slice widths of 2.5cm being used, source positioning errors of up to 1mm for all fractions, 2-3% uncertainty in dose values acquired by the TPS for comparison with the experimental results due to the uncertainty in the air kerma strength calibration measurement, as well as the uncertainty in the AAPM TG-43 dosimetry protocol calculation factors for the source applied to the dose calculation in the treatment planning system. Statistical uncertainty related to the repeated TLD measurements and calibration was also included in the overall error determination. They concluded from their results that the differences between the calculated doses from a commercial planning system and the doses measured with TLDs were acceptable and that the delivered dose was reproducible over the course of treatment for the patients.

Toye et al\textsuperscript{26} aimed to develop an in vivo dosimetry program based investigative action level relevant for the corrective protocol for HDR brachytherapy boost treatment by examining the doses delivered across a large cohort of patients. They examined an array of TLDs measured profiles of the dose delivered along the urethral path of the prostate for 53 patients, and rectum in 31 of the same patients using a separate array of TLDs. Following the evaluation of the differences between the urethral and rectal measurements and TPS calculations with respect to the relative location of the implant
and TLD trains, a clinical protocol was proposed for routine implementation as well as recommendations for action levels. TLD in vivo dosimetry for the initial HDR fraction using LiF:Mg,Ti rods was completed as described in Das et al\textsuperscript{24}, previously mentioned. The corrective action level proposed stated that if more than 50% of the prostatic urethra received a dose greater than 10% above the urethral tolerance (120% prescribed dose) then subsequent fractions would be modified.

The difference between the peak measured and calculated TPS doses exceeding 20% was chosen as the indicator of cases requiring further investigative action due to the uncertainty in the dose difference being in the order of 10% combined with the 10% dose excess above tolerance. Eight of the cases studied showed measured doses that differed from the TPS calculated doses of more than 20% with only one of those cases exceeding the urethral tolerance level for action. The rectal dose for that patient did not however exhibit the same high reading and it was determined from the literature regarding other dose regimes employed that the dose delivered to the urethra should not cause harm.

Issues of catheter stability hampered the accuracy and precision of the rectal dosimetry measurements which were found to have significantly more variability than the urethral measurements. They stated that the in vivo technique used is sensitive to gross errors in dose delivery and movement of needles relative to the urethral catheter, however, the impact of needle movement on treatment quality would largely depend on whether the shift relative to the prostate is greater than the dose margin around the prostate volume provided by the PTV. It was determined that employing their in vivo dosimetry technique does not increase treatment time significantly and is necessary in individual cases to determine whether treatments are being delivered as expected or whether corrective action is required along with further dosimetry.

\textit{Study employing glass dosimeters}

Radiophotoluminescence glass dosimeters (RPLGds) housed within Teflon tubes were employed by Nose et al\textsuperscript{25} to measure point doses to the urethra and rectum of prostate and gynaecological patients. The dosimetry devices were either sutured to the anterior wall of the rectum or marked in relation to a Foley catheter placed inside the urethra. The geometry of the applicators was reconstructed with the use of radiographic films
before CT data was superimposed, with CadplanBT 1.1 used for treatment planning. For each RPLGD three points were reconstructed in the planning system to determine the average theoretical dose received. The deviations between the measured and calculated doses for the urethra and rectum were greater than 20%, which was attributed to independent movement of the organs and applicators between planning and treatment delivery. Again movement of the measurement devices between planning and treatment has been the main cause of error in dose verification.

Diode dosimetry studies

In vivo dosimetry for gynaecological brachytherapy using commercially available PTW rectal probes and bladder probes was conducted by Waldhausl et al.\textsuperscript{28} The rectal probes (type 9112) were a five diode semiconductor array, while the bladder probes (type 9113) consisted of a single diode. Fifty-five patients were examined with rectal measurements taken for all 55 and bladder point dose measurements for 29 of those patients. The physical characteristics of the diodes were investigated thoroughly and included the variation of calibration factors daily and weekly, reproducibility at short, daily and long time intervals, linearity, angular dependence in different planes and temperature dependence. They found that there was large inter-probe variation of inherent characteristics so the measurements were performed with several probe sets to obtain values that represent a reliable average. The short time reproducibility was less than 0.5% with daily and long time reproducibility at 2.8%. The linearity exhibited a response comparable to ionisation chambers and the temperature dependence was given at 0.5% per degree Celsius. Angular directional dependence was seen to vary ±5%.

Phantom studies comparing doses measured to those calculated by the TPS (PLATO v13.2) at different distances from the source were also performed so that an estimate of the clinical uncertainty for the in vivo dosimetry could be obtained. The angular dependence of the diodes was found to vary from -2% to 1.8% in the longitudinal direction and -4.9% to 5.4% in the axial direction. The sensitivity of the diodes was shown to change with distance from the source with difference between the measured and calculated dose ranging from -3.5% at 30mm to -7.3% at 100mm. Taking all of the physical uncertainties into consideration they determined that a 10% tolerance level should be set for clinical applications as there was deemed to be a total 7% uncertainty in the semiconductor measurements. For the rectal measurements the difference
between the calculated and measured dose varied between -31% and 90% with an average of 11% difference and the calculated being higher than the measured in 44/55 cases. The difference was outside the 10% tolerance in 36/55 of the cases. For the bladder the difference between the calculated and measured dose varied between -27% and 26% with an average of 4%. A higher calculated dose was recorded in 19/29 applications.

The measurements were also compared to the ICRU reference rectal and bladder points with 78% of rectal measurements being higher than the calculated ICRU point for the rectum and all of the bladder measurements exceeding the calculated ICRU bladder reference point. Waldhausl et al\(^{28}\) stated that even probe movements of 2.5 and 3.5mm can cause discrepancies in dose of more than 10% indicating that correct identification of the diodes and applicators using the imaging available is crucial in verification of a plan. They indicated that a geometric shift caused by movement of the probe during the time interval between radiographs and the end of irradiation due to movement of the patient, organs or applicator as a possible reason for the differences seen between the measured and calculated values.

It was concluded that diodes allow the performance of in vivo dosimetry provided that the position of the diodes relative to the reference points is determined accurately at the time of irradiation.

\textit{MOSFET dosimetry study}

The characterisation and clinical implementation of a newly developed MOSFET device (MOSkin) was recently investigated by Ian Kwan\(^{29}\) to incorporate into an in vivo dosimetry program measuring point doses to the anterior rectal wall during pulsed dose rate (PDR) brachytherapy of the prostate. The MOSkin device had a sensitive volume <1\(\upmu\)m thickness covered in a thin polyamide film to provide minimal build up, allowing it to be used to measure dose that is indicative of the dose received to the mucosa of the anterior rectal wall. The directional dependence of the diode was determined to vary \(\pm 3\%\), the positional uncertainty in determining detector positioning on CT was \(\pm 1\)mm, and the statistical uncertainty in dose discrepancy was determined to be dependent upon source distance with 2% at 10mm and \(\leq 0.6\%\) at 20-40mm.
The MOSkin was attached to a rectal balloon and positioned inside the rectum while the patient was anaesthetised during the catheter insertion procedure. The position of the detector was determined using the planning CT which was imported into PLATO brachytherapy planning system used to develop the treatment plan and calculate the dose to the detector.

The dose received to the detector was read during treatment and compared to that calculated by the TPS with discrepancies noted. The deviations between the planned and measured values ranged from 5-35% for the 14 fractions studied with the discrepancies attributed to positional uncertainties related to the position of the detector and rectal balloon, which tended to move in a superior direction with the move difficult to measure to a high level of accuracy, and the TPS which treats the anatomy as a homogeneous water phantom and does not take into account the lack of back scatter that results from the volume of air in the rectum. Phantom studies as well as Monte Carlo simulations were undertaken to quantify the difference in expected dose due to the homogeneous TPS calculation with the TPS determined to underestimate the dose to the anterior rectal wall by 15%.

It was concluded that the experimental methodology requires improvement so that balloon migration does not affect the ability to accurately measure dose to the rectal wall during brachytherapy procedures.

Comparative dosimetry study
A comparison of the properties of different dosimeters used for in vivo dosimetry during HDR brachytherapy procedures for prostate cancer treatment was presented by Lambert et al. The physical characteristics, depth dose dependence, angular dependence, and temperature dependence were measured for a MOSFET, diamond detector, TLD and BrachyFOD™ scintillation device and compared to determine which dosimeter had the most favourable characteristics overall for HDR brachytherapy verification.

The physical size of the MOSFET was 4mm³, the diamond detector has a sensitive volume of 6mm³, the TLDs used were 3 x 3 x 0.9mm³ and the BrachyFOD™ had a sensitive measuring volume of 1mm x 5mm coupled to a 0.98mm optical fibre. The
TLD depth dose readings showed a deviation from the predicted values using TG43 ranging from -18% at 10mm to +15% at 100mm. The higher reading at large distances were attributed to the depth dependent sensitivity of LiF chips and the small differences in absorbed dose in solid water than liquid water for kV photons. The dose readings for the MOSFET, BrachyFOD™, and diamond detector were performed in water and normalised to a depth of 50mm where they all closely agreed with TG43. Beyond this depth the MOSFET readings were affected by statistical uncertainty, with their insufficient sensitivity producing readings that varied by up to +40% from the theoretical values. Both the BrachyFOD™ and diamond detector remained consistently within 3% of the theoretical values over the depths measured.

Angular dependence was measured in a custom made Perspex phantom with variation from the theoretical values being 2% for the BrachyFOD™, 3% for the diamond detector, and 10% for the MOSFET over the measured range of angles. The temperature of the three detectors was less than 3% over the 15°C to 40°C temperature range measured.

Based on their measurements and a review of in vivo dosimeters commercially available Lambert et al\textsuperscript{27} concluded that only the BrachyFOD™ and MOSFET are capable of real-time measurements and are small enough to fit into the urethra. The large and rigid structure of the diamond detector prevents its use as an insertable in vivo dosimeter even though its dosimetric properties are favourable and the low sensitivity and angular dependence of the MOSFET and the potentially large errors in the TLD measurement limit the use of these dosimeters for accurate in vivo dosimetry. Therefore the BrachyFOD™ presented the most favourable characteristics and accuracy for verification of HDR brachytherapy.

The main problems associated with rectal dosimetry for prostate HDR brachytherapy involve a lack of reproducibility due to the inconsistent structure of the rectal wall, known positioning of the dosimeters during treatment, as well as movement of organs independent of movement of the target and hence the applicators.\textsuperscript{24, 24, 26, 28} To combat these problems a geometric replica of the B&K ultrasound probe used for imaging during implantation and image capture was developed for this study, which contains a cavity in which measurement devices can be reproducibly placed.
A variety of devices have been employed by various authors to conduct in vivo dosimetry of HDR brachytherapy treatments of the prostate with the studies producing variable results.\textsuperscript{24, 25, 26, 29} The commercial semiconductor array utilised in this study has been previously investigated for in vivo dosimetry during the treatment of gynaecological malignancies with HDR brachytherapy, with the diodes’ physical properties deemed suitable for reliable routine use.\textsuperscript{28}

1.3.4.2 Semiconductor Dosimetry

Semiconductors are used regularly for in vivo verification of brachytherapy plans as well as external beam radiotherapy techniques. They have the advantage of performing instantaneous readouts, high sensitivity, good mechanical stability and small size but are notorious for the characteristics they require correction for including directional dependence, energy dependence, temperature dependence, and changes in sensitivity due to radiation damage.\textsuperscript{28, 30, 31, 32} As these characteristics significantly effect the accuracy of the dosimetry system they must be thoroughly investigated before clinical use.

The suitability of a commercial p-type silicon detector for brachytherapy dosimetry was studied by Piermattei et al\textsuperscript{30} in 1995. They stated that diodes would be particularly suitable for in-medium dosimetry of brachytherapy sources due to their high sensitivity, good mechanical stability, minimum radiation field perturbation, and the absence of an external bias as well as having the advantage of being able to read the results during irradiation. The sensitivity of the detector was determined using an Ir-192 source by measuring the signal produced as the depth of the detector in a tissue equivalent phantom was varied. Measurements were completed both with and without a shielded cylindrical lead cap with thicknesses ranging from 0.15-0.25mm which were used to filter the low energy Compton related photon component which generally makes diode response strongly dependent on source to detector distance. These results were then compared with those measured using a 0.6 cm\textsuperscript{3} ion chamber which were normalised to a depth of 1cm and assumed equal to the relative dose to water. It was found that the sensitivity of the diodes was independent of dose rate between 1cGy/min and 10cGy/min and as expected a flattening of the sensitivity was seen with the use of the
filters with the 0.22mm lead cap proving the most optimal. The uncertainty of the measurements was estimated to be within 4%. Radial dose rate values were also determined with the authors concluding that when the shielded diode is positioned with its longitudinal axis perpendicular to the plane containing the source longitudinal axis, the detector is suitable for accurate dosimetry for high dose rate sources in water or a solid phantom.

As the ideal situation described above is not realistic in terms of patient dosimetry due to non definite angles, further work would have completed examining directional dependence for it to be incorporated clinically.

An in-vivo dosimetry program for the measurement of rectal dose to avoid misadministration in gynaecological intracavity implants was presented by Alecu and Alecu\textsuperscript{31} for 19 patients and 50 fractions in 1999. Silicon diodes were chosen for their study due to their advantages of on-line readout, good spatial resolution, simple instrumentation and absence of bias voltage. The main disadvantage of diodes being their energy dependence was compensated for with the purchase of a commercial product, Isorad\textsuperscript{TM}; model 1141, Sun Nuclear Corp, which contains a low energy filter to make the energy response more uniform over the energy range required.

The dimensions of the product with the outer detector diameter being 4mm makes the product small enough to be inserted into the rectum during gynaecological procedures. The four diodes were able to be used simultaneously with separate calibrations being required for each individual diode. The calibration was performed in a polystyrene phantom at a 2cm catheter to diode distance which simulates the approximate distance from the applicator to the anterior rectal wall in a patient. There is no mention of directional dependence of the diodes being examined during the study.

The diodes were positioned using a commercially available radio opaque rectal marker which was inserted as deep in the patients’ rectums as it would penetrate before anterior-posterior and lateral images were taken and used for planning. The rectal points were defined by the ICRU 38 protocol and identified in the TPS. Knowing the distance of the points from the distal end of the rectal marker, the diodes were mounted using a
semirigid rod with the rod then graduated to the end of the rectal tube so the diodes would be positioned accurately.

Measurements were recorded for the first 20% of treatment time, which is the point where the treatment is either accepted or stopped, and compared with the dose points calculated with the TPS. These values agreed within 11% (2 s.d.) with a maximal discrepancy of 15%. It was concluded that this method of in-vivo dose measurement could be applied for all cases where rectal dose is of concern, including interstitial procedures performed for prostate or gynaecological malignancies.

1.3.5 Catheter and gland movement
Interfraction catheter movement relative to the prostate as well as tissue oedema between the prostate apex and perineum is a significant source of potential error if not checked prior to each treatment.\textsuperscript{33, 34, 35, 36, 37} Quality assurance methods, which monitor this, differ from centre to centre and depend upon the imaging modalities available. Both radiographs and CT scanning methods of verifying catheter positions have been reported and indicate that catheter movement can be as large as 30mm between fractions due to either internal movement of the gland or peri-prostatic oedema and can possibly result in significant inaccuracies in dose delivery unless the position is verified or corrected.\textsuperscript{33, 34, 35, 36, 37}

Treatments of 20 patients receiving a high dose rate brachytherapy boost for prostate cancer were examined by Hoskin et al\textsuperscript{34} to evaluate the interfraction movement of the catheters and prostate gland itself, and to determine any adverse dosimetric effects that may occur if no quality assurance procedures had taken place. A CT scan was taken following the implant procedure and used to produce the dosimetric plan which included catheter reconstruction and definition of the target volume and organs at risk. The same plan was incorporated for the second treatment delivered the following day. To assess the amount of catheter movement a second CT scan was performed prior to the second fraction.

The three possible sources of catheter movement were identified to be:

- External migration of the catheter through the skin fixation site
• Internal prostate movement
• Tissue oedema between the prostate apex and perineum

A total of 332 catheters were used for the 20 patients. The average external movement between fractions was less than 1mm and deemed clinically insignificant. In contrast, significant internal movement was demonstrated between the two CT scans with a mean movement of 11.5mm (range 0-42mm) measured. They proposed that peri-prostatic oedema which develops in the 12-18 hours between treatments and appears primarily in the region between the apex of the gland and the skin displacing the template and catheters is the main cause of the movement. The clinical significance of the movement was apparent when the conformal index and dose to 90% of the prostate (D90) in the subsequent plan, produced using the original reconstruction and dwell times with the new CT data, was compared to the original. A substantial under-dosage of the prostate, in particular the base, as well as an over-dosage of critical structures would result. It was therefore recommended that routine quality assurance, in their case with CT imaging, be incorporated for each fraction.

Needle displacement between high dose rate brachytherapy fractions for prostate cancer was investigated by Damore et al in 96 consecutive patients to determine its impact on treatment delivery. Gold marker seeds were implanted using a transperineal technique into the lateral aspects of the base and apex of the gland before stainless steel needles were positioned to cover the entire prostate and proximal seminal vesicles with the aid of a perineal template.

A simulator was used to obtain anterior-posterior (A-P) and lateral pelvic radiographs which were scanned into the treatment planning computer before dwell times and positions were programmed to produce a homogenous dose distribution within the treatment volume. Prior to receiving their subsequent fractions patients underwent an A/P verification film on the simulator to see whether the needle positions had moved in relation to the gold seeds fixed in the prostate. If some caudal displacement had occurred the implant was adjusted either electronically if there was enough room in the needle tip to adjust the first dwell position to where it needed to be, or manually with a repeat verification film taken prior to treatment. 376 pre-treatment verification films were studied with the displacement of the needles between fractions measured by
alignment of bony structures and then by alignment with the gold marker seeds. In all cases where a vertical displacement was detected the needles moved inferiorly to the target volume and in almost all cases the displaced distance was the same for all needles. The vertical displacement distance of individual gold marker seeds and seed pairs was also investigated.

The greatest amount of displacement for both the needles and seeds was evident between the first and second fractions. They concluded that inferior displacement of interstitial needles between fractions is a potential source of significant error in the delivery of HDR brachytherapy for prostate cancer and that its effect can be minimised by obtaining localisation films with good technique between fractions, noting that neither bony landmarks nor seed position alone is adequate to accurately localise the target volume, and making the necessary adjustments in the treatment volume.

Mullokandov and Gejerman\textsuperscript{35} also analysed the constancy of catheter position and its impact on dose distribution by analysing serial dosimetric CT scans. Using digitally reconstructed radiographs (DRRs) they measured the distance from each catheter tip to the template and to the ischial tuberosity. They chose the ischial tuberosity as opposed to other anatomic landmarks because it was a stable point and unaffected by implant-related oedema. The distance between each catheter tip and the ischial tuberosity was measured, with the mean value calculated to assess catheter movement. Fiducial markers placed in the prostate at the time of implant were used to aid in voluming the prostate for dosimetric analysis but were not incorporated into the determination of catheter movement.

Data sets for fifty patients were analysed with a second CT taken for each patient before either the second, third or fourth fraction. They determined, like Damore \textit{et al}\textsuperscript{33}, that there was no interfraction catheter movement relative to the template and that the template-catheter unit moved in a caudal direction between HDR fractions with the amount of displacement being time dependent, increasing with each fraction. It was also noted that when displacement occurred, almost all the needles moved the same distance, also consistent with what Damore \textit{et al}\textsuperscript{33} reported. The study concluded that significant
changes in catheter position and dosimetric coverage of the target will occur if monitoring between fractions does not occur.

Catheter displacement between fractions was studied by Kim et al\textsuperscript{38} in ten consecutive patients treated with two fractions of 9.5 Gy TRUS guided HDR brachytherapy. Using 3mm CT slices before each of the two fractions a single observer measured the distance between the tip of each catheter and a reference CT slice. The two reference slices contained the most inferior CT slice containing the ischial bone [bony marker (BM)] and the centre of two gold seed markers (COGM) implanted at the base and apex of the gland. These measurements were performed again by another observer to assess inter-observer differences in the measured catheter displacements.

The average displacement between day one and two was 4.1mm (2.7mm for the BM method and 5.5mm for the COGM method) which is quite small compared with the average displacement noted in other reports.\textsuperscript{12, 34, 35} The range of catheter displacement was -6.0mm to 12.5mm for the BM method and -3.8mm to 18.0mm for the COGM method where a negative reading indicates superior movement. Potential errors in their methods that they identified were the CT slice thickness limiting accuracy, artefacts caused by the gold markers therefore making central position difficult to determine, gold seed migration, organ and patient movement, slanting angle of the catheters, and observer error. Assumptions that were made include swelling of the prostate and resolution of oedema between fractions being insignificant, catheters all move together, and ignoring any movement of organs at risk, if the prostate does not move relative to the catheters, then the displacements measured by either the BM or COGM methods should be the same. They concluded that a combination of BM and COGM methods can demonstrate prostate and catheter movement between fractions and they believe that the COGM method is the more accurate method in the present study.

A recent study performed by Tiong et al\textsuperscript{37} examined catheter displacement in patients treated with a fractionated HDR brachytherapy boost for prostate cancer and the impact that this had on tumour control probability (TCP). Twenty patients were retrospectively
replanned with simulated catheter displacements of 3, 6, 9, and 12mm with the original dwell positions and times applied. A DVH analysis and TCP calculation was then completed for the clinical target volumes and compared to the original plan. Several different calculations of TCP were completed to account for the variation in biological parameters reporter in the literature with all of them producing similar results for smaller displacements. Actual catheter displacements for the 91 patients treated that year were also recorded. They found that all patients replanned with a 3mm displacement had a TCP greater than 0.950 compared with only 75% of patients with a 6mm displacement. Greater displacements produced significantly worse results. Of the 91 patients treated, 82.3% of fractions had a displacement greater than 3mm. It was therefore concluded that catheter displacement significantly compromises TCP and that the tolerance for these movements should be ≤3mm.

1.3.6 Fiducial marker validation

Fiducial markers are commonly used to localise the prostate during radiotherapy treatments as prostate motion occurs independently of surrounding bony anatomy and can lead to both random and systematic deviations if not accounted for.38

Organ motion over a course of conformal radiotherapy with respect to bony anatomy was investigated by van Herk et al40, and Balter et al41 in two separate studies. The author van Herk used four CT scans taken over the course of treatment for 11 patients to determine organ motion using a 3D registration technique. They found a strong correlation between rectal volume and A-P translation and rotation around the left-right (L-R) axis of the prostate. Balter et al41 measured prostatic motion using three radiopaque markers implanted into the prostate which were imaged using orthogonal portal films. An image registration tool was used to determine positional changes between bony anatomical structures such as the sacrum, symphysis, femoral heads and ischial tuberosities, and a reference portal image pair. Prostate motion in the patients’ coordinate system was determined using the difference between the components of the transformation that aligns the bony anatomy and the corresponding components of the transformation that aligns the prostate markers.
To determine the precise daily location of the prostate and therefore make dose escalation more feasible, Welsh et al.\(^2\) developed a technique to test the validity of implanting fiducial markers during prostate brachytherapy for use in subsequent guidance in conformal external beam radiotherapy. Gold and silver markers varying in size were tested in a tissue equivalent phantom to determine the material and thickness that would be most visible for conventional x-rays (75-85 kV), CT and 6MV photons. Gold markers were determined to be the most visible under all conditions and were therefore implanted in 29 patients.

Using 6MV port films during the course of treatment, the seeds were seen in different locations daily suggesting prostate motion. The mean daily displacement of the seeds was measured to be 4-5mm in the A-P direction, 4-5mm in the superior-inferior (S-I) direction, and 2-3mm L-R. The possibility of seed migration was also examined in 14 patients with the relative positions of the gold seeds evaluated in CT scans taken 5 weeks apart. The repeated CT scans showed no change in intraprostatic gold marker location, suggesting minimal migration. It was concluded that the implantation of gold marker seeds during prostate brachytherapy represents an easily implemented and practical means of prostate localisation for use in subsequent external beam radiotherapy.

A study was conducted by Schallenkamp et al.\(^3\) to describe the relative motions of the prostate, pelvic bony anatomy, and intraprostatic gold fiducial markers during daily electronic portal localisation of the prostate. Twenty patients were treated with definitive external beam radiotherapy according to an on-line target localisation protocol using three or four gold fiducial markers and an electronic portal imaging (EPI) device. A total of 22,266 data points were obtained from daily pre-therapy and through-treatment EPIs which were compared to digitally reconstructed radiographs from the patients’ treatment plans to identify displacements of the reference markers and bony anatomy.
A three dimensional coordinate system was used to evaluate the position of each marker in relation to typical skeletal landmarks and the centre of mass of the markers. Displacements were measured in the anterior-posterior, superior-inferior and right-left directions with prostate localisation compared between measurements for movements required to match to bony anatomy to those made to the fiducial markers. It was shown that significant interfractional motion exists between the prostate and the pelvic bony anatomy and that the movements are independent of each other. They also investigated marker migration by measuring intermarker distances and found that 79% of the marker positions varied less than 1mm in magnitude with 96% varying less than 1.5mm. Fiducial markers should therefore be relied upon for determining the position of the prostate with imaging devices for external beam radiotherapy.

A comparison of position verification for external beam prostate irradiation based on bony anatomy and implanted fiducials was conducted by Nederveen et al\(^{39}\), 2003. Their aim was to quantify the clinical consequences of the use of image based verification based on both bony anatomy and markers placed in the prostate. A cohort of 23 patients implanted with gold markers were analysed using 2025 portal images and 23 CT images, with statistical data for random and systematic errors calculated using displacements of the bones and markers relative to digitally reconstructed radiographs formed with the initial CT. It was determined that standard deviations for systematic marker displacement were 2.4mm in the left-right direction, 4.4mm in the anterior-posterior direction, and 3.7mm in the superior-inferior direction which could be reduced to below 1mm in all directions with the use of on-line position verification. The use of bone based position verification was seen to reduce the systematic uncertainty by 50% in the AP and LR direction but had negligible effect in the SI direction, with 6 of the 23 patients experiencing an increase in the systematic error. They therefore concluded that while internal body structures decrease some geometric uncertainty, large margins will still be required to account for independent organ motion unless on-line target based position verification is employed.

A pilot study comparing prostate set up accuracy and margins with off-line bony anatomy corrections and online implanted fiducial based corrections was undertaken by
Greer et al. in 2008. Two gold seeds were implanted into eleven patients prior to their radiotherapy planning CT, with one positioned laterally in the base of the prostate and the other in the apex. A daily online correction incorporating the electronic portal imaging device (EPID) and the prostate markers was used to determine set up accuracy, with the position of the gold seeds in the verification image aligned with their positions in the planning digitally reconstructed radiograph (DRR).

Patient set up techniques based on external skin markers were assessed by evaluating the bony anatomy set up positions for the first five fractions with their in-house offline protocol software with any recommended set up shifts recorded. The shifts recorded were then applied and compared to the resulting bony anatomy positions with no intervention to determine set up accuracy.

A further statistical protocol was used to determine whether any inaccuracy was due to systematic or random error. Using the bony anatomy set up errors recorded for the first five fractions, the set up correction shifts were applied to the measured pre-treatment prostate positions to determine the prostate set up accuracy that would have been achieved using the off-line bone protocol. The analysis was repeated using another two protocols with all the simulated results compared to the treatment set up accuracy achieved with the prostate treatment set up accuracy resulting from the daily online corrections using the fiducial markers.

The prostate systematic errors in the medial-lateral, superior-inferior and anterior-posterior directions were 2.2, 3.6 and 4.5mm for skin marker set up, 1.6, 2.5 and 4.4mm for the bony anatomy based offline protocol, and 0.5, 1.4 and 1.4mm for the online fiducial based set up. The set up margins therefore required to encompass 98% of the prostate set up shifts were 11-14mm for the bony offline set up and 4-7mm for the fiducial markers. They concluded that the implantation of fiducial markers for treatment guidance is necessary to reduce the treatment margins required; however, they suggest a larger study of patients is needed to define the margin sizes more accurately.
1.3.7 Volume change between fractions
The dosimetric impact of prostate volume change between HDR brachytherapy fractions was examined by Kim et al.\textsuperscript{45} They analysed the CT scans of 13 consecutive patients which were taken for the planning of fraction 1 and just before treatment of fraction 2 to see whether any changes in prostate volume could be observed and if so what effect that change would have on the implant dosimetry. The initial CT scan was taken within 3 hours of insertion and the average time between the first and second fraction was 20 hours.

Due to inconsistencies that can arise in the subjective method used to contour the prostate and critical organs they chose to compare the implant dose volume histograms (DVH) of the original plan with the implant DVH of the 2\textsuperscript{nd} CT with the original source positions and dwell times entered. By measuring the distance between catheters on particular slices and applying a simple equation they deduced the volume change that had occurred between fractions and noted an average volume change of 7.8\% with maximal volume changes of +16.8\% and -12.8\%.

Possible errors that were noted included selection of the same slice in the second CT scan which could be in the order of the volume change evaluated, and human error in defining the catheter position on the CT slice. No correlation was seen between the changes in volume and the change in implant V100 and V150. They concluded that the volume and dose changes observed are clinically insignificant and that a study incorporating MRIs to calculate DVH for the prostate and organs at risk would be necessary in the future.

During a Phase II prospective study of the use of conformal HDRB as a monotherapy in the treatment of favourable stage prostate cancer, Martinez et al\textsuperscript{36} conducted a volumetric analysis to determine the extent of volume change in the prostate during the course of treatment (four fractions) and the impact that any change would have dosimetrically. TRUS scans were taken prior to catheter insertion for twenty-three patients, just before treatment delivery of fraction 1 (approximately 1.5 – 2 hours later), and at the end of fraction 4 (32 – 36 hours after the first image set). Prostate volumes were derived by contouring each TRUS image at 5mm intervals on their Pinnacle 3D planning system.
It was determined that the largest change in prostate volume occurred between the time prior to needle insertion and following needle placement at fraction 1 with an average prostate expansion of 6.3cc recorded. The mean change in volume of the gland between the first and last fraction was found to be 2.7%, ranging from +17.3% to -13.7%. A comparison was made between the doses received to 90 and 80% of the target (D90 and D80) and 10% of the urethra (D10) for fractions 1 and 4 to determine whether volume change significantly impacts upon dose delivery. After comparing the mean range for D90, D80, and D10 between the fractions they determined that they do not change significantly and that the plan generated for fraction 1 is sufficient for the remainder of the fractions delivered, with no compromise in the dose coverage of the gland and/or urethral dose.

1.3.8 Imaging modality options for treatment planning

Depending on the accessibility and availability of equipment, various imaging modalities are utilised for treatment planning at different institutions. Those commonly used include ultrasound (US), CT and MRI.

The GEC/ESTRO-EAU recommendations from 2005\textsuperscript{4} state that treatment planning can be performed as pre-planning some days before implantation, intra-operative on-line planning in the operation theatre or as a CT-based post-implant procedure. The pre-planning and inter-operative techniques involve TRUS images as ultrasound units are mobile and can be used effectively to image the prostate during implantation in theatre. CT-based post-implant planning is used when on-line planning systems or adequate theatre times are not available.

The American Brachytherapy Society, in 2008, published their guidelines for HDR prostate brachytherapy.\textsuperscript{17} It was stated that treatment planning is volumetric and based on contiguous slice acquisition from either CT, MR or US with a slice spacing appropriate to resolution requirements. They advise that a treatment planning scan performed after the procedure should be achieved with CT or MR.
US planning has the ability to be employed as an intra-operative on-line procedure which seems to be advantageous in terms of patient comfort. The on-line procedures allow the patients to be implanted, planned and treated during a single procedure while under anaesthetic which would be optimal for those facilities who only prescribe single fractions or spread the fractionation out over several procedures. A disadvantage to performing real-time ultrasound planned procedures is that the institution must have a dedicated brachytherapy suite as the necessary theatre time and equipment required may not be available and costly to implement.

For centres without a dedicated suite, post implant planning using CT imaging is a common technique employed. The advantages of using CT are that many radiotherapy departments have them readily available, the spatial accuracy is excellent, and the images are easily incorporated into most planning systems. A disadvantage in comparison to other imaging modalities is that soft tissue delineation can be poor which may make contouring difficult.

MRI has the ability to provide superior visualisation of the prostate gland and surrounding anatomy making it the modality of choice for imaging prostate cancer. There is a strong rationale for using MRI for treatment planning in brachytherapy given that the accuracy is largely dependent on planning image quality. Citrin et al describes a five step procedure for the implementation of inverse planning based solely on MRI for HDR prostate brachytherapy. Those steps include: the correction and verification of spatial distortion in MRI; Digital Imaging and Communications in Medicine (DICOM) header correction for compliance to treatment planning software; validation of a technique for determination of the first dwell position; anatomic evaluation based on MRI; and derivation of inverse planning constraints. They confirmed spatial and targeting accuracy of the MRI and determined that the class solution that they developed for their procedure was effective at achieving excellent target dosimetry while sparing nearby normal tissues. Although an excellent modality for anatomical imaging, MRI is generally less accessible and more costly than both CT and ultrasound and is therefore not used as commonly as the other techniques.
If in-vivo dosimetry is to be performed in conjunction with MRI imaging then the design of the dosimeter chosen is important as it must be non Ferric. TLDs, polymer gels and some MOSFET devices would be suitable for this.

**Summary**

In vivo dosimetry for patients being treated with HDR brachytherapy for prostate cancer has historically been difficult when dosimeters have been placed inside the rectum due to large uncertainties in geometric localisation of the dosimeter during treatment. As many centres do not have the ability to image directly prior to treatment, movement of the dosimeter within the rectum between imaging and treatment is a significant cause of uncertainty in the verification of the dose received to the device. An aim of the study was to combat this issue by developing a device that would retain the position of the dosimeter between imaging and treatment, therefore reducing measurement uncertainty. The use of a semiconductor array instead of other dosimetric devices was based on its availability in the department and its ability to record dose measurements in real time so that plan verification could be evaluated at the time of the patients’ treatment, which is a characteristic that has not been incorporated into many publications.

Even though catheter and gland movement between fractions has been evaluated by many authors as well as the potential effects on patient dosimetry if the movements are not compensated for, there is a lack of published data analysing patient dosimetry for subsequent fractions that incorporate the original plan and have accounted for any changes in catheter positions relative to the gland. A volumetric analysis comparing the volumes encompassed by 100% and 150% of the prescribed dose for subsequent fractions was therefore undertaken to evaluate whether applying the original treatment plan to the prostate following any catheter moves or prostate volume change causes a significant discrepancy in the volume irradiated. An investigation was also undertaken to determine whether the extent of catheter movement is related to interfraction prostatic oedema.
Chapter 2 : Methodology

A dosimetric study investigating the accuracy of a planning systems ability to predict the dose received during treatment for prostate cancer with HDR brachytherapy was conducted at the Mater Hospital in Crows Nest during 2007 and 2008 using a 28 patient cohort. During this time 15 of these patients were analysed to examine the impact, if any, of volumetric changes of the prostate during the course of treatment. The detector utilised in the dosimetric comparison was a commercial semiconductor array whose characteristics were thoroughly examined so that the uncertainties involved in the investigation could be fully understood.

2.1 Patients

Between December 2007 and July 2008, 28 patients with stage T1c to T3a prostate cancer received an Ir-192 HDR brachytherapy boost planned with the Nucletron SWIFT real time treatment planning system which was followed by 50.4Gy external beam radiotherapy. Rectal dosimetry was performed during all of the patients’ first fractions, eleven patients’ 2nd fractions, and thirteen patients’ 3rd fractions. Seventeen patients experienced problems for at least one of their second or third fraction scans with reasons for forgoing measurement including either a high level of pain, excessive gas, or faecal matter preventing the use of the ultrasound probe to collect the images required for the analysis. All except three patients received adjuvant hormone therapy.

2.2 Brachytherapy Procedure

A dose regime of 18Gy in 3 fractions was delivered to each patient as a boost to external beam radiotherapy. The patients were implanted with between 16 and 21 stainless steel (trocar, 1.9mm diameter, 24cm length) or plastic needles (OncoSmart Proguide, 2mm diameter, 24cm length) under transrectal ultrasound guidance using a transperineal approach. The needles were inserted into the base of the bladder. The patients remained in the lithotomy position for the duration of planning and their first treatment. Intraoperative, real-time planning was performed using Nucletron’s SWIFT real time treatment planning system (Netherlands), which has a built in encoder in the probe stepping mechanism that allows instant operator feedback of the probe position.
within the prostate by allowing ultrasound images to be spatially registered against the position of the probe and template. The TPS uses 1mm spaced images captured by ultrasound to reconstruct the implant geometry in three dimensions. The prostate, urethra and rectum were contoured by the Oncologist using the appropriate software tools. The attending Physicist then reconstructed the needle positions, applied appropriate source positions and developed a treatment plan by employing dose optimisation techniques. An example of a SWIFT planning screen is illustrated in Figure 2-1.

![Figure 2-1. SWIFT planning screen showing ultrasound images, prostate, urethra and rectal contours, isodose lines and a 3D reconstruction of the contours, catheters, source and diode positions.](image)

Following the planning ultrasound scan the B&K probe was removed from the rectum and replaced with the detector array placed inside a replica ultrasound probe developed specifically for rectal dosimetry, which is explained in detail in section 2.3. The combined device will be referred to in this thesis as the “replica probe”. A PTW type 9112 dosimetry array consisting of five diodes was placed inside the cavity with the fiducial mark indicating the calibration direction facing the prostate as shown in Figure
The fiducial mark consisted of an arrow marked on sticker which was taped to the required position on the diode array.

A fluoroscopy image taken as part of the regular quality assurance procedure was used to position the diode array in relation to metal marker wires placed within two reference needles centrally located within the prostate. Figure 2-3 shows a typical fluoroscopy image and how the most superior diode was placed at the superior end of the catheters so that the array would encompass the entire prostate. The C-arm angle approximated that of the ultrasound probe so that the image would be close to perpendicular with the implant.

The patients’ treatments were delivered using Nucletrons’ microSelectron HDR afterloading unit and associated equipment. An Ir-192 source was driven out of the unit through a transfer tube which was attached to the indexer (face) plate at its proximal end and connected to the prostate needles at its distal end. Once the source arrived at its most distal planned position it remained in place for the time allocated in the treatment plan before stepping to its next position which was located 2.5mm away. Once the source had remained in a particular needle for the allocated time it was retracted back into the unit before being driven into the next needle in succession.

The diode array was connected via a cable system to an electrometer positioned outside the room near the treatment console. The electrometer was controlled using PTW Multisoft software which was also used to record dose measurements.

The patient and equipment set up, ultrasound scan and dosimetry analysis was replicated for fractions two and three when possible. For each subsequent fraction, needle movement relative to the implant was assessed using fluoroscopy by comparing the positions of three gold fiducial markers in the prostate relative to marker wires positioned in two of the central needles in the gland. The marker wires consisted of pieces of metal spaced 1cm apart which could be inserted into needles. Images of the marker wire are shown in Figure 2-3 inside a needle and positioned next to the diode array in Figure 3-5. The decision of whether to physically shift the needles or not before the patients’ treatment was based upon whether the source could be driven to the required positions toward the base of the prostate as detailed in the treatment plan. If all
of the available source positions at the end of the needles were not occupied with dwell
times then a correction to the indexer length (length defined as the distance from the
indexer plate to the first source position) could occur so that the source could be sent to
the required position relative to the prostate as dictated by the plan. If the needles did
not have the required space then physical adjustments would have to occur. Once it was
deemed that the plan was able to be executed as planned, the treatment was delivered.

Figure 2-2. Dosimetry set up with the replica probe replacing the B&K ultrasound in the stepper
unit. The diode array was then placed within the replica probe and fixated so that the fiducial
marker was positioned in the calibration direction.

Figure 2-3. Fluoroscopic image showing the position of the semiconductor array in relation to the
implant, reference needles and fiducial seed markers in the prostate.
2.3 Replica Probe

The replica of the B&K ultrasound probe was made by 3H Engineering and constructed using an Acetal Polyoxymethylene compound, pictured in Figure 2-4. An 8mm diameter cavity was formed throughout its centre 6mm from the anterior surface. The other dimensions are shown schematically in Figure 2-5.

![Figure 2-4. Photograph of the replica ultrasound probe.](image)

![Figure 2-5. Schematic diagram of the replica probe with the measurements for each section.](image)

2.4 PTW Type 9112 Semiconductor Diodes

The dosimeter chosen for the dosimetric verification was a semiconductor five diode array manufactured by PTW (T9112) and is pictured in Figure 2-6. The diodes in the type 9112 array are 4mm long and spaced 15mm apart centre to centre. The technical specifications state that its intended use is for intracavity dosimetry during afterloading treatment in an energy range from 280kV to 660kV, and that it has an energy response of ± 8% an angular dependence of ± 2% at 1m, and has a temperature dependence of <1%/K. The centre of each diode was chosen as the reference point for dosimetric evaluation with the TPS as directed by the user manual.

An assumption that was made throughout the measurement process was that the diodes lie in the centre of their plastic casing and that the amount and position of cabling is
consistent for each diode. Figure 2-7 shows fluoroscopic images of the diode array taken from different angles. The diode positions with respect to the plastic casing and cabling can be seen and it is apparent that the diodes may not be exactly centred in their encapsulation causing a position uncertainty of ± 0.5mm.

The array was calibrated using a custom designed afterloading calibration phantom (type 9193) pictured in Figure 2-8. The phantom consists of a PMMA (acrylic) cylinder with a diameter of 20cm and a height of 12cm. In the centre, as well as four points equidistant and 2cm from the rim, holes exist which were designed to hold acrylic applicators that contain recesses for commercially available detectors. The holder was designed so that the position of the centre of the radiation source is at the same height as the reference point of the detectors, which for the T9112 is the central detector (detector 3). When positioned the distance between the reference point of the detector and the source was 8cm. To avoid excess scatter conditions the phantom was positioned on a tripod approximately 60cm above the floor.

The characteristics of the diode array were examined thoroughly and these included linearity and reproducibility measurements, temperature dependence, and both radial and longitudinal directional dependence.
2.4.1 Linearity and Reproducibility

The linearity of dose response for each diode was determined using the geometric phantom pictured in Figure 2-8. The diode array was placed in the centre of the phantom with the source positioned 8cm away. Measurements were recorded for sixteen time intervals ranging from 0.1 seconds to 999 seconds, set using dwell times, and analysed using an Excel spreadsheet. A regression analysis was performed from which the sample coefficient of determination (R Square), which is an expression of the strength of the linear relationship, and standard error values, which estimate the variability in the sample, were recorded. ⁴⁷
The reproducibility of the diodes was determined by measuring five consecutive readings for 400s of irradiation using the geometric phantom set up. The standard deviation of the values was recorded and analysed.

2.4.2 Temperature Dependence

The temperature dependence of the diode array was determined at the time of the diode purchase by fixating the array to the side of a plastic tube approximately 5cm in diameter and attaching a plastic catheter to the other side of the tube before immersing in a water phantom. A transfer tube and the afterloading unit were attached to the plastic catheter. A thermometer was placed inside the phantom. Initially a 300s measurement was taken in the water at room temperature (23°C) before the water was removed and replaced with hot water which increased the temperature of the phantom to 35°C. 300s readings were taken consecutively after 5, 10 and 15 minutes to see whether a typical increase in temperature due to the probe being inserted into a patient for a clinical timeframe would affect the sensitivity of the diodes. The diode array was never in direct contact with the patient as it was always contained in over 6mm of plastic inside the replica probe and would therefore not have reached the internal body temperature of 37°C.

2.4.3 Dose Rate Dependence

The dose rate dependence of the diode array was determined using the experimental set up and dimensions depicted in Figure 2-9 and Figure 2-10. A stainless steel needle, used in conjunction with its associated transfer tube as the transfer assembly for the Ir-192 source, was placed against the edge of the water tank 4cm above the end of the diode array so that the first source position (10mm from the tip) was horizontally aligned with diode R3. The diode array was positioned using a Perspex holder provided with the tank which allowed a fixed geometry to be maintained during the measurements. The distance from the diode to the source was determined knowing the thickness of the holder to be 0.55cm, the radius of the diode array to be 0.35cm and the distance of the source from the edge of the tank to be 0.1cm. As the centre of the diode array was positioned 0.3cm closer to the source than the centre of the holder and the source was deemed to be 0.1cm inside the edge of the tank then the distance between the source and
the centre of the diode was determined to be 0.4cm less than the measurement displayed on the tank. Readings were taken for 300s at distances ranging from 2.6cm to 7.6cm from the centre of diode R3 to the source and compared to those predicted with PLATO brachytherapy planning system (BPS) with any deviations noted. Using distance to determine dose rate dependence introduces spectral changes due to photon attenuation and scattering in the medium. As the detectors have an energy dependent response due to their design, it is possible that this response may be a cause of any discrepancy in the results.

Figure 2-9. Photograph of the experimental set up for the determination of dose rate dependence of the diodes.
Figure 2-10. Experimental set up for the measurement of dose rate dependence of the diodes.

2.4.4 Directional Dependence

The directional dependence of the array was investigated in both the radial and longitudinal directions. Radial directional dependence was examined by placing the array in the centre of a geometric phantom and recording the calibration data measured for each diode as the source was moved to each of the four positions outlined in Figure 2-8. The calibration readings were compared for each of the four positions, with the three positions showing the lowest variation in sensitivity averaged and applied to the system, as these three positions would be routinely faced in the direction of the implant during irradiation. A fiducial mark was taped onto the array casing in the calibrated direction, as shown in Figure 2-11, which was faced toward the implant to minimise any radial effects on doses measured. This process was repeated for every diode array calibration procedure.
The longitudinal directional dependence of the diodes was also investigated. This was completed by placing a steel needle parallel to the diode array in a Plastic Water™ stack at a separation of 7cm, and recording the doses received by each diode as the dwell position of the source was moved in 0.5cm increments perpendicular to the length of the array. The calibration direction indicated by the fiducial mark was faced toward the source and a schematic of the set up is displayed in Figure 2-12. Indexer lengths required to match the source to the perpendicular axis of each diode were determined under fluoroscopy. This situation was reproduced in Nucletron’s PLATO Brachytherapy Planning System where the measured readings for each diode position were compared with the predicted values with deviations noted.
2.5 Dosimetry Analysis

A validation of a SWIFT plan exported to PLATO TPS was performed initially to ensure that point dose analysis remained consistent between the two systems. This was completed by planning a basic four catheter plan in SWIFT which was then exported to PLATO with point doses at ten different coordinates inter-compared. The points for comparison were selected by determining the midpoint between 2 source positions in both coordinate systems. Point dose calculations were then performed for each point selected and compared between the two systems.

The position of the diodes relative to the tip of a reference needle containing a marker wire were measured and then used to determine the point coordinates on SWIFT to which the diode dose measurements were compared. The coordinates selected reflect the approximate position of the diodes within the replica probe which when assumed to be positioned in the geometric centre of the 8mm cavity are 9.5mm from the anterior surface of the probe which is further assumed to lie in the same position that the ultrasound probe was in the scan. Figure 2-13 depicts how the coordinates of the diodes were determined using measurements from SWIFT. The plan was then exported to PLATO BPS version 13.6 so that dose points corresponding to diodes outside the range of the ultrasound scan could also be analysed. A three dimensional representation of the implant is depicted in Figure 2-14 using PLATO software.

As the PLATO planning system calculates dose in accordance with the AAPM TG-43 protocol, no corrections are made as to attenuation differences between needle materials. The only aspect modelled by the system is the source itself with the density of the materials through which the photons pass not calculated any differently than water.
Figure 2-13. Determination of the coordinates required for dose comparison using the ultrasound scan taken with SWIFT. Using the ruler function 9.5mm was measured from the anterior aspect of the probe to the point at which the diode was assumed to lie.

Figure 2-14. Three dimensional representation of the implant and diode points in PLATO.

Diode measurements were recorded for 28 patients during the first fraction, 11 patients during their second fraction, and 13 patients during their third fraction. Reasons that all 28 patients were not evaluated for all three fractions included faecal matter preventing adequate ultrasound imaging, inadequate pain management resulting in no imaging due to not being able to reinset the ultrasound probe, and a single patient having to be replanned on CT due to excessive catheter movement between his first and second fraction. For the patients that did have scans taken for subsequent fractions the original SWIFT plan was applied to the new set of images before being exported to PLATO. All
catheter shifts in relation to the prostate between fractions were noted and subsequent shifts in dwell positions were made in the plan accordingly. Adjustments were also made to correct for the depleted activity of the source. Diode dose point comparison was made by selecting points according to diode positioning relative to marker wires on the fluoroscopy image. The measured diode dose readings were compared to the theoretical point doses on PLATO with deviations noted. The individual diode deviations were compared to each other as well as to those taken for the second and third fractions.

2.6 Prostate volume change during the course of treatment

The effect of prostate oedema during the course of treatment on implant dosimetry was investigated using a method developed by Kim et al. In this method the centre of mass of all catheters was used as a reference point to determine volume change in the prostate at the second and third fractions. Catheter coordinates were recorded at the apex, reference and base planes for each fraction imaged with ultrasound. The base plane was determined by the physicist using the images recorded for fraction one with patient anatomy and ultrasound height matched before imaging for subsequent fractions. Reference and apex planes were then set to correspond with the planes contoured by the Oncologist in the first fraction. The centre of mass for each plane was determined by averaging the x and y coordinates with equation 2-1. The average distance \( d_i \) from the reference to a catheter was obtained using equations 2-2 and 2-3.

\[
\begin{align*}
\bar{x}_c &= \frac{\sum_{i=1}^{n} x_i}{n}, \quad \bar{y}_c = \frac{\sum_{i=1}^{n} y_i}{n} \\
\end{align*}
\]

\[
\begin{align*}
d_i &= \sqrt{(x_i - \bar{x}_c)^2 + (y_i - \bar{y}_c)^2} \quad &2-2 \\
\end{align*}
\]

\[
\begin{align*}
d_c &= \frac{\sum_{i=1}^{n} d_i}{n} \quad &2-3 \\
\end{align*}
\]

The variation in prostatic volume over the three fractions was estimated by raising the difference between the global distances to the cubic power (Eq 2-4). This method
assumes that there are no changes in shape of the prostate between fractions and that any oedema occurs isotropically.

\[
\Delta V(\%) = \frac{\Delta V}{V_{1st}} \times 100 = \frac{V_{2nd} - V_{1st}}{V_{1st}} \times 100 = \frac{(d_{c}^{2nd})^{3} - (d_{c}^{1st})^{3}}{(d_{c}^{1st})^{3}} \times 100
\]

The implant dose volume histograms for the irradiated volumes were analysed for each fraction imaged with ultrasound. Organ DVHs were not studied as contouring would have taken considerable time for Radiation Oncologists and could have lead to inconsistencies between fractions due to subjective contouring differences. The DVH statistics recorded for each patient included the volumes receiving 100%, 150%, 200% and 300% of the prescribed dose to the prostate with deviations between fractions noted. Imaging 1mm slices with the ultrasound should reduce the uncertainty experienced by Kim et al.\textsuperscript{45} who imaged using CT and a slice width of 3mm which introduced larger uncertainties in matching anatomical positions.

2.7 Prostatic oedema connection to required catheter movement

The change in prostate volume during the course of treatment was compared to the catheter movements required to deliver the original plan to see whether a link between the two was apparent. The average prostate volume change between fractions was tabulated against the catheter shift required before treatment of each fraction.

2.8 Connection between implant DVH analysis and control/morbidity.

Plato BPS was used to determine the implant DVH statistics for each of the fractions imaged. The differences between volume statistics recorded for the 100%, 150%, 200% and 300% isodose regions (V100, V150, V200 and V300) for each fraction were recorded before being compared with patient follow up PSA levels and any instances of morbidity to see if there was a relation between a decreased V100 and lack of control, or an increase in V150 with increased acute patient morbidity.
2.9 Plastic vs. stainless steel catheter analysis

Patients treated using plastic catheters were compared to those treated using the stainless steel catheters to see whether either group experienced a higher degree of prostatic oedema, required greater overall catheter shifts, or experienced a higher degree of morbidity.

2.10 Reconstruction uncertainty analysis

To estimate the degree of uncertainty related to the catheter reconstruction method and its effects on the dosimetry and volume comparisons, two patients were selected to have their second fraction scans reconstructed a further two times. For consistency both patients had implants that did not require physical adjustment of the catheters before scanning had taken place. The first patient selected had an image of good quality where all of the catheters could be detected easily. The second patient was selected as his images were of poorer quality, with catheters toward the anterior lateral portions of the implant difficult to see and therefore accurately geometrically position. The effect of image quality on accurate reconstruction is currently not known and is a factor that can theoretically alter a patient’s treatment if dose is delivered to an area which differs to that which was planned, therefore requiring investigation. Once reconstructed on SWIFT the implants were exported to PLATO where marker points were added to determine the diode theoretical doses for the new reconstructions. Implant DVH statistics were also recorded for V100, V150, V200, and V300 before being compared with results of the initial second fraction implant reconstruction. To compare the implants volumetrically, catheter coordinates were recorded on the apex, reference, and base planes using SWIFT.
Chapter 3 : Results

3.1 PTW Type 9112 Semiconductor Diode analysis

3.1.1 Linearity and Reproducibility

The linearity of each diode is expressed in Table 3-1, represented by the R-Squared and standard error values determined using a regression analysis in excel. All diodes exhibit a linear response with dose, depicted in Figure 3-1, exhibiting $R^2$ values which only become different from 1 after the 5th place. The diodes all demonstrate very reproducible results for the 400s readings demonstrated by the small deviation between the five consecutive readings, shown in Table 3-2.

![Linearity of the five diodes (R1 - R5) in the PTW semiconductor array](image)

**Figure 3-1.** Linearity of the five diodes as a function of dose.

<table>
<thead>
<tr>
<th>Diode</th>
<th>R-Squared</th>
<th>Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1</td>
<td>0.999996</td>
<td>0.000254</td>
</tr>
<tr>
<td>R2</td>
<td>0.999988</td>
<td>0.000483</td>
</tr>
<tr>
<td>R3</td>
<td>0.999996</td>
<td>0.000271</td>
</tr>
<tr>
<td>R4</td>
<td>0.999995</td>
<td>0.000302</td>
</tr>
<tr>
<td>R5</td>
<td>0.999995</td>
<td>0.000282</td>
</tr>
</tbody>
</table>

Table 3-1. Diode linearity representation expressed with the coefficient of determination and standard error of each measurement set.
Table 3-2. Reproducibility of diode measurements recorded for 400s.

<table>
<thead>
<tr>
<th>Diode</th>
<th>R1</th>
<th>R2</th>
<th>R3</th>
<th>R4</th>
<th>R5</th>
</tr>
</thead>
<tbody>
<tr>
<td>rdg 1 (Gy)</td>
<td>0.180</td>
<td>0.197</td>
<td>0.193</td>
<td>0.193</td>
<td>0.178</td>
</tr>
<tr>
<td>rdg 2 (Gy)</td>
<td>0.180</td>
<td>0.197</td>
<td>0.194</td>
<td>0.193</td>
<td>0.179</td>
</tr>
<tr>
<td>rdg 3 (Gy)</td>
<td>0.180</td>
<td>0.197</td>
<td>0.194</td>
<td>0.193</td>
<td>0.179</td>
</tr>
<tr>
<td>rdg 4 (Gy)</td>
<td>0.180</td>
<td>0.197</td>
<td>0.194</td>
<td>0.193</td>
<td>0.179</td>
</tr>
<tr>
<td>rdg 5 (Gy)</td>
<td>0.180</td>
<td>0.197</td>
<td>0.194</td>
<td>0.193</td>
<td>0.178</td>
</tr>
<tr>
<td>Standard Deviation (%)</td>
<td>0</td>
<td>0</td>
<td>0.2</td>
<td>0</td>
<td>0.3</td>
</tr>
</tbody>
</table>

3.1.2 Temperature Dependence

A change in temperature of similar magnitude to that expected clinically did not significantly impact upon any of the diode readings for a 300s measurement, displayed by the variation in the readings in Table 3-3. These diodes therefore do not exhibit significant temperature dependence in the clinical range which differs from other published data showing a 0.5%/°C variation.26

Table 3-3. Temperature dependence of the individual diodes for the temperature range experienced clinically.

<table>
<thead>
<tr>
<th>Diode</th>
<th>R1</th>
<th>R2</th>
<th>R3</th>
<th>R4</th>
<th>R5</th>
</tr>
</thead>
<tbody>
<tr>
<td>23°C</td>
<td>0.724</td>
<td>0.855</td>
<td>0.932</td>
<td>0.846</td>
<td>0.705</td>
</tr>
<tr>
<td>35°C – 15 mins</td>
<td>0.726</td>
<td>0.857</td>
<td>0.933</td>
<td>0.848</td>
<td>0.705</td>
</tr>
<tr>
<td>35°C – 10 mins</td>
<td>0.725</td>
<td>0.856</td>
<td>0.933</td>
<td>0.847</td>
<td>0.706</td>
</tr>
<tr>
<td>35°C – 5 mins</td>
<td>0.728</td>
<td>0.858</td>
<td>0.933</td>
<td>0.846</td>
<td>0.703</td>
</tr>
<tr>
<td>R5 Standard Deviation (%) 23-35°</td>
<td>0.2</td>
<td>0.2</td>
<td>0.1</td>
<td>0.1</td>
<td>0.2</td>
</tr>
</tbody>
</table>

3.1.3 Dose Rate Dependence

No clear trend was observed for all diodes when dose rate dependence was investigated. R2 – R5 however expressed a trend where differences between the planned and measured values moved in a positive direction (positive indicating calculated result was greater than that measured) with an increase in distance from the source. The opposite occurred for diode R1. The maximum and minimum differences between the PLATO
and measured point doses are displayed in Table 3-4. As the effect is not consistent for all diodes it is unclear as to whether energy dependence, as a result of a spectral change with depth, is a cause of the discrepancies evident in Figure 3-2.

Table 3-4. Range of deviations exhibited between the PLATO and measured dose values recorded.

<table>
<thead>
<tr>
<th>Diode</th>
<th>Range in %</th>
<th>Difference Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1</td>
<td>-3.5 to 2.2</td>
<td></td>
</tr>
<tr>
<td>R2</td>
<td>-6.9 to -1.5</td>
<td></td>
</tr>
<tr>
<td>R3</td>
<td>-2.5 to 5.9</td>
<td></td>
</tr>
<tr>
<td>R4</td>
<td>-3.5 to 2.8</td>
<td></td>
</tr>
<tr>
<td>R5</td>
<td>-0.3 to 2.1</td>
<td></td>
</tr>
</tbody>
</table>

Figure 3-2. Discrepancy between measured diode results and those calculated by the PLATO software as a function of distance from the source. Positive discrepancies relate to calculated results being greater than those measured.

The uncertainties related with this procedure include: the position of the diodes inside the array, the position of the array in the holder, the holder position at the level of the source, the needle position, the distance from the source to the holder, as well as the TPS calculation. The combined uncertainty for the measurements was equal to ± 5.8% and is described in Table 3-6. When the uncertainties are taken into account the range of
dose variations is almost entirely enveloped but the trend observed in four of the diodes suggests a possible systematic variation of diode response with dose rate.

3.1.4 Directional Dependence

The directions referring to the radial and longitudinal planes of the diode array are shown schematically in Figure 3-3. Radial directional dependence was exhibited by the variation in calibration factors for each diode in the array, depicted in Figure 3-4. Due to the consistency of the calibration factors for positions 1, 3 and 4, they were averaged and employed as the overall calibration factor for the array. A fiducial marker was then placed at the position indicating the centre of the three averaged positions. This process was repeated every time a new calibration factor was measured. The variation in calibration factor between the four measurements and their average was used to determine the directional dependence in the radial direction which was ± 3.4%.

The orientation of the longitudinal directional dependence experiment on the five diodes is depicted schematically in Figure 3-5. Figure 3-6 depicts the longitudinal directional dependence of the five diodes by showing the percentage deviation between the measured results and those predicted by PLATO with respect to the perpendicular angle between the diode and the source.

The same source position represents a different angle from each diode displayed by the schematic and fluoroscopy image in Figure 3-5. Sources positioned on the right of each diode in the diagram are indicative of the positive angle in the plot while those on the left of the diode position represent negative angles. All of the diodes exhibit a similar trend in that the dose points predicted by PLATO as the source moves in a positive direction with respect to the diode are greater than the dose measurements physically recorded, while becoming slightly less before tending greater again as the source moves in the opposing direction. The similar trends indicate that the diodes are all positioned in a similar fashion within their casing. The plot indicates that the discrepancies recorded exhibit two changes in direction, at approximately -20° and +45° relative to the centre of the diode. A possible reason for this occurrence lies in the structure of the device where wires surround the diode as shown in the fluoroscopy image in Figure 3-5. This wiring may inhibit the signal measured with the effect increasing with angle from the source to a point where a maximum amount of wire is being passed through. This
explanation does not describe the trend seen with the source positions on the negative side of the diodes though.

A wide range of angles were investigated as the source positions used clinically form a vast array of varying angles with each of the diodes, especially diodes R1 and R5 which are generally positioned with no aspect of the diode perpendicular to the prostate. The average deviation between the planned and measured values for the angles investigated was $2.2 \pm 3.6\%$ with a range from -3 to 11%. The angular response quoted by the manufacturer is $\pm 2\%$ at 1m distance for a Cs-137 source.

AAPM TG-43 calculations in commercial systems incorporate a polynomial fit to the radial dose function, which accounts for photon scattering and attenuation in the medium. This fit is limited though to a certain radial range and it is possible that data calculated outside this range may produce erroneous results. Nucletron applies the dose rate table derived by Daskalov et al\textsuperscript{48} using Monte Carlo simulations into their planning software. This table extends up to 7cm from the source in directions parallel and perpendicular to the longitudinal axis of the source. Errors in the calculation of dose at relatively large distances from the source (all distances in longitudinal dependence investigation between 7 and 12 cm) could therefore be a reason for the considerable discrepancies indicated by the plot. As any calculation inconsistencies would be expected to be the same at equivalent distances from the source in either the positive or negative direction the dose calculation cannot be the overall reason explaining the trend in the discrepancies evident in Figure 3-6.

Plastic Water was used as it was the only solid phantom material available at the time of the study. Meigooni et al\textsuperscript{49} conducted a comparative study of the dosimetric properties of Plastic Water in brachytherapy applications using Monte Carlo simulations and determined that the composition of the material, which includes almost 8% calcium, has a significant effect on absorption for energies below 100keV. The difference is due to the photoelectric cross section of Plastic Water being markedly different to that of liquid water at the same energy. The Plastic Water therefore attenuates and absorbs lower energy photons more rapidly than liquid water and produces more photoelectric absorption and less scattering. The differences decrease as energy increases and become insignificant for Co-60. As the average energy for the Ir-192 source is 380keV, the
differences between the chemical compositions of Plastic Water and liquid water should not be a large contributor to the discrepancy between the calculated and measured data.

The uncertainties apparent for this measurement include: the position of the diodes inside the array, the position of the array in the plastic water, the position of the source within the needle, the position of the needle in the plastic water, and the position of the source relative to the diodes. The combined uncertainty of the measurements was ± 2.1%. Error bars indicating this uncertainty are not shown in Figure 3-6 for clarity.

![Radial and longitudinal planes of the diode array.](image)

**Figure 3-3. Radial and longitudinal planes of the diode array.**
Figure 3-4. Radial directional dependence exhibited by the diode array.
Figure 3-5. Schematic diagram and fluoroscopic image showing the position of the diodes in relation to the source used to determine longitudinal directional dependence.

Figure 3-6. Longitudinal directional dependence of the five diodes. The angles noted are those projected from the perpendicular of each diode to the source. Positive deviations indicate that the dose points calculated using the PLATO software were greater than those measured.

3.1.5 Uncertainty Analysis

The uncertainties for the sets of measurements taken to characterise the diode array were estimated using the methodology from the ISO guide to the expression of uncertainty in measurement. Uncertainties were considered from the measurement set
up for the diode array and water tank assembly, diode array and plastic water assembly, diode array and geometric phantom assembly, as well as the positioning of the source within the applicator, source calibration, plus uncertainty related to the TPS. The lists of uncertainties for the various measurements are shown in Table 3-6. A thorough description of the uncertainty analysis can be found in Appendix A.

Due to the inverse square law a positional uncertainty in diode placement of ± 0.5mm corresponds to dosimetric uncertainties ranging from ± 9% at 1cm to ± 1% at 8cm as shown in Table 3-5. The distances between the source positions and diodes vary considerably for each catheter and source position within that catheter. The closest catheter positions were approximately 2cm from the derived position of the diodes so the uncertainty quoted for a position error of ± 0.5mm was chosen to be ± 5%.

<table>
<thead>
<tr>
<th>Distance from source (cm)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positional uncertainty (%)</td>
<td>9</td>
<td>5</td>
<td>3</td>
<td>2.5</td>
<td>2</td>
<td>1.7</td>
<td>1.4</td>
<td>1.2</td>
</tr>
</tbody>
</table>

An uncertainty in the position of the diodes relative to the implant arises due to only an A-P image being used for its determination. It is possible that the needles are angled with respect to the fluoroscopy arm which was aligned to the angle of the replica probe. As the marker wires are placed inside two of those needles there is therefore an uncertainty in determining the position of the most distal diode using the known distance between the markers. Figure 3-7 illustrates an extreme case where a 30° angle exists between the catheters and probe. Using trigonometry the maximum deviation from the expected 1cm gap between markers is 2mm. The angles for the plastic implants are likely to be greater than that for the metal implants due to them not being rigid and having a tendency to bend anteriorly toward the base of the gland.
Figure 3-7. Uncertainty in diode position due to angle between implant and probe.

Table 3-6. Estimated uncertainties associated with the experimentally measured data using the ISO methodology.

<table>
<thead>
<tr>
<th>Source of uncertainty for the calibration, linearity, reproducibility and radial directional dependence</th>
<th>Type A</th>
<th>Type B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source position within needle (3mm diameter)</td>
<td>1.7%</td>
<td></td>
</tr>
<tr>
<td>Diode position in array</td>
<td>0.6%</td>
<td></td>
</tr>
<tr>
<td>Position of needle &amp; array within geometric phantom</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>Statistical</td>
<td>0.5%</td>
<td></td>
</tr>
</tbody>
</table>

Total uncertainty (8cm measurement distance) 1.9%

<table>
<thead>
<tr>
<th>Source of the uncertainty for the dose rate data</th>
<th>Type A</th>
<th>Type B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diode position in array</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Array position in holder</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Needle placement in tank</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Source position within needle</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Tank distance indicators</td>
<td>0.5%</td>
<td></td>
</tr>
<tr>
<td>Diode calibration</td>
<td>1.9%</td>
<td></td>
</tr>
<tr>
<td>Statistical</td>
<td>0.5%</td>
<td></td>
</tr>
<tr>
<td>Ir-192 reference AKS</td>
<td>5.0%</td>
<td></td>
</tr>
<tr>
<td>TPS algorithm</td>
<td>&lt;1.0%</td>
<td></td>
</tr>
</tbody>
</table>

Total uncertainty (source – detector distance) 5.8%
### Source of uncertainty for the longitudinal directional dependence

<table>
<thead>
<tr>
<th>Source of uncertainty</th>
<th>Type A</th>
<th>Type B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diode position in array</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Array position in solid water</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Distance between needle and array</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Source position within needle</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Statistical</td>
<td>0.5%</td>
<td></td>
</tr>
</tbody>
</table>

**Total uncertainty** 2.1%

### Source of uncertainty for the patient dosimetry measurements

#### Positional

<table>
<thead>
<tr>
<th>Source of uncertainty</th>
<th>Type A</th>
<th>Type B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diode position in array</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Array position in replica probe</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Position of replica probe in relation to implant</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Implant angled with respect to array</td>
<td>2.0%</td>
<td></td>
</tr>
</tbody>
</table>

#### TPS

<table>
<thead>
<tr>
<th>Source of uncertainty</th>
<th>Type A</th>
<th>Type B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ir-192 reference AKS</td>
<td>5.0%a</td>
<td></td>
</tr>
<tr>
<td>TPS algorithm</td>
<td>&lt;1.0%</td>
<td></td>
</tr>
</tbody>
</table>

#### Measurement

<table>
<thead>
<tr>
<th>Source of uncertainty</th>
<th>Type A</th>
<th>Type B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose response of diodes</td>
<td>7.0%</td>
<td></td>
</tr>
<tr>
<td>Diode calibration</td>
<td>1.9%</td>
<td></td>
</tr>
</tbody>
</table>

#### Statistical

<table>
<thead>
<tr>
<th>Source of uncertainty</th>
<th>Type A</th>
<th>Type B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement repeatability (long term)b</td>
<td>2.7%</td>
<td></td>
</tr>
<tr>
<td>Resolution of readout system</td>
<td>&lt;0.1%</td>
<td></td>
</tr>
</tbody>
</table>

**Total uncertainty** 10%

---

*a Calibration certificate states uncertainty in AKS to be ±5% at 1m.

*b Long term (daily/weekly) reproducibility quoted from Waldhausl26 paper.

---

**Table 3-7. Point dose comparison between SWIFT and PLATO treatment planning systems.**

<table>
<thead>
<tr>
<th>Point Dose (cGy) -SWIFT</th>
<th>Point dose (cGy) -PLATO</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1296.62</td>
<td>1296.90</td>
<td>0.02</td>
</tr>
<tr>
<td>1836.57</td>
<td>1836.08</td>
<td>-0.03</td>
</tr>
<tr>
<td>1202.87</td>
<td>1202.88</td>
<td>0.00</td>
</tr>
<tr>
<td>1938.02</td>
<td>1938.07</td>
<td>0.00</td>
</tr>
<tr>
<td>1967.45</td>
<td>1967.20</td>
<td>-0.01</td>
</tr>
<tr>
<td>1533.94</td>
<td>1533.76</td>
<td>-0.01</td>
</tr>
<tr>
<td>1234.59</td>
<td>1234.11</td>
<td>-0.04</td>
</tr>
<tr>
<td>1879.43</td>
<td>1878.91</td>
<td>-0.03</td>
</tr>
<tr>
<td>1884.96</td>
<td>1884.44</td>
<td>-0.03</td>
</tr>
<tr>
<td>1253.48</td>
<td>1253.00</td>
<td>-0.04</td>
</tr>
</tbody>
</table>
3.2 Dosimetry Analysis
A validation between the SWIFT treatment planning system and PLATO BPS was performed for ten points selected in a basic four catheter plan. The maximum difference recorded between the two systems for the ten points analysed was 0.04% indicating that analysis can be performed accurately on either system no matter which system the treatment plan was originally performed upon. Table 3-7 displays the results for the percentage deviations apparent between each point selected for comparison.

The percentage dose differences between the measured and planned data for the five diode positions are shown for each individual fraction in Figure 3-8, Figure 3-9, and Figure 3-10. Data is displayed for the 28 patients’ first fractions, 11 patients’ second fractions and 13 patients’ third fractions. Figure 3-11 displays the percentage deviation between the measured and planned results for the entire treatment course. A total of 71.5% of the measured points lie within ± 10% of the theoretical values. The percentage of points within the ± 10% range varies from diode to diode with the central diode, R3, indicating the highest agreement with 88.7% of data points falling in that range. Table 3-8 lists the percentage of measured points within ± 10% of the theoretical values for each of the five diodes.

R3 was generally positioned in a plane close to perpendicular from the central region of the prostate and usually received the highest signal recorded out of the five diodes. Diodes R1 and R5, in contrast, were positioned at or outside either end of the prostate where signals were weaker due to the diodes being further away from the sources and received from highly oblique angles where directional dependence has a more dominant effect. If a measurement uncertainty of 10% is included in the comparison of dose points and a 10% dose differentiation is tolerated as a treatment delivery error then the proportion of comparison points falling within ± 20% of the calculated dose increases from 71.5% to 95.8%. The statistics for each individual diode are expressed in Table 3-9.

The deviations between the measured and calculated values ranged from -42 to +35% with a mean of -3%. The spread of those deviations in 5% blocks are shown in Figure 3-12 which illustrates a Gaussian like distribution around agreement between the
values. The variation is also displayed by the scatter plot in Figure 3-13, which shows how closely the measurements as a whole are to the ideal.

Figure 3-8. Dose differences between measured and planned diode points for Fraction 1.
Figure 3-9. Dose differences between measured and planned diode points for Fraction 2.

Figure 3-10. Dose differences between measured and planned diode points for Fraction 3.
Figure 3-11. Percentage deviations between measured and theoretical points for the patients first, second and third fractions.

Table 3-8. Percentage measurements for each diode that were within ±10% of the planned values.

<table>
<thead>
<tr>
<th></th>
<th>R1</th>
<th>R2</th>
<th>R3</th>
<th>R4</th>
<th>R5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>71.2%</td>
<td>78.9%</td>
<td>88.7%</td>
<td>77.4%</td>
<td>41.5%</td>
</tr>
</tbody>
</table>

Table 3-9. Percentage of measurement points for each diode that lie within ±20% of the calculated values.

<table>
<thead>
<tr>
<th></th>
<th>R1</th>
<th>R2</th>
<th>R3</th>
<th>R4</th>
<th>R5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>96.2%</td>
<td>96.2%</td>
<td>98.1%</td>
<td>98.1%</td>
<td>90.6%</td>
</tr>
</tbody>
</table>
Figure 3-12. Deviation spread of total data collected from all the diodes.

Figure 3-13. Scatter diagram showing the correlation between the calculated and measured dose points. The linear trend line equates to the ideal scenario where the measured and calculated dose points are equal.
3.3 Prostate volume change during the course of treatment

The change in prostate volume throughout treatment was examined for the 15 patients who had more than one fraction imaged. The percentage change in volume was recorded between fractions 1 & 2, 2 & 3, and 1 & 3 which were then separated into corresponding time periods from implantation. The average deviations observed for the base, mid and apex were all determined separately being 10.2, 8.8 and 7.1% respectively showing a variation of 3% between the three areas of the prostate. They were therefore averaged to determine the overall average change in volume (overall difference between fractions 1 and 3) for the treatment which was 8.5%, with the magnitude of either an increase or reduction ranging from 0.1 to 19.0%.

A Paired t-test was performed using the volumes determined for fractions 1 and 2 and fractions 1 and 3 resulting in p values of 0.32 and 0.36 respectively, indicating that no observable trend was evident linking the degree of prostate volume change between fractions. The results for each patient evaluated are separated into time intervals between fractions and depicted in Figure 3-14.

Implant DVH statistics were calculated in PLATO for each of the fractions imaged and compared with any deviations from the first fraction noted. The percentage deviations between volumes receiving 100% and 150% of the prescribed dose are shown in Figure 3-15 for fractions 1&2 and fractions 1&3. For an increase in V100 there is a corresponding decrease in V150 and vice versa for all patients. Patients who experienced a prostate volume change of greater than ± 10% also exhibited a related change in V100 and V150. For volume changes greater than 10% a corresponding change in V100 of <5% and change in V150 of >10% was evident. The average change in V100 and V150 for this group of patients was 0.2 and 3.1% respectively with ranges of -3.7 to 1.9% and -12.6 to 16.8%. Paired t-tests were performed on the sets of DVH volumes in cubic centimetres to analyse whether the changes in V100 and V150 were significant. For the V100 analysis P values of 0.34 and 0.26 were produced for fractions 1 and 2 and between 1 and 3 indicating that the variation in volumes is due to chance. Similarly, P values of 0.14 and 0.22 were recorded for the V150 data which does not confirm that the change in V150 is significant.
Figure 3-14. Percentage prostatic volume change for various time intervals between fractions.
3.4 Prostatic oedema connection to required catheter movement

Any movement, physical or indexer offset, required to shift the source to its planned position within the prostate was recorded for each patient fraction. Each shift was then related to the percentage volume change determined for that fraction. No direct correlation was made between a change in prostatic oedema and catheter position adjustment as significant volume changes of greater than 10% did not necessarily equate to a required adjustment which is graphically depicted in Figure 3-16. Only 3 out of the 15 patients studied volumetrically required physical catheter adjustments greater than 10mm. Of these, 2 patients appeared to experience significant volumetric change (~17%). Surprisingly a decrease rather than an increase in volume was apparent for both patients. When the shifts required for all 28 of the patients studied were examined it became apparent that larger physical moves (10-30mm) coincided with the patients that were not able to be imaged for second and third fractions with 8 out of 13 patients falling into this category.

Figure 3-15. Differences in DVH statistics between fractions 1&2 and fractions 1&3 for V100 and V150.
There was no correlation apparent between patient age and catheter movement indicated by the spread of results in Figure 3-17. The results were not normally distributed so a test for significance was not applied.

Figure 3-16. Relationship between the percentage volume change between fractions and the catheter movement required to reposition the implant with regards to the original plan.

Figure 3-17. Relationship between patient age and required catheter movements for fractions 2 and 3.
3.5 Connection between implant DVH analysis and control/morbidity.

Patient follow up data was collected for all of the patients studied volumetrically to see whether a link existed between a decreased V100 and lack of control or an increased V150 and a higher degree of acute morbidity. Only one patient exhibited lack of local control in the follow up period of 12 – 18 months, discovered by his Oncologist due to a PSA reading of 11.5 which was an increase on prior tests. This patient had exhibited a slight increase in his V100 and decrease in V150 statistics over the course of treatment. His Oncologist attributed the rise in PSA to micrometastatic disease that was present initially but not included in his staging prior to radiotherapy. Only two of the patients studied who experienced urinary problems showed an increase in V150 between their first and third fractions. These included acute urinary symptoms in patient “o” which had diminished after 5 months and nocturia (x2) for patient “g”. Other patients experiencing urinary problems such as frequency, urgency and nocturia did not exhibit and increase in V150 with some even experiencing a decrease. A total of five out of the fifteen patients evaluated were recorded to have experienced urinary problems as a result of their overall treatment with problems ceasing in the long term. One patient exhibited slight bowel irritation. No post radiotherapy problems were recorded for 9 of the 15 patients.

3.6 Plastic vs. Stainless steel catheter analysis

16 of the 28 patients were treated with metal needles while the remaining 12 were treated with plastic. The Oncologists’ reason for changing from metal to plastic was the belief that the metal needles caused an increase in hematuria compared with the plastic and therefore cause patients to have a longer stay in hospital due to increased bleeding and clot formation in the bladder. Of those studied volumetrically over the three fractions 10 from 15 were metal implants with the remaining 5 plastic.

A total of 35 fractions using metal needles were compared dosimetrically to the theoretical planned data as opposed to 19 fractions using plastic catheters. A comparison between the absolute dose differences was made between the two for each diode as well as the total number of measurements for each needle type with the averages of the absolute magnitudes of discrepancies shown in Table 3-10. The average
results for the total diode comparison are very similar with an average magnitude of discrepancy from the planned dose values for the metal and plastic implants being 0.123 ± 0.089 Gy and 0.121 ± 0.103 Gy respectively.

The numbers of patients requiring total catheter movements (including physical and indexer corrections) ≥ 10mm were studied with 11 out of the 28 patients falling into this category. Of these 11 patients 7 had plastic implants, with a maximum physical movement of 30mm required for one patient who was subsequently replanned with CT before his second fraction. The 4 patients with metal implants all required moves ≤ 12mm. Of these 11 patients 8 were not able to be scanned for second or third fractions so volumetric analysis was not able to be performed. 6 out of those 8 patients were implanted with plastic catheters.

Of the 13 patients who were unable to be scanned for subsequent fractions 6 were implanted with metal needles. 6 out of the 7 patients with plastic implants that could not be scanned required large (10mm – 30mm) interfractional catheter movements. A summary of the metal and plastic comparison is displayed in Table 3-11. With regard to the dosimetry analysis, neither the plastic or metal implants tended to agree more than the other to the calculated data. The type of needle material used for implantation does therefore not affect implant dosimetry.

<table>
<thead>
<tr>
<th></th>
<th>Metal (Gy)</th>
<th>Plastic (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Diode Av</td>
<td>0.078</td>
<td>0.105</td>
</tr>
<tr>
<td>StDev Av</td>
<td>0.060</td>
<td>0.067</td>
</tr>
<tr>
<td>(Total)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>StDev (Total)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3-11. Summary of comparison between metal and plastic needle insertions.

<table>
<thead>
<tr>
<th></th>
<th>Metal</th>
<th>Plastic</th>
</tr>
</thead>
<tbody>
<tr>
<td># Patients</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td># Studied Volumetrically</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td># Requiring adjustments ≥ 10mm</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Maximum adjustment</td>
<td>12mm</td>
<td>30mm</td>
</tr>
<tr>
<td># Not studied volumetrically who had adjustments ≥ 10mm</td>
<td>2</td>
<td>6</td>
</tr>
</tbody>
</table>

3.7 Reconstruction Uncertainty analysis

The effects of repeated catheter reconstruction on the dosimetry and volume comparisons were evaluated for two patients, one with clear imaging of the catheter positions, and the other with poorer image quality where the positions of the anterior lateral needles were quite difficult to determine. The variation in theoretical diode doses between the first, second and third fraction reconstructions for both patients are shown in Table 3-12. The maximum variation in dose for Patient 1 was 0.9cGy compared with 1.2cGy for Patient 2 which equates to less than 1% variation for delivered doses of 150cGy, which is of the order of that delivered to the diodes inside the rectum. The differences in the volumes containing 100%, 150%, 200% and 300% of the prescription dose were recorded for both patients and are displayed in Table 3-13. The magnitudes of the variations were similar for both patients with a maximum of 1.5cc seen for Patient 1 with the 150% comparison, and 1.6cc for the 100% comparison in Patient 2.

Table 3-12. Diode point dose differences between the three reconstructed implants.

<table>
<thead>
<tr>
<th>Diode</th>
<th>Patient 1 (difference in cGy)</th>
<th>Patient 2 (difference in cGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>0.3 0.3 0.5 0.5 0.3 0.5 0.8 0.9 0.7 1.1</td>
<td>0.5 0.7 0.9 0.8 0.4 0.6 0.9 1.1 0.9 1.2</td>
</tr>
<tr>
<td>1-3</td>
<td>0.5 0.7 0.9 0.8 0.4 0.6 0.9 1.1 0.9 1.2</td>
<td>0.2 0.4 0.4 0.3 0.2 0.1 0.2 0.2 0.2 0.1</td>
</tr>
<tr>
<td>2-3</td>
<td>0.2 0.4 0.4 0.3 0.2 0.1 0.2 0.2 0.2 0.1</td>
<td></td>
</tr>
</tbody>
</table>
Table 3-13. Differences in DVH statistics based on the volumes receiving 100%, 150%, 200% and 300% of the prescribed dose.

<table>
<thead>
<tr>
<th></th>
<th>Patient 1 (difference in cc)</th>
<th>Patient 2 (difference in cc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>0.1 0.0 -0.1</td>
<td>0.0 -1.6 -1.5</td>
</tr>
<tr>
<td>150</td>
<td>-1.4 -1.5 -0.1</td>
<td>-0.9 -0.8 0.1</td>
</tr>
<tr>
<td>200</td>
<td>-0.2 -0.3 0.0</td>
<td>-0.2 0.0 0.3</td>
</tr>
<tr>
<td>300</td>
<td>0.0 -0.1 0.0</td>
<td>0.0 0.3 0.3</td>
</tr>
</tbody>
</table>

The variations in the volume comparison indicated larger differences between the two patients. These were compared using the average distance between the catheters and the centre of mass \(d_c\) raised to the cubic power. The values recorded for the apex, reference and base planes were averaged to determine a global volume. The maximum difference observed between the three reconstructed implants for Patient 1 was 0.5% compared to 4.4% for Patient 2. Even though larger volume differences were apparent for Patient 2, they did not equate to obvious differences in dosimetry.
Chapter 4: Discussion

A commercial semiconductor array was evaluated for routine clinical use by initially examining the detectors’ dosimetric characteristics before performing in vivo dose measurements in patients receiving HDR brachytherapy for the treatment of prostate cancer. The patient results were then compared with related point doses selected from the real time planning system used to determine their treatment plan. Twenty-eight patients treatments were studied whose ages ranged from 54 – 82 years with an average of 69.5 years.

Diode Dosimetric Properties

The linearity of the diodes response with dose is comparable to that of ion chamber measurements. The short term reproducibility of <0.5% was excellent and comparable to the measurements completed by Waldhausl et al. Long term reproducibility was not examined but the daily and weekly reproducibility measured by that group for the same diode system resulted in a standard deviation of 2.7 ± 1.5% for both time periods indicating that performing weekly calibrations is sufficient to maintain dosimeter accuracy. They also determined that the angular dependency was ± 0.9% in the longitudinal direction and ± 2.7% in plane, which could be explained by the presence of the cables. In comparison, the radial and longitudinal directional dependence determined in this study was ± 3% and 2.2 ± 3.6% respectively. The exact details regarding the measurement set up employed and whether or not a phantom was used were not published and may account for the differences evident between the studies. A contributor to the uncertainty in the present study was the accuracy of the planning system in calculating dose at distances greater than 7cm from the source. Temperature dependence was less apparent than demonstrated in the Waldhausl publication, with a maximum of 0.2% deviation measured for a clinical temperature change of 12°C compared to the 0.5% per °C presented by them. No dose rate dependence was observed with all variations from the theoretical being within the measurement uncertainty. The overall measurement uncertainty of 10% determined in this study is close to the 7% expressed by Waldhausl.
**Rotational Symmetry**

As the five diodes are encapsulated in a synthetic sheath and connected by identical wiring it was difficult to identify each diodes’ individual orientation with fluoroscopy. It could however be seen that the system had the shortcoming that the diodes were rotated differently with respect to each other in a longitudinal direction as well as slightly in a radial direction. This rotation may account for the differences seen in the directional dependence for the individual diodes. The fluoroscopic images also showed that not all diodes looked to be positioned in the exact geometric centre of the array. This positional uncertainty was an important aspect to consider when evaluating the overall uncertainty in the dose comparisons.

**Spatial Resolution**

Due to the effect of the inverse square law, positional errors have a much greater significance at shorter distances than at longer ones. For example a 0.5mm positional error at a distance of 1cm from the source will produce a 9% deviation from the theoretical value, 5% at 2cm, 2% at 5cm, and 1.2% at 8cm. Knowing the exact position of the diodes in relation to the source is therefore crucial in determining whether they can accurately measure dose at clinical distances. Any inaccuracies related to the reconstruction could therefore significantly impact upon results if catheters close to the diodes had considerable dwell times.

**Impact of Image Quality**

An assumption that has been made is that the catheter position reconstruction using the ultrasound image was accurate for every fraction of every patient. This was not the case and is a source of error in the results, especially for subsequent fractions where image quality was inferior to the initial planned fraction. Anterior needles were particularly difficult to identify for some patients due to being shadowed by posterior needles closer to the US probe. In those cases, the first fraction reconstruction was assessed to determine the most probable catheter alignment in relation to adjacent catheters.

The impact of inaccurate reconstruction on the diode results would vary from patient to patient depending upon the distance between the diodes and the particular catheter, the number of source positions in the catheter, and the dwell times of those source positions. The small investigation conducted to examine the differences between the
effects of repeated catheter reconstruction on the dosimetric and volume analysis indicated that even though a variation in volume may result, the difference that the position variation has dosimetrically is small. Where those differences are in relation to the anatomical structures though is not known as the organ DVH statistics were not analysed. For the two patients investigated poor image quality, leading to possible inaccurate catheter positioning, appeared comparable to the implant reconstructed with the superior image quality. As only two separate patients’ fractions were examined to determine this, a larger study investigating the effect of image quality on implant position reconstruction and therefore patient dosimetry would be required to come to a global conclusion on the importance on reconstruction accuracy.

**Measured vs. Calculated Dose Points**

A 72% level of agreement between measured and calculated values varying less than 10% is relatively high compared to other studies investigating rectal dosimetry. The study conducted by Waldhaeusl et al., for example, found a difference in dose of greater than 10% in over 65% of their clinical cases and determined that their method was sufficiently accurate and reproducible for clinical applications provided that the position of the diodes are determined accurately. Toye et al. showed a variation between -36 and +101% for 31 patients with an average difference of 20%. They proposed setting an investigation level at 20%, which was defined in terms of a 10% dose excess combined with a 10% uncertainty in the measurements. If that level was reached then the cause would be investigated and evaluated so that a clinical decision on whether the case would require re-planning could be made. If the same ideals were employed for this study then over 95% of the dosimetric measurements would fall within ±20% calculated values, assuming a measurement uncertainty of 10%. Setting a tolerance on what level of disagreement is unacceptable and determining the clinical ramifications is difficult and patient specific. Due to the high dose gradients in brachytherapy the most important aspect of in vivo dosimetry program is to ensure gross dosimetric delivery errors do not occur.

Even though the results indicated a variation from the calculated values of between -42 and +35%, not all diodes in the one measurement experienced that same variation. In general, when large discrepancies were evident it was only for one or two of the five diodes in the measurement, with the remaining recording values much closer to that
expected or deviating in the opposing direction. A criterion would therefore also have to be set based on which points would be selected for comparison and what significance single measurements indicating a large deviation would have clinically.

Diodes 1 and 5 displayed a significantly higher level of disagreement with the planned data in comparison with diodes 2, 3 and 4. This was likely to be attributed to the high degree of directional dependence shown by the diodes as the angle away from perpendicular increases, with sources at large angles from the diodes contributing the majority of measured signal. For diode to bottom row catheter distances of 2cm, these angles could be as large as 70° for certain source positions. Due to the signal acquired coming from hundreds of positions in the implant, it was difficult to quantify the total effect of longitudinal directional dependence as the magnitude of the effects varies with angle.

**Volume Expansion due to Oedema**

Isotropic expansion of the prostate was assumed for the simple volumetric analysis when in reality some areas of the prostate may swell while other regions shrink down.\textsuperscript{45} The analysis was based upon catheter positions and not anatomy though in an attempt to make the evaluation independent of patient to patient variations and the subjective nature of contouring. A true representation of the actual anatomical changes that occurred within each patient would only be accurately defined by an MRI at each fraction, which was not a feasible form of imaging considering the cost and logistics. The clinically significant aspect is prostate DVH, not implant DVH. Even though the study conducted shows that a variation in catheter expansion/contraction, and therefore volume variation, is patient specific it does not provide any anatomical information regarding where increases in hot spots due to a rise in V150, or a reduction in coverage due to a decrease in V100 occur. The only connection that can be investigated is whether an apparent increase or decrease in DVH statistics due to an apparent change in volume is related to patient morbidity.

Volumetric analysis of the prostate over the course of treatment showed significant variations between patients. The magnitude of the average change for all patients was 8.5% with either an increase or reduction ranging from 0.1 to 19%. This is similar to that found by Kim \textit{et al}\textsuperscript{45} who showed an average change of 7.8% with a range of 2% to
17%. A smaller difference was presented by Martinez et al\textsuperscript{36} who found a 2.7% average change in volume with a range of -13.7% to 17.3%. If sign is included then the average volume change of this study is -2.4% with a range of -19.0% to 11.3%. These volume changes correspond to average dosimetric variations in V100 of 0.2% ranging from -3.7 to 1.9% and 3.1% for V150 ranging from -12.6% to 16.8%.

The variations recorded from the first fraction statistics did not appear to affect any of the patient outcomes with no lack of control or acute morbidity able to be linked with either a decrease in V100 or increase in V150. This shows that the initial treatment plan generated is sufficient for the remainder of the fractions delivered and agrees with the conclusions drawn by Martinez et al\textsuperscript{36}. They determined that the majority of prostatic volume change occurs in the time between an initial scan of the prostate prior to any needle insertion and the planning scan prior to the treatment delivery of fraction 1, with little further change throughout the treatment. This presumes that volume change is caused by either intraprostatic bleeding and/or oedema inflicted by the mechanical trauma of needle insertion and that little change occurs after this time due to no further trauma being inflicted to the prostate.

Of the 15 patients examined volumetrically 6 experienced acute urinary effects post treatment. Of those 6 only 2 showed an increase in their V150 DVH statistics with the others either indicating little change or a reduction in their V150 data. Knowing the position of the hot spots relative to the urethra would provide more clinically relevant information and allow an investigation of a relationship between the two to occur. An increase in V150 in the periphery of the prostate is unlikely to cause adverse effects and may even increase the probability of tumour control.

The adjustment of catheter positions relative to the three gold seeds in the prostate was completed by taking the average move required by two catheters in the central region of the prostate. This method assumes that all the needles move the same distance and that there is no cranial-caudal motion relative to each other. The error in this assumption was minimised in this study by marking the catheters relative to the template at implantation, with any necessary movements moved the same amount using a ruler. Based on the various methods of determining tumour control probability (TCP) performed by Tiong et al\textsuperscript{37} a 3mm displacement resulted in most patients having a TCP
that was close to or greater than 95% of the original. Based on these results any small motion of the catheters relative to each other would not adversely effect patient treatment.

There was no correlation evident between a change in implant volume between fractions and the catheter adjustment required to position the implant in the same place relative to the initial plan. Larger variations in volume did not necessarily equate to large required catheter moves and small variations were sometimes associated with larger movements. Similarly, no correlation was seen between patient age and apparent prostate mobility, indicated by the catheter movements required for second and third fractions to match the patients implant to that planned for the initial fraction.

**Metal vs. Plastic Needles**

Metallic implants accounted for 16 of the 28 patients studied. Of this 16, 63% were able to be imaged adequately so that a volumetric analysis could be performed. Conversely 12 of the 28 patients were implanted with plastic catheters with 42% analysed volumetrically. 39% of the patients studied required catheter adjustments ≥10mm. 73% of the patients who required those large catheter adjustments were not able to be scanned for their second or third fractions. There is evidence to suggest that metal implants are more geometrically sound as 64% of those patients that required catheter adjustments had plastic implants which accounted for 58% of the total patients with plastic implants. In comparison only 25% of the patients implanted with metal needles required adjustments ≥10mm.

Clinically, no difference was evident between the patients implanted with plastic as opposed to metal needles. The dosimetric study produced very similar results for both sets of patients indicating that the choice of needle material did not affect the implant dosimetry. Similar variations in volume change and DVH statistics were seen for both sets of patients demonstrating that following needle position adjustment, if required, the implants are effectively the same.

**Ultrasound Replica Probe**

The geometric consistency provided with the introduction of the replica ultrasound probe was an improvement on past techniques where rectal dosimetry proved to be
difficult, in most cases due to the anatomical changes that can occur between imaging and treatment times. A disadvantage with the process is that it can only be practically employed in departments that have their own operating theatre as it is based on a real time planning process. A second disadvantage is the possibility that the replica probe system cannot always be applied for subsequent fractions due to inadequate pain relief or the development of faecal matter inhibiting imaging. This would mean that only select patients could have their dosimetry tracked through their entire treatment as shown in this study where only 15 of the 28 patients investigated were able to have their second and third fractions analysed.

**Barriers to Implementation**

The process of performing dosimetry verification long term on a regular basis may not be economical due to the extra work involved. Each fraction requires the set up of the ultrasound unit and planning system with the addition of imaging and matching anatomy which adds approximately 10 to 15 minutes to each fraction. In addition the time required to retrospectively replicate the original plan for subsequent fractions and analyse dosimetry can take approximately 2 hours per patient, with this depending upon the extent of adjustments required.

If anatomical dosimetric data were to be collected, the Oncologists would have to contour the prostate and each critical structure for each fraction which is also a time consuming procedure. Even if the Oncologists were able to contour each patient fraction, the subjective nature of contouring, and degradation of image quality may cause inconsistencies between fractions and subsequent DVH analysis may not be consistent.

The initial fraction alone could readily be employed into general practice and be adequately used to identify dosimetric errors at the time of the first treatment with little extra work involved. The in vivo program may therefore be more viable long term if only the initial fraction is examined with the initial diode readings used to decide on whether treatment will continue as planned or be re-examined. That decision would have to be based upon the extent of disagreement between the planned and measured values, whether all or only a few of the diodes are indicating this disagreement and where the diodes are positioned relative to sources.
Chapter 5: Conclusion

In vivo dosimetry is an important verification tool in avoiding gross errors in radiotherapy applications. Due to high dose gradients and issues with dosimeter localisation, dosimetry for brachytherapy has historically been difficult to accurately measure. This study has shown that a commercially available PTW diode array (T9112) can effectively be incorporated into an in vivo dosimetry program as long as the properties and limitations of the device are fully understood and accounted for. Positional discrepancies and inherent diode characteristics such as directional dependence can greatly influence results, as shown in this investigation. By accounting for the related uncertainties, a reliable dosimetry system can be established to an accuracy of ±10%.

Changes in prostate volume can occur throughout the duration of a patients’ treatment. Following the analysis of individual patients dosimetry data, volume changes between fractions and related variations in DVH statistics, and control rates, it was determined that the treatment plan derived based upon the patient anatomy and implant positioning for fraction 1 could adequately be applied for subsequent fractions without negatively impacting upon patient outcomes.

Catheter movement relative to the prostate can occur between fractions. The data collected from the small set of patients did not indicate a correlation between the size of the adjustment required to restore the original relation between the implant and prostate and the extent of swelling in the gland or between the moves required and patient age. The mobility of the gland therefore appears to be patient specific.

The in vivo dosimetry program employed at the Mater hospital during 2007 and 2008 could adequately be used to detect gross errors in treatment delivery for HDR prostate brachytherapy, and if utilised during delivery of the patient’s first fraction only, become part of an ongoing dosimetry program that validates the treatment planning system at five points and does not require any additional staffing or resources. Retrospective analysis indicates that treating subsequent fractions with the patient’s initial treatment plan has no detrimental effects on patient outcomes as long as an assessment of the position of the implant in relation to the prostate is conducted prior to treatment.
Appendix A – Expression of Uncertainties

The uncertainties for the measurements made in this study were estimated using the methodology provided by the International Organisation for Standardisation (ISO) in the document entitled “Guide to the Expression of Uncertainty in Measurement” and Appendix IV in IAEA TRS-398.

An error is traditionally defined as the difference between a measured and a true value. It is made up of a random and a systematic component which have both a numerical value and a sign and can theoretically be corrected for to obtain the true value. In reality though, errors are not known exactly and are estimated in the best possible way so that it is the uncertainty of these qualities which are of interest. The uncertainty of a measurement characterises the dispersion of the values that could be reasonably attributed to the measurand and is usually assumed to be symmetrical, having no known sign.

Uncertainties of measurements are classified into type A and type B and are generally expressed as relative standard uncertainties. Type A standard uncertainties are those determined by statistical analysis of a series of measurements, whereas type B uncertainties cannot be estimated statistically and are intelligent guesses or scientific judgements of the non-statistical uncertainties related to the measurement.

Type A Uncertainties

If a measurement of a dosimetric quantity \( x \) is measured \( N \) times, then the best estimate for \( x \) is the arithmetic mean value

\[
\bar{x} = \frac{1}{N} \sum_{i=1}^{N} x_i
\]

The average uncertainty for an individual result can be characterised by the standard deviation

\[
\sigma_x = \sqrt{\frac{1}{N-1} \sum_{i=1}^{N} (x_i - \bar{x})^2}
\]
The quantity of interest is generally the standard deviation of the mean which is given by
\[
\sigma_x = \frac{1}{\sqrt{N}} \sigma = \frac{1}{\sqrt{N(N-1)}} \sum_{i=1}^{N} (x_i - \bar{x})^2
\]
The standard uncertainty of type A, denoted by \( u_A \), is defined in this study as the standard deviation of the mean value, i.e. \( u_A = \sigma_x \).

**Type B Uncertainties**
Measurement uncertainties that cannot be estimated by repeated measurements are referred to as type B uncertainties. They include influences such as the set up in the measuring process, application of correction factors and physical data taken from the literature. It is often assumed that this type of uncertainty has a probability distribution that corresponds to an easily recognisable shape such as a rectangle, which has equal probability within the given limits, or a normal (Gaussian) distribution. There are no rigid rules for estimating type B standard uncertainties and they can be derived by estimating the limit beyond which the value of a factor is not going to lie, with a fraction of that limit taken as \( u_B \) according to the distribution assumed.

**Combined and Expanded Uncertainties**
The statistical rules for combining variances, which are the squares of a standard deviation, can be used to combine type A and type B uncertainties as they are both estimated standard deviations. The combined standard uncertainty \( u_C \) associated with a quality is a quadratic summation of type A, \( u_A \), and type B, \( u_B \), uncertainties:
\[
u_C = \sqrt{u_A^2 + u_B^2}
\]
If the combined uncertainty is assumed to exhibit a Gaussian distribution than the standard deviation corresponds to a confidence limit of 68%. By multiplying this by a suitable coverage factor, \( k \), an expanded uncertainty can be determined which will act to increase confidence limits. For example, values of the coverage factor of \( k = 2 \) or \( 3 \) correspond to confidence limits of about 95 or 99% which are more useful in determining the overall accuracy of the measurement quality.
References

2. Cancer Institute NSW. Fact Sheet: Prostate Cancer in NSW. (CI) 080360.
3. American College of Radiology. Practice guideline for transperineal permanent prostate brachytherapy. 2005


