Daily Image Guided Radiation Therapy for Prostate Cancer:

An assessment of treatment plan reproducibility.

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A thesis submitted in fulfilment of the requirements of the degree of Doctor of Health Science.

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Declaration

I hereby declare that this thesis is my original work. To the best of my knowledge it contains no previously published material unless otherwise acknowledged or has been accepted for an award or diploma by any other institution of higher learning.

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Summary:

It is well documented that for prostate cancer patients undergoing radiation therapy, there is a correlation between target volume displacement and changes in bladder and rectal volumes. However, these studies have used a methodology that has captured only a subset of all treatment positions. This research used daily Computer Tomography (CT) imaging to comprehensively assess organ volumes, organ motion and their effect on dose, something that has never been performed previously, thus adding considerably to the understanding of the topic.

Daily CT images were obtained using a Siemens Primus Linear Accelerator equipped with an in-room Somatom CT unit in the accelerator suite, marketed as ‘Primatom’, to accurately position the patient prior to treatment delivery. The internal structures of interest were contoured on the planning workstation by the investigator. The daily volume and location of the organs were derived from the computer to assess and analyse internal organ motion. The planned dose distribution was then imported onto the treatment CT datasets and used to compare the planned dose to i) the actual isocentre, where the isocentre was actually placed for that fraction, ii) the uncorrected isocentre, by un-doing any on-line corrections performed by the treatment staff prior to treatment delivery, and iii) the future isocentre, by placing the isocentre relative to internal organ motion on a daily basis.

The results of this study did not confirm a statistically significant decrease in rectum volumes over time (hypothesis 1), however large fluctuations in bladder volume were confirmed (hypothesis 2). Internal organ motion for the rectum and bladder was demonstrated to be related to organ filling. Ideal planning volumes for these organs have been reported to minimise systematic and random uncertainty in the treatment volumes. An observed decrease in prostate volume over time, a systematic uncertainty in the location of the prostate at the time of the planning CT scan and a significant relationship between prostate centre of volume and rectum and bladder volumes has resulted in a recommendation that patients should be re-scanned during treatment to ensure appropriate clinical target volume coverage. A significant relationship between rectal and bladder volumes and the dose delivered to these organs was found (hypothesis 3). The dose delivered to the planning target volume was not related to the rectal or bladder volumes, although it was related to the
motion of these organs. Despite these results only minimal effects on the dose delivered to any of the three isocentres occurred, indicating that the planned dose was accurately delivered using the methodology presented here (hypothesis 4). However the results do indicate that the patient preparation instructions need to be improved if margins are to be reduced in the future.

It is unrealistic to assume that Image Guided Radiation Therapy will ever become routine practice due to infrastructure costs and time limitations. This research will inform radiation therapy centres of the variables associated with prostate cancer treatment on a daily basis, something that has never before been realistically achievable. As a result centres will be able to devise protocols to improve treatment outcomes.
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1. Introduction

Prostate cancer is to men what breast cancer is to women. Both have the highest incidence of cancer for their sex and radical radiation therapy is a mainstay of curative treatment.

The development of Prostate Specific Antigen (PSA) testing has lead to an increase in early detection of low stage localised prostate cancers. However, “there is no recognised single best treatment for localised prostate cancer, as each patient is unique and different. The current treatment options for localised prostate cancer include surgery, radiation therapy, hormone manipulation and observation as well as various combinations thereof” (Eng, Thomas & Herman 2002, p. 239).

Radiation therapy can consist of External Beam Radiation Therapy (EBRT) and/or Brachytherapy (radioactive implant). The most common form of radiation therapy to the prostate is EBRT. Three-Dimensional Conformal Radiation Therapy (3D-CRT) is widely used to treat localised prostate cancer during a standard fractionated course of around seven to eight weeks. The intention of 3D-CRT is to deliver high target doses to the prostate while optimally reducing irradiation of critical non-target structures such as the rectum and the bladder. This has been made possible by advances in imaging techniques, planning computer systems and treatment technology (Martinez et al. 2001; Fiorino et al. 1998). As a result of 3D-CRT the incidence of severe bladder and rectal toxicity has decreased compared to previous treatment techniques. The continued use of 3D-CRT relates to its suitability for “medically non-surgical candidates, relatively low morbidity, cost, preservation of normal sexual function in some patients, less time lost from work and patient preference.” (Eng, Thomas & Herman 2002, p. 239)
1.1 Importance of prostate positioning

During a seven to eight week course of radical External Beam Radiation Therapy (EBRT) there are several variables that affect the accuracy with which the patient’s treatment can be delivered. These include daily patient set-up uncertainties, organ volume uncertainties and organ motion.

Numerous authors have demonstrated that there is a correlation between target volume displacement and variations in rectal and/or bladder volume (Antolak et al. 1998; Dawson et al. 1998; Miralbell et al, 2003a; Roeske et al. 1995; Zelefsky et al. 1999; Zellars et al. 2000). These volumes are affected on a daily basis by fluid intake, fibre supplements and patient diet. Although conventionally the accuracy of treatment set-up in prostate cancer patients has been verified according to bony anatomy, the bladder status, rectal distension and pelvic muscle contraction may all affect daily prostate motion. Patient treatment position and stabilisation methods also affect treatment accuracy.

These uncertainties all contribute to an inability to deliver the planned dose distribution which may lead to an under-dosage of part of the target or to the over-dosage of healthy tissues.

Throughout this thesis anterior-posterior refers to the Z direction on the Cartesian axis and will be abbreviated to AP, superior-inferior (SI) refers to the Y direction and right-left (RL or Lateral where more appropriate) refers to the X direction.
1.2 Hypotheses

Based on the published literature and clinical observations, the following hypotheses were proposed in the context of prostate radiotherapy and tested during this research study.

1.2.1 Hypothesis 1: Rectal volumes decrease

That rectal volume decreases across a course of radiotherapy.

1.2.2 Hypothesis 2: Bladder volumes fluctuate

That bladder volume fluctuates/alters during a course of radiotherapy.

1.2.3 Hypothesis 3: Reduced rectal volumes lead to increased dose

That reducing rectal volume leads to increasing rectal radiation dose; i.e. that more of the rectum is inside the high dose region.

1.2.4 Hypothesis 4: Current instructions are inadequate

That the current patient preparation instructions regarding bladder filling and rectal emptying are inadequate to maintain the planned dose distribution.