Post-implant dosimetry analysis of brachytherapy patients using pre and post-implant MRI

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POST-IMPLANT DOSIMETRY ANALYSIS OF BRACHYTHERAPY PATIENTS
USING PRE AND POST-IMPLANT MRI

by

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Bachelors in Secondary Education
Arizona State University
1990

A thesis submitted in partial fulfillment of the requirements for the

Master of Science Degree in Health Physics
School of Allied Health Sciences
Division of Health Sciences

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ABSTRACT

Post-implant Dosimetry Analysis of Brachytherapy Patients Using Pre and Post-implant MRI

by

Deana Tuttle

Dr. Phillip Patton, Examination Committee Chair
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University of Nevada Las Vegas

Post-implant dosimetry analysis is a critical step in brachytherapy for identifying the quality of the implant based on seed localization in relation to the volume of the prostate. However, the accuracy of post-implant dosimetry analysis is dependent on accurate delineation of the prostate from surrounding tissue in post-implant CT images. Research has shown that adequately delineate the prostate from surrounding tissue in CT images is difficult, resulting in significant variation between the dose received by the prostate and the dose prescribed by the physician. This research compared prostate volumes delineated from pre-implant US, post-implant CT, and pre and post-implant MR images in order to develop a more reliable methodology to delineate the prostate. The results illustrated the superiority of MR imaging over CT imaging in delineation of the prostate thereby producing more individual and mean dosimetry values, D90 and V100, above their respective cut points of 140 Gy and 85%.
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CHAPTER 1

INTRODUCTION

1.1 Purpose

Permanent seed implant brachytherapy has been proven to be a successful treatment for patients with early stages of prostate cancer with approximately 40,000 procedures being performed in 2000 (Potters et al. 2001). The increase in permanent seed brachytherapy by clinical physicians has propelled research into developing better methods of determining dose to the prostate by accurately delineating the prostate from surrounding tissue using computed tomography (CT) and magnetic resonance (MR) imaging.

Post-implant dosimetry analysis for permanent seed implant brachytherapy patients is a crucial step in identifying the difference in the dose prescribed by the physician in pre-planning to the actual dose delivered to the prostate and surrounding tissue during surgery. In addition, it provides the physician a means of evaluating the seed distribution in relation to prostate volumes for future brachytherapy procedures. Though research agrees that post implant dosimetry analysis is critical for evaluating the quality of the implant, currently there appears to be a lack of standard procedures or guidelines in post-implant dosimetry for practicing physicians (Nag et al. 2000).

Post-implant dosimetry analysis identifies the extent patients are being under or overdosed. Therefore, the purpose of this research is to compare the actual total dose the
prostate received to the dose prescribed by the physician in Iodine-125 brachytherapy patients based upon prostate volume differences by (1) determining differences in prostate volumes calculated from pre-implant transrectal ultrasound (TRUS) images and pre-implant magnetic resonance (MR) images, (2) determining differences in prostate volumes calculated from post-implant computed tomography (CT) images and post-implant MR images, (3) determining differences in prostate volumes by fusing pre-implant ultrasound images with post-implant CT and MR images, (4) determining the differences in the D90 value, the percent of dose delivered to 90% of the prostate volume, the V100 value, the percent of the prostate volume receiving 100% of the dose, and the dose prescribed by the physician in the pre-planning stage to the total dose calculated in the post-implant stage based upon prostate volumes differences, and (5) determine systematic differences in MR and CT modalities by eliminating the problem of delineation of the prostate from surrounding tissue by imaging phantoms of known volumes.

1.2 Anatomical Characteristics of the Prostate and Surrounding Tissue

The prostate is a chestnut-sized organ located between the bladder and urogenital diaphragm, just in front of the rectum. It weighs approximately 8 grams and has the dimensions of 4 cm at the base, 2 cm anterior-posterior, and 3 cm vertically. It is situated in the pelvis cavity just below the internal urethra orifice and the symphysis pubis and above the superior fascia of the urogenital diagram. The prostate surrounds the urethra with the ejaculatory ducts passing through the posterior section of the prostate from the seminal vesicles and connecting with the urethra (Gray et al. 1918).
The prostate is characterized by the base, apex, and four surfaces, the posterior surface, the anterior surface, and two lateral surfaces. The base of the prostate is located inferior to the wall of the bladder where the urethra enters the prostate’s anterior region. The apex of the prostate is located at the superior fascia of the urogenital diagram as shown in Fig. 1.

Figure 1. Illustration of the prostate showing the seminal vesicles, prostatic urethra, apex, and base of the prostate (Bostwick et al. 1994).

The posterior surface is about 4 cm from the anus and is separated from the rectum by its sheath and connective tissue. The anterior surface of the prostate is located about 2 cm behind the pubic symphysis and is where the urethra emerges from the prostate in front and above the apex. The lateral surfaces of the prostate are surrounded by the anterior part of the Levator ani muscles and are separated from the muscles by an array of veins (Gray et al. 1918).
The majority of the prostate’s mass is composed of glandular tissue which is defined by zonal anatomy (Gray et al. 1918). The transition zone (TZ) is located between the anterior fibromuscular stroma and the peripheral zone (McLaughlin et al. 2005). About 20% of prostate cancer will originate in the transition zone (Rangabashyam et al. 2001). The peripheral zone (PZ) is located between the rectum wall and the transition zone (McLaughlin, et al. 2005, Watson et al. 1997) and encompasses about 70% of the prostate gland. This zone is where 70% of prostate cancer will originate (Rangabashyam et al. 2001, Watson et al. 1997). The central zone (CZ) represents the tissue at the base of the prostate and encompasses the ejaculatory ducts located within the prostate. Approximately 10% of prostate cancer will originate here (Rangabashyam et al. 2001).

1.3 Permanent Seed Prostate Brachytherapy

Permanent seed brachytherapy is the placement of radioactive seeds in the prostate using interstitial brachytherapy techniques which include 3D anatomically based dosimetry planning and guidance from real-time diagnostic imaging. This method of treating prostate cancer is currently the most prescribed plan in the United States (Peschel et al. 2003). It is widely chosen because it is low cost, has a short recovery time, produces excellent long-term results from biochemical failure, and has low morbidity (Peschel et al. 2003). Application of brachytherapy for treatment of prostate cancer can be prescribed two ways, as a monotherapy (a treatment plan with just permanent seed brachytherapy) or as a combination therapy (a treatment plan with permanent seed brachytherapy in addition to external beam radiation) (Peschel et al. 2003). In a study by Potters et al. (2004), prostate cancer patients were treated with radical prostatectomy, external beam
radiation, or permanent seed brachytherapy. Results indicate similar rates in freedom from biochemical failure for all three treatment plans. The overall survival was 97% for radical prostatectomy, with 96% for external beam, and 93% for brachytherapy. Compared to external beam radiation and radical prostatectomy, brachytherapy has fewer cases of urinary or rectal complications and sexual dysfunction (Yu et al. 1999).

With the increase of brachytherapy treatment as an option for many prostate cancer patients due to the early diagnoses obtained from monitoring PSA levels (Yu et al. 1999), research has begun to focus on identifying the variables that affect the outcome of the procedure. The goal of prostate brachytherapy is to deliver the prescribed dose to the prostate while minimizing the dose received by the urinary and rectal areas using a 3D anatomically based treatment plan, an interoperative treatment plan, and an analysis of post-implant dosimetry (Yu et al. 1999). However, research conducted by the clinical research committees of the American Brachytherapy Society (ABS) and the Prostate Brachytherapy Quality Assurance Group (PBQAG) conclude that there is a wide variation in indicators, techniques, treatment regiments, and dosimetry for treating prostate cancer with brachytherapy. Two major areas of concern the committees addressed were pre-implant treatment planning and post-implant dosimetry analysis, both of which are dependent upon being able to acquire accurate prostate volumes from 2D images.

1.4 Dose Margin

One factor that has been identified that contributes directly to post-implant dosimetry is the dose margin used for the implant (Yu et al. 1999, Waterman et al. 1998).
Because of uncertainties in seed distribution, the percent of the prostate volume receiving the prescribed dose is almost always less than what was planned. To ensure adequate dose coverage, a planning volume larger than the prostate volume is used to ensure dose coverage beyond the prostate capsule. Alternatively, the physician can increase the strength of the seeds or increase the number of seeds to be implanted until the prescribed isodose line extends several millimeters beyond the prostate (Yu et al. 1999).

The 1998 study by Waterman et al. illustrates how margin determination during pre-implant planning can directly affect dose coverage. In a comparison between a dose margin which closely contoured the pre-implant prostate volume to a standard dose margin that extended several millimeters beyond the periphery of the prostate, the pre-implant plan with little or no margin had less dose coverage than the pre-plan with a standard dose margin due to post-implant edema. As the prostate swelled from the edema after the implant, it was still covered by the isodose lines from the dose margin being extended past the peripheral of the prostate capsule during the pre-planning stage (Waterman et al. 1998).

1.5 Edema

Edema also influences the dose coverage due to the increase in prostate volumes from implant trauma. Compared to pre-implant volumes, edema can increase prostate volume as much as 96% with an average increase in prostate volumes of 52% (Waterman et al. 1998). This increase in prostate volume results in an increase in the separation between the implanted seeds thus lowering the percentage of the prostate volume that is receiving 100% of the prescribed dose (Yu et al. 1999, Waterman et al. 1998, Taussky et
al. 2005). However, a CT scan done after the edema has completely resolved will result in an overestimation of the dose delivered to the prostate because the dose being delivered during the time the edema is resolving will not be accurately accounted for by the post-implant dosimetry analysis is calculated (Yu et al. 1999). Since Iodine-125 delivers 90% of its total dose in the first 197 days after the implant, scheduling the time for post-implant CT scans is not only dependent upon the edema, it is also dependent upon the type of seed used in the implant (Yu et al. 1999, Waterman, et al. 1998). Therefore, a CT scan performed immediately after the implant will underestimate the dose delivered to the prostate while CT scans performed after all the edema has resolved will overestimate the dose delivered to the prostate. Studies suggest the optimal time for I-125 post-implant dosimetry analysis is 30 days after treatment (Yu et al. 1999, Helmick et al. 2002, Taussky et al. 2005).

1.6 Source Type and Source Distribution

The two radionuclides used for low-dose rate brachytherapy are I-125 and Pd-103. Both are similar in dose distribution, dimensions, and photon energy. Iodine-125 seeds are encapsulated in titanium with outer dimensions of 4.5 mm x 0.8 mm for the most commonly used type of seed, Model 6711. Model 6711 contains I-125 in the form of silver iodide deposited on the surface of a silver rod, which serves as a radiographic marker. The average overall energy for all I-125 emissions is 27.4 keV with a half-life of 59.4 days. Since clinical studies do not show any difference in patient outcomes or complications with either I-125 or Pd-103, the ABS does not make a radionuclide preference for prostate brachytherapy.
There are three different types of seed distribution that can be applied in brachytherapy: uniform loading, modified peripheral loading, and peripheral loading. The uniform loading spaces the seeds 1 cm apart throughout the prostate resulting in a higher dose in the center of the prostate. The modified peripheral loading is similar to the uniform loading distribution except some seeds are deleted in the center of the prostate to reduce the central dose. Peripheral loading places the seeds along the peripheral of the prostate sparing the urethra from receiving unnecessary dose. Also, with 70% of prostate cancer being located in the peripheral zone, peripheral loading for seed distribution is the most commonly applied method of source distribution. This method of seed distribution can maximize the prescribed dose to the periphery of the prostate while minimize the dose to the urethra (Yu et al. 1999).

1.7 Freedom from Biochemical Failure

One of the most important applications of post-implant dosimetry is determining the time in which the patient is cancer free or free from biochemical failure after completion of the treatment. The success of the treatment is measured by the patient’s prostate specific antigen (PSA) scores, Gleason scores, and/or biopsy results. Current research can support evidence to directly correlate the freedom from biochemical failure in permanent seed implant to two post-implant parameters, D90, the dose delivered to 90% of the prostate volume, and V100, the amount of prostate volume receiving 100% of the prescribed dose (Gong et al. 2002). Of these, the best dosimetry parameter to describe the amount of dose delivered to the prostate is the D90 parameter (Nag et al. 1999). The D90 parameter is more commonly used instead of the D100 parameter because there are
small errors in contouring the prostate in addition to small areas within the prostate that have been under dosed, making the D100 parameter an incorrect representation of the actual dose being delivered to the prostate volume. In addition, D90 is the only dosimetric parameter that has been directly correlated to PSA response (Stock et al. 2002).

Research has identified a D90 cut point value of 140 Gy (Polo et al. 2004, Stock et al. 2000, Wallner et al. 2003, McNeely et al. 2004, Merrick et al. 1999, Kollmeier et al. 2003) and a V100 cut point of 85% (Polo et al. 2004, Wallner et al. 2003) for 1-125 sources using CT based dosimetry. The relationship between freedom from biochemical failure and D90 value is illustrated in a study by Stock et al. (1998) which showed 68% of patients who received a D90 less than 140 Gy were free from biochemical failure compared to 92% of patients who received D90 greater than 140 Gy. A similar study by Wallner et al. (2003) illustrated the relationship between V100 and biochemical failure where 97% of the patients that had a V100 greater than 90% were free from biochemical failure compared to only 87% of the patients who had V100 less than 90%.

In the 2004 study by Polo et al. that compared CT and CT/MR dosimetric parameters, D90 and V100, showed superior results from CT/MR imaging due to volume definition from the MR images instead of CT images. D90 values were only 116 Gy for the CT images yet the CT/MR fused images resulted in D90 values of 158 Gy. The V100 also showed the same results with 82% coverage measured from the CT images compared to 88% coverage measured from the CT/MR fused images (Polo et al. 2004).

Research has determined the accuracy of post-implant dosimetry analysis is dependent upon successful delineation of the prostate from surrounding tissue, and that
current imaging practices are unable to adequately produce true prostate volumes. As a result, MR imaging of the prostate or applying multiple imaging modalities and fusing the images is being proposed in this research as a method of enhancing current post-implant dosimetry analysis by more accurately measuring the prostate volume.

1.8 Brachytherapy Imaging Modalities

1.8.1 Pre-implant Ultrasound (US) Volume Study and Computed Tomography (CT) Imaging

Transrectal ultrasound (TRUS) imaging is used by practicing clinical oncologists for pre-planning, implantation, and post-implant dosimetry analysis. During the pre-planning stage, ultrasound images are obtained during a volume study two to three weeks before the implant using TRUS images. The volume study provides pre-implant treatment planning information including the number and strength of the seeds to be implanted, grid coordinates for needle placement during surgery, and the dose distribution. Peripheral dose distribution is emphasized to reduce central hot spots in the prostate thus reducing urinary complications (Nag et al. 1999). The pre-implant US images obtained during the volume study are also used by physicians during the implant stage for seed distribution in relation to the border of the prostate. For post-implant dosimetry analysis, the US images are fused with CT images, which provide seed localization information. Using US images solely for post-implant dosimetry analysis would have advantages of being more accurate, less expensive, and faster, than CT imaging. However, US can not be used after implantation because of the frequency disruption the titanium seeds produce which manifests as a shadowing of the seeds farthest from the probe (Solhjem et al 2004).
The optimum post-implant imaging modality would be able to determine seed location and to delineate the prostate from the surrounding tissue. Fusion of the pre-implant ultrasound images to post-implant CT images are commonly used for post-implant dosimetry analysis with the prostate volume information being supplied by the US and seed localization information being supplied by the CT. The posterior border of the prostate and urethra can be used to register the two images with the calculated isodose curves being superimposed on the resulting fused image (Nag et al. 1999).

The issue with applying CT imaging for fusion with US images for post-implant dosimetry analysis is illustrated in previous studies that show prostate volumes delineated from CT images are on the average 30% to 50% larger than prostate volumes delineated from MR or US images making the difference in prostate volumes from the CT images a major concern in regards to the accuracy of post-implant dosimetry analysis (Helmick et al. 2002, Steggerda et al. 2004, Prete et al. 1998, Solhjem et al. 2004). Even with an experienced oncologist, research has concluded that the contouring of prostate volumes in CT images is difficult and the uncertainty in adequately defining the volume can significantly affect the post-implant dosimetry analysis (Crook et al. 2002, Anderson et al. 1999).

The importance of CT based post-implant dosimetry lay not only in being able to precisely delineate prostate volumes, but being able to do it consistently among different observers. Research has also shown that there has even been a large discrepancy in outlining the CT prostate volumes among different physicians. From the study by Narayana et al. (1995), the volumes contoured on pre-implant CT images were 13%, 35%, and 92% larger than volumes contoured on pre-implant US images by three
different physicians. On average, the prostate volumes defined in the pre-implant CT images were 47% larger and 0.6 cm longer than the volumes defined in the US images. The difference in prostate volumes delineated by the three observers illustrates the difficulty in distinguishing the prostate from surrounding tissue in CT images.

1.8.2 Computed Tomography (CT) and Magnetic Resonance (MR) Imaging

Several studies have reported large discrepancies in prostate volumes delineated from CT images compared to volumes delineated from US or MR images (Polo et al. 2004). In one study by Rasch et al. (1999) prostate volumes contoured from CT images were 30% larger than volumes contoured from MR images. Another study illustrated the ability of MR imaging to accurately represent the actual volume of the prostate (Amdur et al. 1999) where prostate volumes were measured using US and MR imaging prior to radical prostatectomy. The prostate volumes delineated from the US images were 8% larger and volumes delineated from the MR images were only 6% larger than the actual surgical specimen.

The specific problem reported with using CT imaging is the difficulty in delineating the apex, base, and seminal vesicles from surrounding tissue and distinguishing the prostate from the prostatic muscles and the periprostatic venous plexus (Nag et al. 1999, Dubois et al. 1998, Potters et al. 2001, Crook et al. 2004, Rasch et al. 1999, Amdur et al. 1999, McLaughlin et al. 2002, Polo et al. 2004, Helmick et al. 2002, Badiozammani et al. 1999, Algan et al. 1995). Other crucial problems identified in using CT imaging include distinguishing the posterior section of the prostate from the anterior wall of the rectum, difficulty in distinguishing between the posterior-inferior apical portion of the prostate from the anterior portion of the levator ani muscles, the inclusion
of neurovascular bundles as part of the prostate, and distinguishing the superior edge of
the prostate from the bladder (Al-Qaisieh et al. 2002, Crook et al. 2004, Potters et al.
uncertainty in defining boundaries in CT images is located at the most inferior or apical
portion of the prostate. This region is of major concern to oncologists since 75% to 85%
of prostate cancers involve the apical region of the prostate requiring optimum dose
coverage to this area (Roach et al. 1996).

Inter-observer variation is also a significant factor when comparing the
delineation of prostate volumes from CT and MR images. Inter-observer differences on
CT prostate volumes were significantly larger with volume differences ranging from 35
\( \text{cm}^3 \) to 70 \( \text{cm}^3 \), a 100% difference in half of the patients in a study by Amdur et al.
(1999). In comparing prostate volume differences using CT and MR fused images, the
study revealed prostate volumes contoured in the CT images were 32% larger than the
volumes contoured in the MR images.

A solution to the overestimation of prostate volumes delineated in CT images is
the application of MR imaging. MR imaging offers better soft tissue delineation and can
be correlated with US evaluations and pathological results. In addition, MR imaging can
produce better inter-observer reproducibility and fusion of CT and MR imaging is being
researched as a means of assessing implant quality (Polo et al. 2004). MR imaging is
favored over CT imaging because of its reproducible and consistent delineation of
prostate volumes (Crook et al. 2003). Dubois et al. (1998) showed a difference of 18.2%
between the mean inter-observer variations of prostate volumes contoured on CT images
among two different observers. However, the mean inter-observer variation in prostate
volumes contoured on the MR images had an 8.3\% difference and more consistency. Prostate volumes contoured from MR images have also shown to correlate closely with volumes measured from pathological examinations (Dubois et al. 1998) and are considered to be the gold-standard for prostate volume definition (Parker et al. 2003, Amdur et al. 1999).

1.9 Post-implant Brachytherapy Dosimetry Analysis

Post-implant dosimetry is used to identify any variation in the treatment plan in order for the physician to evaluate the quality of the implant by calculating the actual dose delivered to the prostate, urethra, rectum, and surrounding tissue (Yu et al. 1999, Nag et al. 1999). The post-implant dosimetry parameter used to determine the quality of the implant and to predict freedom from biochemical failure is D90. Studies conducted at Memorial Sloan-Kettering have shown the D90 dosimetry value is very sensitive to small differences and perturbations in the location of the seeds and target delineation (Nag et al. 1999). A study by Polo et al. (2004) illustrated that post-implant dosimetry is so sensitive to volume definition that if prostate boundaries are enlarged on CT images by 4 mm from the actual volume, D90 values will decrease from 171 Gy to 98 Gy and V100 will decrease from 95\% to 72\%, well below their respective cut points. But when permanent seed prostate brachytherapy is pre-planned with the sources having D90 and V100 dosimetry parameters greater than their cut point values, patients have a 10-year local recurrences-free survival rate which is twice that of patients having dosimetry parameters below the cut point values (Nath et al. 1998). With post-implant dosimetry values dependent upon prostate volumes delineated from CT imaging with studies concluding...
that volumes contoured from CT images are significantly overestimated, research is supporting the implementation of MR imaging for prostate radiation treatment planning (Parker et al. 2003).

The goal of this research is to calculate the difference in prostate volumes delineated from pre-implant US, post-implant CT, and pre and post-implant MR images to identify the impact volume definition has on post-implant dosimetry values, D90 and V100.
CHAPTER 2

VOLUME ESTIMATION OF 25 ML, 50 ML, AND 100 ML FLASKS USING COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING

2.1 Introduction

The accuracy of post-implant dosimetry analysis in the evaluation of prostate cancer patients depends upon being able to delineate the prostate in 2D images. The ability to obtain accurate prostate volumes from either CT or MR images is dependent upon various factors. Two such variables are differentiation of prostate tissue from surrounding tissue and the problem of subjectivity. Due to poor definition of soft tissue in CT images, the inclusion of surrounding tissue with the delineation of the prostate in CT images has resulted in an increased volume estimate that differs significantly from the actual volume of the prostate (Al-Qaisieh et al. 2002). Previous research has shown prostate volumes delineated from CT images are on the average 40% larger than prostate volumes delineated from other imaging modalities (Steggerda et al. 2004) raising questions in the accuracy of post-implant dosimetry analysis (Helmick et al. 2002, Steggerda et al. 2004, Prete et al. 1998, Solhjem et al. 2004). Subjectivity has also been a concern in prostate brachytherapy post-implant dosimetry analysis where dosimetry parameters, D90 and V100 are calculated based on delineating prostate volumes from CT images (Badiozamani et al. 1999). Dubois et al. (1998) showed that there are smaller inter and intra observer differences with volumes contoured from MR images than
volumes contoured from CT images concluding that MR imaging is more precise and more accurate in delineating the prostate for evaluation of permanent seed prostate implantation. These results suggest that the subjectivity associated with delineating prostate volumes on CT images makes the accuracy of the dosimetric evaluation based on CT imaging questionable.

The purpose of this portion of the research is to determine systematic differences in MR and CT modalities by eliminating the problems of subjectivity in prostate contouring and delineation of the prostate from surrounding tissue by imaging phantoms of known volumes.

2.2 Research Methodology

Three borosilicate volumetric flasks with defined volumes of 25 ml, 50 ml, and 100 ml were used as phantoms. These particular flasks were selected for their ellipsoidal shape which mimics the shape of the prostate. The flasks were filled with distilled water and submerged in water to simulate a prostate gland inside the pelvic region (Fig. 2). The flasks were placed on top of a clay pedestal to ensure the boundary between the glass flask and glass jar didn’t interfere with delineation in the CT and MR images. Styrofoam cones were bored out with the stem of the flasks placed inside to ensure stability and to prevent changes in the water level inside the flasks and jars.

The phantoms were imaged individually with a GE SIGNA LX EXCITE 1.5 T MRI scanner with a GE Toropa coil and a Medrad endorectal coil interface. The phantoms were scanned in the axial plane with a T2 FRFSE (Fast Recall, Fast Spin Echo
sequence with an 18 cm field of view and 24 slices of 3.0 mm thickness. A 2D MRI slice of the 50 ml flask is shown in Fig. 3.

![2D MRI slice of the 50 ml flask](image)

Figure 2. 25 ml, 50 ml, and 100 ml flasks filled with distilled water and placed inside water phantoms.

The three flasks were also imaged with a Philips CT helical scanner in the axial plane with 16 slices of 3 mm thickness with a 3 mm gap. Figure 4 shows a 2D CT image of the 100 ml flask. The axial T2 MR and axial CT image sets were loaded onto the Varian Variseed software in order to contour the flask volumes.
Figure 3. A 2D 3 mm slice obtained from the MR image of the 50 ml flask filled with distilled water and placed inside a water phantom.
2.3 Results

The results of contouring the 25 ml, 50 ml, and 100 ml flasks from MR and CT images are given in Table 1. The contoured volumes of the three flasks from the CT images showed significant differences from the actual volumes of the flasks. The
contoured volume of the 25 ml flask was 18.0 cm$^3$, a percent error of 27.9%. Similar results were seen with the 50 ml and 100 ml flasks. The contoured volume of the 50 ml flask was 37.4 cm$^3$, a percent error of 25.2% and the 100 ml flask's contoured volume was 77.0 cm$^3$, a percent error of 23.0%.

Table 1. Volumes of the 25 ml, 50 ml, and 100 ml flasks contoured from the CT and MR images along with the percent error from the original volumes in parenthesis.

<table>
<thead>
<tr>
<th>Flask Volumes (ml)</th>
<th>CT Volume (ml)</th>
<th>MR Volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>18.0 (27.9)</td>
<td>23.3 (6.8)</td>
</tr>
<tr>
<td>50</td>
<td>37.4 (25.2)</td>
<td>47.5 (5.0)</td>
</tr>
<tr>
<td>100</td>
<td>77.0 (23.0)</td>
<td>96.6 (3.4)</td>
</tr>
</tbody>
</table>

Compared to CT imaging, the volumes contoured from the MR images were closer to actual volumes of the three flasks. The contoured volume of the 25 ml flask from the MR images was 23.3 cm$^3$ or 6.8% smaller than the actual volume. The contoured volume of the 50 ml flask was 47.5 cm$^3$, a 5.0% percent error and the contoured volume of the 100 ml flask was 96.6 cm$^3$, a 3.4% percent error. These results show that the volumes contoured from the CT images underestimated the actual volumes of the flasks from 23.0% to 27.9% but the volumes contoured from the MR images only underestimated the actual volumes of the flasks by 3.4% to 6.8%.

The data also indicate that smaller contoured volumes experience larger differences from the actual volume in both CT and MR images. The difference of the 25 ml volume contoured in the CT images was 27.9% compared to 25.2% for the 50 ml flask and 23.0% for the 100 ml flask. Similar results were seen in the MR images with the 25
ml flask having a percent error of 6.8% compared to the 5.0% for the 50 ml flask and 3.4% for the 100 ml flask. Since the optimum prostate volume for brachytherapy is in the 25 ml to 50 ml range, the larger differences seen with the delineation of smaller volumes in the CT and MR images will greatly impact dosimetry analysis.

The volumes contoured from CT and MR images of the 25 ml, 50 ml, and 100 ml flasks are plotted versus the actual volumes of the flasks in Fig. 5. Figure 5 shows a linear relationship with a correlation coefficient of 0.999 for both imaging modalities.

![Flask Volumes versus Contoured CT and MR Volumes](image)

Figure 5. The contoured volumes from the CT and MR images are plotted against the actual volumes of the flasks illustrating a linear relationship between the flask volumes and the CT and MR volumes.

Graphical analysis of the flasks in Fig. 5 shows a correlation of 0.79 to the volumes contoured from the CT images (blue line) and 0.98 to the volumes contoured from the MR images. From these results, volumes contoured from CT images will
consistently be 21% smaller than the actual volume but volumes contoured from MR images will only be 2% smaller.

2.4 Conclusion

The discrepancy in the contoured volumes of the flasks from CT and MR images was larger in the CT imaged volumes than from the MR imaged volumes. The contoured volumes of the flasks from the CT images were 23.0% to 27.9% smaller than the original volumes of the flasks. But the contoured volumes of the flasks from the MR images were only 3.4% to 6.8% smaller than the volumes of the original flasks. These results agree with results of previous research showing that volumes contoured on MR images correlate more closely to pathological specimen (Roach et al. 1996, Polo et al. 2004, Prete et al. 1998, Dubois et al. 1998). Furthermore, these results illustrate why prostate volumes contoured from MR images are considered to be the gold-standard in prostate brachytherapy pre-implant dosimetry planning and in post-implant dosimetry analysis (Amdur et al. 1999, Parker et al. 2003).

Graphical analysis of the three flasks show a linear relationship between the volumes of the original flasks and the volumes contoured from the CT and MR images. Graphing the volume of the flask with the volumes contoured from the CT images illustrates that the CT images underestimated the volume of the flasks by 21%. However, graphing the volume of the three flasks with the volumes contoured from the MR images shows that the MR images only underestimated the volumes by 2%.

Though there is a significant difference in the magnitude in which the CT images underestimated the volumes of the flasks compared to the MR images, there was one very
distinct similarity between the two imaging modalities. The data illustrated that the smaller volumes delineated in both CT and MR images had larger differences from the actual volumes of the flasks than the larger volumes. The significance of these results indicate that images of prostate volumes ranging from 25 ml to 35 ml will exhibit larger differences in volumes contoured from MR and CT images than prostate volumes of 40 ml to 50 ml, making post-implant dosimetry analysis less accurate for smaller prostate volumes. This result is supported in a study by McNeely et al. (2004) where 20% of small prostate volumes had D90 dosimetry values less than 140 Gy while medium prostate volumes had 9% and larger prostate volumes had only 3% less than 140 Gy.

The prostates imaged in vivo show an increase in volumes in both CT and MR images rather than a decrease as shown from imaging the flasks. The discrepancy in volume differences between in vivo imaging of prostates and imaging of the flasks illustrates the difficulty in delineating prostate tissue from the surrounding soft tissue in the images. The results also show the CT images of the flasks created well defined glass/water boundaries, eliminating any ambiguity in defining the glass from the water. Yet, there was still a significantly larger difference between the volumes contoured from the CT images than the volumes contoured from the MR images. This indicates that CT imaging will generate images that have a larger difference from the actual volume then MR images. The research illustrates how volumes contoured in MR images represent a more accurate definition of the actual volumes in comparison to images contoured in CT images with smaller volumes experiencing larger differences than larger volumes in both imaging modalities.
CHAPTER 3

COMPARISON OF ULTRASOUND, COMPUTED TOMOGRAPHY, AND MAGNETIC RESONANCE IMAGING FOR POST-IMPLANT DOSIMETRY ANALYSIS

3.1 Introduction

Post-implant dosimetry analysis for brachytherapy permanent seed implant is a crucial step in identifying differences in the dose prescribed by the physician in pre-planning and the actual dose delivered to the prostate and surrounding tissue. This analysis identifies the extent patients are under or overdosed based on delineation of the prostate volume using current imaging modalities and image fusion software. Though research agrees that post implant dosimetry analysis is critical for evaluating the quality of the implant and is needed to improve future brachytherapy procedures, currently there appears to be a lack of standard procedures or guidelines in post-implant dosimetry for practicing physicians (Nag et al. 2000).

Permanent seed implantation of the prostate occurs in three stages, pre-implant, implant, and post-implant. In the pre-implant stage, TRUS is used to determine the clinical target volume (CTV). This is the standard volume used by the physician to define the prostate geometry for pre-implant dosimetry which allows the physician to correctly determine seed distribution. The ultrasound images are also used during the implant stage for prostate delineation and correct seed localization and distribution. However, for the
post-implant stage, post-implant CT images have to be fused with pre-implant US images because physicians have difficulty in distinguishing the prostate from the surrounding soft tissue in the CT images used for seed localization (McLaughlin et al. 2002, Rasch et al. 1999, Potters et al. 2001, Yu et al. 1999, Roach et al. 1996). A CT image of the prostate and surrounding tissue shown in Fig. 6 illustrates the problems with contouring the prostate from the surrounding tissue.

Figure 6. CT image of post-implant Iodine-125 seed implant illustrating excellent seed localization but poor delineation of prostate from surrounding tissue.

To overcome the limitations of CT imaging in defining prostate volumes, MR imaging is proposed in post-implant stages of brachytherapy. Post-implant comparison between MR and CT imaging conducted by Dubois et al.(1998) shows MR images have significantly better boundary definition of prostate volumes and offers better apex definition than CT.
Though tissue differentiation in MR imaging is superior to CT imaging as seen in Fig. 7, seed location and distribution is better defined in CT images. To resolve this issue, fusion of CT images for seed localization information and MR images for volume information is currently being investigated (Graves et al. 2001).

Figure 7. MR image of post-implant Iodine-125 permanent seed implant illustrating the excellent delineation of the prostate from surrounding tissue but the poor resolution of the seeds.

In this research, prostate volumes delineated from pre and post-implant MR images were compared to prostate volumes delineated from pre-implant US and post-implant CT to determine the differences in volume measurements among the different imaging modalities. After the US, CT, and pre and post-implant MR images were acquired, the prostate glands were contoured and the images were fused for comparison. In addition, the dosimetry parameters, D90 and V100 were compared between the imaging modalities to identify how they are affected by the delineation of the prostate volumes.
3.2 Research Methodology

3.2.1 Participant Selection

Eight patients that elected to have permanent seed implant for treatment of prostate cancer participated in this research. Since this research is investigating delineation of prostate volumes with different imaging modalities, any outside variable that would change the prostate volume, such as hormone therapy or external beam radiation, excluded patients from being able to participate.

Before the study began, approval was granted by each patient according to the Institutional Review Board (IRB). The research was approved by the IRB of the Northwest Hospital Medical Center in Tucson, Arizona on June 8, 2005.

3.2.2 Pre-implant Brachytherapy Transrectal Ultrasound Volume Study

In the pre-implant stage, the oncologist determined the patient’s prostate volume in using TRUS. The TRUS uses a rectal probe in conjunction with a Foley Catheter to introduce contrast into the urethra. The ultrasound was performed in 5 mm increments starting at the base of the prostate and continuing to the apex with the patient in a dorsal lithotomie position.

The pre-implant US images were used for dose distribution calculations using the Varian VariSeed™ Version 7.1 software and for seed distribution and seed placement during the implant. Figure 8 illustrates a brachytherapy dosimetry plan with isodose lines and seed distribution according to grid coordinates. The urethra and rectum walls are located in order to avoid overdosing these organs during implantation.

* Varian Medical Systems, 3100 Hansen Way, M/S MGM, Palo Alto, CA 94304-1038

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The planning target volume (PTV) was extended 5 mm beyond the prostate capsule to ensure all cancer cells were dosed. The seeds were distributed according to the peripheral seed distribution method. The activity of the seeds and the number of seeds to be implanted were determined based on the prostate volume and surgery date with an average dose prescribed of 145 Gy.

3.2.3 Pre and Post-implant MR Scans

Before the implant surgery, the patients had an MR scan at a diagnostic imaging center. The MR spectrometer used in this research for pre and post implant scans was a GE SIGNA LX EXCITE 1.5 T spectrometer with a GE Toropa coil and a Medrad endorectal coil interface. Each patient was scanned with an axial T2 FRFSE (Fast Recall, Fast Spin Echo), and axial T1 FRFSE with fat saturation. Fat saturation gave us the
ability to change the contrast of fatty tissue in the pelvic area to better delineate the prostate from the surrounding tissue. These MR imaging parameters were defined as the optimum settings to provide the best images of the prostate and surrounding tissue. Parameters for the axial T2 FRFSE and the axial T1 FRFSE scans are given in Table 2.

Table 2. MR imaging parameters for pre and post-implant axial T2 FRFSE (Fast Recall, Fast Spin Echo) and T1 FRFSE pulse sequences.

<table>
<thead>
<tr>
<th></th>
<th>Axial T2 FRFSE</th>
<th>Axial T1 FRFSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of Echo (TE)</td>
<td>85 ms</td>
<td>14 ms</td>
</tr>
<tr>
<td>Time of Repetition (TR)</td>
<td>4750 ms</td>
<td>375 ms</td>
</tr>
<tr>
<td>Field of View (FOV)</td>
<td>18 cm</td>
<td>18 cm</td>
</tr>
<tr>
<td>Slice Thickness</td>
<td>3.0 mm</td>
<td>3.0 mm</td>
</tr>
<tr>
<td>Number of Slices</td>
<td>24</td>
<td>24</td>
</tr>
</tbody>
</table>

Time of Echo (TE) is the time between the initial pulse and the peak of the echo. Time of Repetition (TR) is the time between excitation pulses. Both TE and TR are imaging parameters selected based upon T1 or T2 weighted imaging.

3.2.4 Implant Procedure

Approximately two to three weeks after the volume study, the patients were admitted to Northwest Medical Center for outpatient brachytherapy permanent seed implant. After being brought into the operating room and placed under general anesthesia, the patients were positioned in a dorsal lithotomie position. During the implant, ultrasound images obtained during the volume study, in addition to fluoroscopy imaging, were used for accurate seed placement within the prostate.
The patients were implanted with pre-loaded Iodine-125 seeds. After implantation, the bladder was drained by the patient’s urologist. The patient was taken to post-op, brought out of the anesthesia, and released.

3.2.5 Post-implant Procedure

Approximately 30 days after surgery, the patients returned for a post-operative exam. At this time each patient had a CT and MR scan. The CT scanner is a helical multi-slice, 16 channel scanner. The images were acquired in 3 mm increments. The MR scan had the same parameters as the pre-implant MR scan.

The Pre-implant US, Post-implant CT, and Planning Target Volume (PTV) data were the only information used for patient pre and post treatment planning and analysis. All other images and data were used solely for research purposes.

3.2.6 Prostate Volume Delineation, Seed Localization, and Dosimetry Parameters

The prostate volumes were determined by contouring the CT images and the pre and post-implant MR images on the Varian Variseed software. The pre-implant ultrasound volumes and post-implant CT images were contoured by the oncologist (Observer 1). The radiologist (Observer 2) contoured the pre-implant and post-implant MR images. This researcher (Observer 3) contoured the pre-implant MR, post-implant MR, and post-implant CT images. All prostate volumes were contoured without a margin. The dosimetry values, D90 and V100, were generated from the pre-implant US images, post-implant CT images, and post-implant MR images.

Seed localization was determined for all 8 patients on the post-implant CT images that were contoured by Observer 1 using the automatic seed finder on the Variseed software program. Seed localization was determined on the post-implant MR images...
using information from the pre-implant US volume study images and the knowledge of the distribution of the seeds within the prostate according to the peripheral loading method. Seed localization on the post-implant MR images were determined for patients 2 through 8. The seeds could not be successfully identified in patient one's post-implant MR images due to artifacts and patient motion. Patients 3, 4, and 7 were randomly selected by Observer 3 for seed localization on the post-implant MR images and for subjectivity comparisons.

3.2.7 Image Fusion

Two sets of image fusions were performed during this research. The pre-implant US images were fused with the pre-implant MR images and the pre-implant US images were also fused with the post-implant CT and post-implant MR images. To obtain the most accurate alignment of the two image sets, all of the images were aligned and fused with the Variseed software program using the urethra and the bony features in the pelvic area, with the prostate projected in the transverse, sagittal, and coronal planes. The images were aligned in the transverse plane by translating and rotating the images from the two imaging modalities in relation to each other until the prostate, urethra, and bony features were in agreement. Once the features were aligned in the transverse plane, the same process was performed in the sagittal and coronal planes. An example of a 2D slice of a fused image is illustrated in Fig. 9.
3.2.8 Statistical Analysis

The difference, percent difference, mean, and standard deviation were calculated for prostate volumes delineated from the pre-implant US images, pre and post-implant MR images, and post-implant CT images.

The Paired Student’s t-test was used to determine if there was a significant difference between the calculated mean volumes produced from each imaging modality. The Student’s t-test was calculated for (1) pre-implant US and pre-implant MR, (2) post-
implant CT and post-implant MR, (3) pre-implant MR contoured by Observer 2 and pre-implant MR contoured by Observer 3, (4) post-implant CT contoured by Observer 1 and post-implant CT contoured by Observer 3, and (5) post-implant MR contoured by Observer 2 and post-implant MR contoured by Observer 3. An example of the calculations of the paired Student’s t-test for pre-implant US and pre-implant MR is given in Appendix I.

3.3 Results

3.3.1 Patient Information

Table 3 lists the age, number of needles, number of seeds, activity per seed, total activity, dose, and planning target volume (PTV) for the eight patients in this study. The PTVs were determined by the physician during pre-implant planning and includes a 5 mm margin added to the gross tumor. Each patient’s cancer stage fell into the T1a to T1c range with Gleason scores of 6 and PSA scores ranging from 2.0 ng/ml to 10.0 ng/ml. The majority of the prostate cancer was located at the right apex or right mid-base with two patients having the cancer located at the left mid-gland and left base.
Table 3. Patient demographics and treatment details for all eight patients in the study.

<table>
<thead>
<tr>
<th>ID #</th>
<th>Age</th>
<th>Needles</th>
<th>Seeds</th>
<th>Activity per Seed (mCi)</th>
<th>Total Activity (mCi)</th>
<th>Dose (Gy)</th>
<th>PTV (cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65</td>
<td>34</td>
<td>112</td>
<td>0.338</td>
<td>35.806</td>
<td>145</td>
<td>58.69</td>
</tr>
<tr>
<td>2</td>
<td>71</td>
<td>30</td>
<td>94</td>
<td>0.383</td>
<td>33.153</td>
<td>145</td>
<td>50.92</td>
</tr>
<tr>
<td>3</td>
<td>61</td>
<td>31</td>
<td>110</td>
<td>0.353</td>
<td>36.687</td>
<td>145</td>
<td>57.72</td>
</tr>
<tr>
<td>4</td>
<td>59</td>
<td>32</td>
<td>116</td>
<td>0.338</td>
<td>37.158</td>
<td>145</td>
<td>58.58</td>
</tr>
<tr>
<td>5</td>
<td>62</td>
<td>38</td>
<td>100</td>
<td>0.325</td>
<td>30.568</td>
<td>145</td>
<td>49.06</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
<td>40</td>
<td>114</td>
<td>0.354</td>
<td>40.394</td>
<td>145</td>
<td>66.37</td>
</tr>
<tr>
<td>7</td>
<td>74</td>
<td>34</td>
<td>107</td>
<td>0.333</td>
<td>33.72</td>
<td>145</td>
<td>53.55</td>
</tr>
<tr>
<td>8</td>
<td>66</td>
<td>30</td>
<td>103</td>
<td>0.357</td>
<td>34.599</td>
<td>145</td>
<td>54.83</td>
</tr>
</tbody>
</table>

3.3.2 Pre-implant US and Pre-implant MR

The pre-implant US mean prostate volume was 37.9 cm³ with a standard deviation of 4.5 cm³. The pre-implant MR mean volume was 41.5 with a standard deviation of 7.7 cm³. In comparing these mean prostate volumes, the pre-implant MR volumes mean is 3.6 cm³ or 9.5% larger than the pre-implant US volumes mean. Since prostate volumes contoured from MR images are considered to be the gold standard in brachytherapy, the prostate volumes means from pre-implant US images underestimate the correct volume mean by 9.5%. Table 4 lists the contoured volumes from the pre-implant US, pre-implant MR, post-implant CT, and post-implant MR images.
Table 4. Individual and mean prostate volumes with standard deviation contoured from the pre-implant US, pre-implant MR post-implant CT, and post-implant MR images for the eight patients in the study.

<table>
<thead>
<tr>
<th>Patient ID #</th>
<th>Pre-implant US Volume (cm³)</th>
<th>Pre-implant MR Volume (cm³)</th>
<th>Post-implant CT Volume (cm³)</th>
<th>Post-implant MR Volume (cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38.4</td>
<td>43.9</td>
<td>51.9</td>
<td>50.5</td>
</tr>
<tr>
<td>2</td>
<td>33.7</td>
<td>28.2</td>
<td>31.0</td>
<td>36.7</td>
</tr>
<tr>
<td>3</td>
<td>35.9</td>
<td>42.4</td>
<td>33.8</td>
<td>48.9</td>
</tr>
<tr>
<td>4</td>
<td>41.7</td>
<td>51.0</td>
<td>42.3</td>
<td>57.3</td>
</tr>
<tr>
<td>5</td>
<td>32.7</td>
<td>36.2</td>
<td>36.0</td>
<td>40.1</td>
</tr>
<tr>
<td>6</td>
<td>45.8</td>
<td>48.5</td>
<td>37.0</td>
<td>56.9</td>
</tr>
<tr>
<td>7</td>
<td>34.4</td>
<td>35.7</td>
<td>46.4</td>
<td>35.8</td>
</tr>
<tr>
<td>8</td>
<td>40.5</td>
<td>46.1</td>
<td>53.3</td>
<td>46.2</td>
</tr>
<tr>
<td>Mean</td>
<td>37.9 ± 4.5</td>
<td>41.5 ± 7.7</td>
<td>41.5 ± 8.4</td>
<td>46.5 ± 8.4</td>
</tr>
</tbody>
</table>

However, the results from the Student’s t-test calculated for the mean pre-implant US and pre-implant MR prostate volumes was 2.25 (p = 0.058), showing that there is not a statistical difference between the two means at the 95% confidence interval for seven degrees of freedom.

Though the means between the pre-implant US and pre-implant MR are not statistically different, there is a large difference among the individual prostate volumes delineated from the US and MR images. Patient seven had a difference of only 1.3 cm³ between contoured volumes. Yet patient four had a difference of 9.3 cm³ in contoured volumes.

The mean and individual D90 and V100 dosimetry values for pre-implant US are listed in Table 5. The mean D90 and V100 values are 166.9 Gy with a standard deviation of 9.3 Gy and 99.4% with a standard deviation of 0.79%, respectively.
The fused image of the pre-implant US and pre-implant MR images shown in Fig. 10 illustrates the difference in size, shape, and positioning of the contoured prostate volumes from the two imaging modalities. The prostate volume delineated in the pre-implant MR image extends further out from the contoured volume of the pre-implant US image, resulting in a larger volume. It is also less uniform in shape and positioned more anterior and to the patient’s left in relation to the prostate delineated in the pre-implant US. The urethra is shown in green with a virtual seed as a green dot with red and green concentric circles.

Table 5. Individual and mean D90 and V100 dosimetry values for pre-implant US, post-implant CT, and post-implant MR images for the eight patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Pre-implant US</th>
<th>Post-implant CT</th>
<th>Post-implant MR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D90 (Gy)</td>
<td>V100 (%)</td>
<td>D90 (Gy)</td>
</tr>
<tr>
<td>1</td>
<td>165.1</td>
<td>100.0</td>
<td>128.1</td>
</tr>
<tr>
<td>2</td>
<td>158.9</td>
<td>99.6</td>
<td>152.4</td>
</tr>
<tr>
<td>3</td>
<td>177.2</td>
<td>100.0</td>
<td>133.8</td>
</tr>
<tr>
<td>4</td>
<td>160.4</td>
<td>99.0</td>
<td>137.0</td>
</tr>
<tr>
<td>5</td>
<td>155.8</td>
<td>97.7</td>
<td>114.2</td>
</tr>
<tr>
<td>6</td>
<td>162.6</td>
<td>100.0</td>
<td>120.9</td>
</tr>
<tr>
<td>7</td>
<td>180.7</td>
<td>99.2</td>
<td>99.6</td>
</tr>
<tr>
<td>8</td>
<td>174.4</td>
<td>99.8</td>
<td>106.5</td>
</tr>
<tr>
<td>Mean</td>
<td>166.9±9.3</td>
<td>99.4±0.79</td>
<td>124.0±17.3</td>
</tr>
</tbody>
</table>
3.3.3 Pre-implant US, Post-implant CT, and Post-implant MR

The mean post-implant CT prostate volume was 41.5 cm$^3$ with a standard deviation of 8.4 cm$^3$. The mean prostate volume contoured from the post-implant MR images was 46.5 cm$^3$ with a standard deviation of 8.4 cm$^3$. Table 4 lists the individual mean prostate volumes delineated from the post-implant CT and post-implant MR images for all the patients in the study.

The mean prostate volume contoured from the post-implant CT images were similar in size to the mean pre-implant US prostate volume of 37.9 cm$^3$ and identical to
the mean prostate volume contoured from the pre-implant MR images of 41.5 cm$^3$. The least difference in individual prostate volumes between the pre-implant US and post-implant CT of 0.4 cm$^3$ was seen in patient four with the largest difference of 13.5 cm$^3$ from patient one. However, the mean prostate volume contoured from the post-implant MR images was larger than the mean from either the pre-implant US or post-implant CT images. But a similar difference in the individual prostate volumes between the pre-implant US and post-implant MR is seen with 1.4 cm$^3$ from patient seven and 15.6 cm$^3$ from patient four.

In comparing the results of the mean prostate volumes among these three imaging modalities, the mean pre-implant US volume was 9.5% or 3.6 cm$^3$ smaller than the post-implant CT volumes and 22.7% or 8.6 cm$^3$ smaller than the post-implant MR volumes. The data also shows a difference between post-implant CT and post-implant MR of 12.0% or 5.0 cm$^3$ with the CT volumes smaller than the post-implant MR volumes. However, the result of the Student's t-test for post-implant CT and post-implant MR is 1.30 (p= 0.235) indicating that there is no statistical difference between their means. Though the post-implant CT and post-implant MR means are not statistically different, the individual volumes varied greatly. The prostate volumes contoured from the CT and MR images of patient one varied by only 1.4 cm$^3$. However, the prostate volumes contoured from the CT and MR images of patient six varied by 19.9 cm$^3$.

The fused image of the pre-implant US, post-implant CT, and post-implant MR images shown in Fig. 11 illustrate the volume differences between the US image and the CT image. Figure 11 also shows how the CT contouring excludes seeds from the delineated prostate while the MR image matches the shape and contours of the US image.
This indicates that MR images are more accurate in representing the actual dimensions of the prostate than CT images.

![Image](image.jpg)

**Figure 11.** Fused pre-implant US (yellow), post-implant CT (red), and post-implant MR (burgundy) images illustrating the difference in prostate volumes between the three different imaging modalities.

Though there was not a significant difference in the pre-implant US and post-implant CT prostate volumes, there is a difference between their dosimetric values. The results of the mean D90 values for pre-implant US, post-implant CT, and post-implant MR listed in Table 5 show a difference of 34.6% between pre-implant US and post-implant CT values. However, there was only a difference of 10.5% between the pre-implant US D90 and the post-implant MR D90 values even though the largest difference in prostate volumes was between these two imaging modalities. The mean D90 of 151.0
Gy with a standard deviation of 21.8 Gy for MR imaging is also above the cut point of 140 Gy but the D90 for CT is only 124.0 Gy with a standard deviation of 17.3 Gy. Similar results are seen with the V100 values. The CT mean V100 value is 81.9% with a standard deviation of 5.9% which is below the V100 cut point of 85% while the MR mean V100 value is 90.3% with a standard deviation of 5.8%.

In identifying the number of D90 dosimetric values for the CT and MR imaging modalities that were above an established cut point of 140 Gy, the results show post-implant CT imaging generating only one out of eight D90 values above the cut point while post-implant MR imaging had four out of seven. Additionally, at a cut point of 85% for V100, post-implant CT imaging had only three out of eight V100 values that were above the cut point while post-implant MR imaging had six out of seven. With the correlation of freedom from biochemical failure to D90 values greater than 140Gy and V100 values greater than 85%, these results indicate that MR imaging offers more accurate dosimetry analysis than CT imaging.

The difference in the individual D90 values between the pre-implant US and post-implant CT ranged from 6.5 Gy for patient two to 81.1 Gy for patient seven. The difference in the individual V100 values ranged from 8.1% also for patient two to 22.2% for patient five. However, a smaller difference was seen in the individual D90 values between the pre-implant US and post-implant MR with values ranging from 0.9 Gy for patient six to 27.4 Gy for patient eight. The individual V100 values that range from 1.2% for patient seven to 19.1% for patient four. There was also a larger difference in the individual D90 and V100 values between post-implant CT and post-implant MR imaging. The least difference between these two imaging modalities in the D90 values was seen in
patient four with 15.5 Gy with the largest difference of 83.6 Gy for patient seven. The least difference was seen in patient two with 3.3% and the largest difference was 22.4% for patient seven.

3.3.4 Pre-implant MR, Post-implant CT, and Post-implant MR

Though pre-implant US images are currently being used for pre-treatment planning, pre-implant MR images could offer better prostate definition resulting in more accurate dose coverage. In comparing the difference between the mean prostate volume from the pre-implant MR to the mean prostate volume from the post-implant CT, the two imaging modalities had the same mean of 41.5 cm$^3$. But the difference between the pre-implant US and post-implant CT was 9.5%. The ability to easily contour prostate volumes in MR images is illustrated in the comparison between the mean pre-implant MR volume of 41.5 cm$^3$ and the mean post-implant MR volumes of 46.5 cm$^3$. The difference between the volumes contoured from the pre-implant MR and post-implant MR images was only 6.0 cm$^3$ or 12.0% compared to a difference of 8.6 cm$^3$ or 22.7% between the pre-implant US and post-implant MR.

3.4 Subjectivity

3.4.1 Pre-implant Prostate Volumes

To determine the extent subjectivity affects prostate volume delineation, different observers contoured the images of the prostate from different imaging modalities. Results illustrate very little difference in the mean value among different observers for MR imaging as shown in Table 6. The mean pre-implant MR prostate volume contoured by Observer 2 was 41.5 cm$^3$ with a standard deviation of 7.6 cm$^3$ compared to a mean pre-
implant MR prostate volume contoured by Observer 3 of 40.3 cm$^3$ with a 5.8 cm$^3$ standard deviation. This resulted in a 3.0% difference between the mean prostate volumes with the volumes contoured by Observer 2 being larger. A Student’s t-test for the mean pre-implant MR volumes showed that there wasn’t a statistical difference between their means with a t-value of 1.16 (p= 0.283). Little difference was seen among the individual prostate volumes contoured by Observer 2 and Observer 3 from the pre-implant MR images. Patient three had the least difference of only 0.4 cm$^3$ and patient two had the largest difference of 5.1 cm$^3$.

Table 6. Individual and mean pre-implant MR prostate volumes with standard deviation contoured by Observer 2 and Observer 3.

<table>
<thead>
<tr>
<th>Patient ID #</th>
<th>Pre-implant MR Volume (cm$^3$) Observer 2</th>
<th>Pre-implant MR Volume (cm$^3$) Observer 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43.9</td>
<td>39.5</td>
</tr>
<tr>
<td>2</td>
<td>28.2</td>
<td>33.3</td>
</tr>
<tr>
<td>3</td>
<td>42.4</td>
<td>42.8</td>
</tr>
<tr>
<td>4</td>
<td>51.0</td>
<td>46.9</td>
</tr>
<tr>
<td>5</td>
<td>36.2</td>
<td>35.4</td>
</tr>
<tr>
<td>6</td>
<td>48.5</td>
<td>47.4</td>
</tr>
<tr>
<td>7</td>
<td>35.7</td>
<td>33.3</td>
</tr>
<tr>
<td>8</td>
<td>46.1</td>
<td>43.4</td>
</tr>
<tr>
<td>Mean</td>
<td>41.5 ± 7.6</td>
<td>40.3 ± 5.8</td>
</tr>
</tbody>
</table>

3.4.2 Post-implant Prostate Volumes

The effect of subjectivity was more evident in the contouring of prostate volumes in the post-implant CT images as shown in Table 7. The mean post-implant CT prostate volume contoured by Observer 1 was 41.5 cm$^3$ with a standard deviation of 8.4 cm$^3$ and the mean post-implant CT prostate volume contoured by Observer 3 being 61.3 cm$^3$ with
a standard deviation of 9.6 cm$^3$. This shows a difference in means between the contouring of the two CT images of 47.7% with larger volumes resulting from Observer 3. However, the mean post-implant MR prostate volume contoured by Observer 2 of 46.6 cm$^3$ with a standard deviation of 8.4 cm$^3$ was very similar in size to the mean post-implant MR prostate volume contoured by Observer 3 of 48.7 cm$^3$ with a standard deviation of 7.1 cm$^3$. This shows a difference of 4.7% with the larger volumes resulting from Observer 3. The individual and mean prostate volumes for the two post-implant MR images are also given in Table 7.

Table 7. Individual and mean post-implant prostate volumes with standard deviation calculated from CT and MR images by different observers for the eight patients in the study.

<table>
<thead>
<tr>
<th>Patient ID #</th>
<th>CT Volume Observer 1 (cm$^3$)</th>
<th>CT Volume Observer 3 (cm$^3$)</th>
<th>MR Volume Observer 2 (cm$^3$)</th>
<th>MR Volume Observer 3 (cm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>51.9</td>
<td>65.2</td>
<td>50.5</td>
<td>50.1</td>
</tr>
<tr>
<td>2</td>
<td>31.0</td>
<td>52.4</td>
<td>36.7</td>
<td>37.4</td>
</tr>
<tr>
<td>3</td>
<td>33.8</td>
<td>58.1</td>
<td>48.9</td>
<td>50.3</td>
</tr>
<tr>
<td>4</td>
<td>42.3</td>
<td>74.8</td>
<td>57.3</td>
<td>58.1</td>
</tr>
<tr>
<td>5</td>
<td>36.0</td>
<td>50.7</td>
<td>40.1</td>
<td>41.7</td>
</tr>
<tr>
<td>6</td>
<td>37.0</td>
<td>73.5</td>
<td>56.9</td>
<td>56.4</td>
</tr>
<tr>
<td>7</td>
<td>46.4</td>
<td>52.0</td>
<td>35.8</td>
<td>44.7</td>
</tr>
<tr>
<td>8</td>
<td>53.3</td>
<td>63.4</td>
<td>46.2</td>
<td>50.6</td>
</tr>
<tr>
<td>Mean</td>
<td>41.5 ± 8.4</td>
<td>61.3 ± 9.6</td>
<td>46.6 ± 8.4</td>
<td>48.7 ± 7.1</td>
</tr>
</tbody>
</table>

The difference in the individual prostate volumes contoured from two post-implant CT images varied the most with a difference of 5.6 cm$^3$ for patient seven to 36.5 cm$^3$ for patient six. Smaller individual differences were seen between the prostate

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volumes contoured from the two post-implant MR images with a difference of 0.4 cm³ for patient one and a difference of 8.9 cm³ for patient six.

Of the four mean post-implant prostate volumes, the prostate volumes contoured by Observer 3 from the CT images was the largest with 61.3 cm³ with 48.7 cm³ contoured by Observer 3 from the MR images followed by 46.5 cm³ contoured by Observer 2 from the MR images. The smallest mean of 41.5 cm³ was contoured from the CT images by Observer 1. These results illustrate MR imaging as having the least variability among different observers compared to CT imaging, providing consistent volume definition among different observers.

A large difference among different observers in delineating prostate volumes in CT images is illustrated in the results of the paired Student’s t-test. The result for the mean CT volumes contoured by Observer 1 and Observer 3 was 5.15 (p= 0.001) indicating a significant statistical difference at the 99% confidence interval using seven degrees of freedom. However, the paired Student’s t-test for the mean MR volumes contoured by Observer 2 and Observer 3 was 1.90 (p= 0.099). This indicates no statistical difference between the two means from the different MR images.

The mean D90 and V100 values calculated from CT images by Observer 1 and Observer 3 are given in Table 8. This shows very similar results with a difference of 7.5% between the mean D90 values and a difference of 3.9% between the mean V100 values. The two post-implant CT mean D90 values were below the cut point of 140 Gy with dosimetry values of 124.0 Gy with a standard deviation of 17.3 Gy and 133.3 Gy with a standard deviation of 9.0 Gy. The mean V100 value for post-implant CT contoured by Observer 1 was also below the 85% cut point with 81.8% with a standard deviation of
5.9%. The only mean dosimetry value above the cut point was the mean V100 value from the post-implant CT contoured by Observer 3 of 85.8% with a standard deviation of 3.3%.

There was also a large difference between the individual D90 values from the CT images ranging from 0.41 Gy for patient four to 24.4 Gy for patient five. A similar difference was also seen between the V100 values with a 0.2% difference from patient four to 12.7% difference from patient five.

Table 8. The individual and mean D90 and V100 values for post-implant CT images contoured by Observer 1 and Observer 3 for all eight patients in the study.

<table>
<thead>
<tr>
<th>Patient ID#</th>
<th>Post-implant CT (Observer 1)</th>
<th>Post-implant CT (Observer 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D90 (Gy)</td>
<td>V100 (%)</td>
</tr>
<tr>
<td>1</td>
<td>128.1</td>
<td>83.7</td>
</tr>
<tr>
<td>2</td>
<td>152.4</td>
<td>91.5</td>
</tr>
<tr>
<td>3</td>
<td>133.8</td>
<td>86.3</td>
</tr>
<tr>
<td>4</td>
<td>137.0</td>
<td>86.0</td>
</tr>
<tr>
<td>5</td>
<td>114.2</td>
<td>75.2</td>
</tr>
<tr>
<td>6</td>
<td>120.9</td>
<td>78.4</td>
</tr>
<tr>
<td>7</td>
<td>99.6</td>
<td>75.6</td>
</tr>
<tr>
<td>8</td>
<td>106.5</td>
<td>78.1</td>
</tr>
<tr>
<td>Mean</td>
<td>124.0±17.3</td>
<td>81.8±5.9</td>
</tr>
</tbody>
</table>

The number of patients who had D90 values above the cut point of 140 Gy for the post-implant CT contoured by Observer 1 was one out of eight with the post-implant CT contoured by Observer 3 having only two out of eight. The number of V100 values from the volumes contoured by Observer 1 above 85% was three out eight. The number of V100 values from the volumes contoured by Observer 3 above 85% was five out of eight.
A comparison of the D90 and V100 calculated from volumes obtained from MR images contoured by Observer 1 and Observer 3 from three randomly selected patients shows smaller differences than those seen from CT images. The mean D90 and V100 values calculated from contours produced by Observer 2 and Observer 3 from post-implant MR images are listed in Table 9. Comparing the mean MR D90 value contoured by Observer 2 of 157.4 Gy with a standard deviation of 32.9 Gy and the mean MR D90 value contoured by Observer 3 of 153.9 Gy with a standard deviation of 18.8 Gy, there was only a difference of 2.3%. And a difference of only 1.4% was calculated between the mean MR V100 value contoured by Observer 2 of 90.4% with a standard deviation of 9.4% and the mean MR V100 value contoured by Observer 2 of 91.7% with a standard deviation of 4.5%. Not only were there smaller differences between the post-implant MR D90 and V100 means compared to the post-implant CT D90 and V100 values, but all the mean D90 and V100 dosimetry values for both post-implant MR images were above their respective cut points of 140 Gy and 85%.

Table 9. Individual and mean dosimetric values, D90 and V100, of the post-implant MR images calculated from contours produced by Observer 2 and Observer 3 for three patients in the study

<table>
<thead>
<tr>
<th>Patient ID#</th>
<th>Post-implant MR (Observer 2)</th>
<th>Post-implant MR (Observer 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D90 (Gy)</td>
<td>V100 (%)</td>
</tr>
<tr>
<td>3</td>
<td>164.4</td>
<td>93.3</td>
</tr>
<tr>
<td>4</td>
<td>121.6</td>
<td>79.9</td>
</tr>
<tr>
<td>7</td>
<td>186.2</td>
<td>98.0</td>
</tr>
<tr>
<td>Mean</td>
<td>157.4±32.9</td>
<td>90.4±9.4</td>
</tr>
</tbody>
</table>

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In addition, there were more individual D90 and V100 values for both post-implant MR images that were above their respective cut points than the individual D09 and V100 values for both post-implant CT images. The post-implant MR contoured by Observer 2 had four out of seven D90 values above 140 Gy and six out of seven V100 values above 85% as shown in Table 5. Similar results were seen with the post-implant MR contoured by Observer 3 with three out of three D90 and three out of three V100 values that were above their respective cut points as shown in Table 9.

Though the mean D90 and V100 values were similar, there was a large difference seen in the individual D90 and V100 values between the two post-implant MR images. The least D90 difference of 11.1 Gy was seen in patient three with the largest difference of 41.4 Gy from patient seven. Similarly, the least V100 difference of 3.4% was also seen from patient three with the greatest difference of 8.4% from patient four.

Compared to the two post-implant CT mean and individual D90 and V100 values, the two post-implant MR had mean dosimetry values and more dosimetry values above their respective cut points. This suggests MR imaging is capable of providing more consistent volume information resulting in better dosimetry information compared to CT imaging.

3.5 Dose-volume Histograms (DVH)

Dose-volume histograms (DVH) are a crucial analytical tool for providing qualitative information of dose distribution and dose coverage to the prostate. DVH were generated from the pre-implant US, post-implant CT, and post-implant MR images for patients one through six for comparison to the dose coverage for the PTV. The ability to
accurately delineate the prostate volumes from the different imaging modalities will produce greater dose coverage to the volumes.

The DVH were used to determine the amount of prostate volume that received the prescribed dose of 145 Gy from delineation of the prostate volumes from the pre-implant US, post-implant CT, and post-implant MR images. The dose coverage to the prostate is determined by locating the prescribed dose of 145 Gy on the independent axis and measuring the volume associated with this value on the individual lines of the DVH.

From the six patients in the research that had DVH generated from prostate volume information, five patients’ DVH showed the dose coverage from the post-implant MR images were superior over the dose coverage from the pre-implant US or post-implant CT images. The DVH in Fig. 12 is from patient three. From this DVH at the 145 Gy prescribed dose, the prostate volume from the post-implant MR images (blue line) had a dose coverage of 38.5 cm³ compared to 33.8 cm³ from the pre-implant US images (light blue line) or 29.1 cm³ from the post-implant CT images (red line). Compared to the PTV prostate volume of 52.3 cm³ (burgundy line) for this patient, the post-implant MR imaging offered better dose coverage due to better prostate volume delineation. Of the DVH generated for patients one through six, five DVH showed the prostate volumes contoured from the post-implant MR images provided better dose coverage information.
Figure 12. DVH from patient three showing the dose coverage from the post-implant MR imaging (blue line) had better dose coverage at the prescribed dose of 145 Gy than from pre-implant US (light blue line) or post-implant CT (red line) imaging and came closer to the PTV dose coverage (burgundy line). This type of DVH was seen in patients two through six.

Table 10 gives the individual and mean prostate volumes receiving 145 Gy for the post-implant CT, post-implant MR, pre-implant US, and PTV for patients two through six illustrating excellent dose coverage from post-implant MR imaging. The mean dose coverage to the prostates from the post-implant MR imaging for the five patients was 39.1 cm$^3$ with a standard deviation of 8.6 cm$^3$, 34.0 cm$^3$ with a standard deviation of 4.4 cm$^3$ for the post-implant US imaging, and 30.1 cm$^3$ with a standard deviation of 3.6 cm$^3$ for the pre-implant CT imaging. Compared to the mean PTV dose coverage of 48.5 cm$^3$ with a standard deviation of 6.6 cm$^3$, post-implant MR imaging provided better dose coverage to the prostates than the pre-implant US or post-implant CT imaging.
Table 10. The individual and mean prostate volumes covered at the prescribed dose of 145 Gy for the post-implant CT, post-implant MR, pre-implant US, and PTV for five out of six patients.

<table>
<thead>
<tr>
<th>Patient ID#</th>
<th>Post-implant CT Volume (cm^3)</th>
<th>Post-implant MR Volume (cm^3)</th>
<th>Pre-implant US Volume (cm^3)</th>
<th>PTV Volume (cm^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>28.3</td>
<td>32.7</td>
<td>32.6</td>
<td>48.0</td>
</tr>
<tr>
<td>3</td>
<td>29.1</td>
<td>38.5</td>
<td>33.8</td>
<td>52.3</td>
</tr>
<tr>
<td>4</td>
<td>36.4</td>
<td>49.5</td>
<td>38.8</td>
<td>53.7</td>
</tr>
<tr>
<td>5</td>
<td>27.4</td>
<td>29.0</td>
<td>27.5</td>
<td>37.5</td>
</tr>
<tr>
<td>6</td>
<td>29.3</td>
<td>45.9</td>
<td>37.4</td>
<td>51.7</td>
</tr>
<tr>
<td>Mean</td>
<td>30.1±3.6</td>
<td>39.1±8.6</td>
<td>34.0±4.4</td>
<td>48.5±6.6</td>
</tr>
</tbody>
</table>

The only DVH that showed the prostate volume delineated from the post-implant CT imaging as providing better dose coverage than post-implant MR or pre-implant US imaging was generated from patient one. The DVH for patient one is shown in Fig. 13. In this DVH, the dose coverage from the post-implant CT imaging of 43.5 cm^3 was closer to the dose coverage from the PTV of 51.6 cm^3. This DVH also shows the prostate volume from the post-implant CT images received more dose coverage at the prescribed dose of 145 Gy than from the volumes delineated from the pre-implant US images of 35.5 cm^3 or from the post-implant MR images of 39.1 cm^3.
Figure 13. DVH from patient one showing the dose coverage from the post-implant CT (red line) came closer to the PTV dose coverage (burgundy line) than from the pre-implant US (light blue line) or post-implant MR (blue line). This was the only type of DVH among the six patients.

Comparing the prostate volumes contoured from the pre-implant US, post-implant CT, and post-implant MR images shown in Table 4, the volumes contoured from the MR images were larger than the US or CT images for patients two through six. However, for patient one, the prostate volume contoured from the post-implant CT images was larger than the volumes contoured from the US or MR images. This result is illustrated in the superior dose coverage to the prostate from MR imaging in Fig 12.
3.6 Conclusion

The results of this research determined that there was a significant difference from the prostate volumes delineated from the pre and post-implant MR images to prostate volumes contoured from the pre-implant US or post-implant CT images.

There was a 9.5% or 3.6 cm³ difference between the prostate volumes contoured from the pre-implant US images to the volumes contoured from the pre-implant MR images. The difference in the individual prostate volumes between the pre-implant US and pre-implant MR ranged from 1.3 cm³ to 9.3 cm³. The fused image of the prostate from the pre-implant US and pre-implant MR images show the prostate delineated in the MR image extending more anterior and to the patient’s left in relation to the prostate delineated in the pre-implant US images. This illustrates that almost 10% of the prostate volume is not accounted for in the pre-treatment planning stage of brachytherapy.

In comparing the means of the prostate volumes contoured from the pre-implant US to the volumes contoured from the post-implant CT images, there was also a difference of 3.6 cm³ or 9.5%, suggesting that, on average, the images contoured from CT images produced similar volume estimates. However, the D90 dosimetry values for the CT imaging were suboptimal with a difference of 34.6% between pre-implant US and post-implant CT values. In addition, the post-implant CT imaging had only one out of eight D90 value above the cut point of 140 Gy and three out of eight V100 values above the cut point of 85%. Even the mean D90 of 124.0 Gy and the mean V100 values of 81.9% from the post-implant CT images were below their respective cut points. These differences are due to seeds being located outside the volume contoured on the CT images suggest poor contouring due to poor prostate definition.
The prostate volumes contoured from the post-implant MR images were significantly larger than the volumes from pre-implant US images probably due to edema. Compared to the mean pre-implant US prostate volumes, the mean prostate volume from the post-implant MR images was 22.7% or 8.6 cm$^3$ larger. However, there was a difference of only 10.5% between the pre-implant US and the post-implant MR D90 values. The post-implant MR images also provided more individual D90 and V100 values above their respective cut points with four out of seven D90 values above 140 Gy and six out of seven V100 values above 85%. Even the mean D90 value of 151.0 Gy and the mean V100 value of 90.3% for the post-implant MR were above their respective cut points.

Though the mean prostate volumes differed, the difference in the individual prostate volumes between the pre-implant US, post-implant CT, and post-implant MR was similar. The least difference in the individual prostate volumes was 0.6 Gy between the US and CT with 1.4 Gy between CT and MR and between US and MR. The largest difference in the individual prostate volumes was between the CT and MR of 19.9 Gy followed by 15.6 Gy between US and MR and 13.5 Gy between US and CT. However, the same can not be said for the difference between the individual D90 and V100 values for the post-implant CT and post-implant MR with the least difference in the D90 values of 15.5 Gy with the largest difference of 83.6 Gy. The same was seen in the V100 values with the least difference of 3.3% and the largest difference of 22.4%. A large difference was also seen in the individual D90 and V100 values between the pre-implant US and post-implant CT with D90 values ranging from 6.5 Gy to 81.1 Gy and V100 value ranging from 8.1% to 22.2%. The smallest difference in the individual D90 and V100
values between the pre-implant US and post-implant MR images with the D90 values ranging from 0.9 Gy to 27.4 Gy and the V100 values ranging from 1.2 to 19.1%.

The ability to distinguish prostate volumes in MR imaging provides more accurate volume definition than CT imaging resulting in better dose coverage as illustrated in the DVH. In five of the six DVH generated from the research, prostate volumes contoured from MR imaging resulted in superior dose coverage to the prostate compared to volumes contoured from CT imaging. The mean prostate volume receiving the prescribed dose of 145 Gy for the post-implant MR imaging was 39.1 cm$^3$ compared to 33.8 cm$^3$ from the pre-implant US images and 30.1 cm$^3$ from the post-implant CT images. This supports results from previous research that determined DVH from MR imaging are more accurate than from CT images (Badiozammani et al. 1999).

Results from this research also show that replacing pre-implant US imaging with pre-implant MR imaging would create better volume definition for pre-treatment planning and fusion with either post-implant CT imaging or post-implant MR imaging for post-implant dosimetry analysis. The mean pre-implant MR prostate volume was the same as the mean volume from the post-implant CT images compared to a 9.5% difference between the mean volume from pre-implant US and the mean volume from the post-implant CT volumes. Similar results were seen with the pre-implant MR and post-implant MR, with a difference of only 12.0% compared to 22.7% between the prostate volumes contoured from the pre-implant US and post-implant MR images.

MR imaging also provided better results than CT imaging for delineation of prostate volumes among different observers. There was only a 3.0% difference between the pre-implant MR prostate volumes contoured by Observer 2 and Observer 3 with a
difference of 4.7% between the post-implant MR prostate volumes that were contoured by Observer 2 and Observer 3. But a difference of 47.7% was seen in the prostate volumes contoured from the post-implant CT images by Observer 1 and Observer 3. When identifying the number of individual D90 and V100 values that were above their respective cut points of 140 Gy and 85%, the two post-implant MR images were clearly superior with a total of seven out of ten D90 values and a total of nine out of ten V100 values. However, the two post-implant CT images had only a total of three out of sixteen D90 values and eight out of sixteen V100 values that were above their respective cut points.

There was even a significant difference in the individual prostate volumes, D90, and V100 values between the two CT images and the two MR images. The individual prostate volumes from the two MR images had the least difference with the smallest difference of 0.4 cm$^3$ and the largest difference of 8.9 cm$^3$ compared to 5.6 cm$^3$ and 36.5 cm$^3$ from the two CT images. However, the same can not be said of the difference in the D90 values. The smallest difference in the D90 values between the two CT images was 0.41 Gy with the largest difference of 24.4 Gy. But the smallest difference in the D90 values between two MR images was 11.1 Gy with the largest difference being 41.4 Gy. The difference in the V100 values were less pronounced with the smallest difference between the two CT images of with a 0.2% and the largest difference of 12.7%. compared to of 3.4% and 8.4% for the two MR images.
CHAPTER 4

CONCLUSION

4.1 Delineation of Defined Volumes in CT and MR Images

The results from this research showed a larger discrepancy in the contoured volumes from the CT images of the 25 ml, 50 ml, and 100 ml flasks compared to the contoured volumes from the MR images. The contoured images of the flasks from the MR images generated volumes that were smaller than the actual volume of the flasks, but to a lesser degree than the volumes contoured from the CT images. Though there was a significant difference in the magnitude in which the CT images decreased the volumes of the flasks compared to the MR images, there was one very distinct similarity between the two imaging modalities which is crucial in prostate brachytherapy post-implant dosimetry analysis. The data illustrated that the contoured volume of the 25 ml flask from the CT and the MR images had a greater degree of difference compared the contoured volumes of the 50 ml and 100 ml flasks, suggesting that post-implant dosimetry analysis would be less accurate for smaller prostate volumes.

4.2 Comparison of US, CT, and MR Imaging for Post-implant Dosimetry Analysis

The results from this portion of the research showed that, though prostate volumes delineated from pre and post-implant MR images differed in comparison to prostate
volumes delineated from pre-implant US and post-implant CT images, MR imaging generated more D90 and V100 dosimetry values above their respective cut points.

The prostate volumes delineated from the pre-implant MR images differed by 9.5% compared to the volumes contoured in the pre-implant US and post-implant CT images. But between the mean post-implant MR prostate volume and the mean pre-implant US prostate volume there was 22.7% difference. Though prostate volumes contoured from CT images were closer to the volumes contoured from US images, the true shortcoming of CT imaging for brachytherapy was seen in the dosimetry values. The majority of the dosimetry values, D90 and V100, from the post-implant CT images were suboptimal. Compared to the dosimetry values from the post-implant CT images, the post-implant MR images produced 44.6% more D90 values and 48.2% more V100 values above their respective cut points even though the prostate volumes contoured from the MR images differed the greatest compared to the volumes contoured from the US images. Even the mean D90 and V100 values from the post-implant MR images were above the cut points, but neither mean D90 nor V100 values from the post-implant CT images were above the cut points. These results were illustrated in Figure 11 which showed how the prostate contoured from the post-implant CT image was closer in shape and size to the volume contoured from the pre-implant US image, but the CT contouring excluded seeds from the delineated prostate resulting in extremely poor dosimetry information. It also showed how the prostate contoured from the post-implant MR image extended beyond the contouring from the pre-implant US, encompassing more implanted seeds and producing better dosimetry information.
The criticality of obtaining accurate prostate volume definition relates to the implementation of pre-implant US imaging for pre-treatment planning, implantation information, and post-implant dosimetry analysis. The results from this research suggest that replacing pre-implant US imaging with pre-implant MR imaging would generate better prostate volume definition and dosimetry information. The prostate volumes delineated from the pre-implant MR and the post-implant CT images had the same mean volume of 41.5 cm³ but there was a 9.5% difference between the prostate volumes delineated from the pre-implant US and post-implant CT images. In addition, there was a 12% difference between the mean prostate volumes contoured from the pre-implant MR and post-implant MR images but between the mean prostate volumes contoured from the pre-implant US and the post-implant MR images there was a 22.7% difference. Since the prostate boundary is well defined in MR images resulting in a more accurate representation of the true prostate volume, the 12% difference can be related to edema resolution. Research has shown that, on average, edema will typically resolve by 88% after 28 days. Since all eight of the patients in the study had the post-implant MR scans performed approximately 30 days after the implant, the 12% difference between the pre-implant and post-implant MR images can be attributed to edema. The benefit of MR imaging for dosimetry analysis was also illustrated in the DVH generated from six of the patients in the study. Five of the six DVH showed dose coverage from the post-implant MR imaging was superior over post-implant CT and pre-implant US imaging. From the six DVH generated, there was only one DVH which illustrated where the dose coverage from post-implant CT imaging was superior to dose coverage from the post-implant MR imaging.
Subjectivity is a major concern in all prostate brachytherapy post-implant dosimetry analysis where dosimetry parameters, D90 and V100 are calculated based on delineating prostate volumes from CT images. The results from this research showed prostate delineation from MR imaging is less affected by subjectivity than CT imaging. The difference between the mean prostate volumes from the pre-implant MR images that were contoured by Observer 2 and Observer 3 was only 3.0% with little difference between the individual prostate volumes. Similar results were obtained with the post-implant MR images with a difference of 4.7% between the prostate volumes contoured by Observer 2 and Observer 3. However, a difference of 47.7% was seen between the mean post-implant CT prostate volumes contoured by Observer 1 and Observer 3. Consequently, the difference in individual prostate volumes contoured from the two post-implant CT images were larger compared to the difference in individual prostate volumes contoured from the two post-implant MR images. In addition, the post-implant MR images produced better dosimetry values than the post-implant CT images. The post-implant MR images had a total of seven out of ten D90 values above 140 Gy and nine out of ten V100 values above 85%. But the post-implant CT images had a total of three out of sixteen D90 values and eight out of sixteen V100 values. The post-implant CT contoured by Observer 3 had only one additional D90 value above 140 Gy and two more V100 values above 85% than the post-implant CT contoured by Observer 1 even though the prostate volumes contoured by Observer 1 was 47.7% larger. However, there was a larger difference in the individual D90 values between the two post-implant MR images than between the two post-implant CT images. The difference in volumes and dosimetry values between the two CT images illustrates that the prostate volumes contoured in CT
images produced dosimetry values below their respective cut points. This suggests that subjectivity associated with delineating prostate volumes from CT images makes the accuracy of the dosimetric evaluation based on CT imaging questionable, concluding that MR imaging is more precise and accurate in delineating prostate volumes for post-implant dosimetry analysis.

4.3 Overall Conclusion

The results from this research concluded that MR imaging provides more mean and individual D90 and V100 values above their respective cut points than CT imaging due to the ability to adequately delineate the boundary of the prostate from surrounding soft tissue in MR images. The data also indicate that MR imaging is less affected by subjectivity that CT imaging. Though the prostate volumes delineated from the CT images were closer to the volumes from the pre-implant US images, the individual D90 and V100 values were suboptimal, indicating that post-implant dosimetry analysis based on CT imaging gives incorrect dosimetry information in regards to the quality of the implant and to the patient's rate from freedom from biochemical failure. The results of this research supports MR imaging for prostate brachytherapy I-125 pre-treatment planning, implantation information, and post-implant dosimetry analysis by either replacing pre-implant US for volume information, replacing CT imaging for seed localization, or by fusing MR images with CT images to provide correct volume definition.
4.4 Recommendations

The results from this research suggest the implementation of MR imaging for pre-treatment planning and post-implant dosimetry analysis. Implementing MR imaging for pre-treatment planning can provide a more accurate prostate volume definition resulting in optimum seed placement within the prostate. For post-implant dosimetry analysis, the fusion of MR imaging to provide volume information with CT imaging to provide seed localization information, would generate more accurate dosimetry information resulting in a more accurate evaluation in freedom from biochemical failure. Also, the development of new MR T2-sequences could provide better seed visualize in addition to the excellent prostate definition in MR images thereby eliminating the need for post-implant CT imaging.
APPENDIX I

STUDENT'S T-TEST FOR PRE-IMPLANT US AND PRE-IMPLANT MR
Table 11. Student’s t-test Calculation for Pre-implant US and Pre-implant MR

<table>
<thead>
<tr>
<th>Patient</th>
<th>Pre-implant US (cm$^3$)</th>
<th>Pre-implant MR (cm$^3$)</th>
<th>Difference (z)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38.4</td>
<td>43.9</td>
<td>-5.5</td>
</tr>
<tr>
<td>2</td>
<td>33.7</td>
<td>28.2</td>
<td>5.5</td>
</tr>
<tr>
<td>3</td>
<td>35.9</td>
<td>42.4</td>
<td>-6.5</td>
</tr>
<tr>
<td>4</td>
<td>41.7</td>
<td>51.0</td>
<td>-9.3</td>
</tr>
<tr>
<td>5</td>
<td>32.7</td>
<td>36.2</td>
<td>-3.5</td>
</tr>
<tr>
<td>6</td>
<td>45.8</td>
<td>48.5</td>
<td>-2.7</td>
</tr>
<tr>
<td>7</td>
<td>34.4</td>
<td>35.7</td>
<td>-1.3</td>
</tr>
<tr>
<td>8</td>
<td>40.5</td>
<td>46.1</td>
<td>-5.6</td>
</tr>
</tbody>
</table>

$\sum z = 29.1$

$n = 8.0$

$\bar{z} = 29.1/8$

$= 3.6$

$\sum z^2 = 242.4$

$(\sum z)^2 / n$

$= (29.1)^2 / 8$

$= 105.9$

$\sum d^2 = \sum z^2 - (\sum z)^2 / n$

$= 242.4 - 105.9$

$= 136.5$

$a_d^2 = \sum d^2 / n - 1$

$= 136.5 / 8 - 1$

$= 19.5$
\[ \sigma_d = \sqrt{\langle \sigma_d^2 \rangle} \]
\[ = 4.4 \]
\[ \sigma_n = \sigma_d / \sqrt{n} \]
\[ = 4.4 / \sqrt{8} \]
\[ = 1.6 \]
\[ t = \frac{\bar{x}}{\sigma_n} \]
\[ = 3.6 / 1.6 \]
\[ = 2.25 \]
APPENDIX II

HUMAN SUBJECTS RESEARCH PROTOCOL
Human Subjects Research Protocol

Project title: Post-implant Dosimetry Analysis of Iodine-125 Brachytherapy Patients by Delineation of Prostate Volumes Using Pre- and Post-implant MRI Imaging

Principal Investigator/Title/Section/Branch/Institute:
Dr. Curtis Mack, MD Arizona Oncology, Tucson, Arizona
Deana Tuttle, Graduate Student, Department of Health Physics, University of Nevada, Las Vegas, NV

Associate Investigators [include name, institution, and city]:
(1) Michael Taylor, Medical Physicist, Arizona Oncology, Tucson, Arizona
(2) Mark Yoshino, MD, Southern Arizona Diagnostic Imaging, Tucson, Arizona
(3) Phillip Patton, Ph.D. UNLV, Las Vegas, Nevada

Study type (check all that apply):

- [X] Archived biological specimens/medical information
- [ ] Natural history; definition of phenotype, genotype/phenotype correlation
- [ ] Prospective linkage/gene identification, NOT providing information to participants
- [ ] Prospective linkage/gene identification, providing information provided to participants
- [ ] Social science; assessments of knowledge, attitudes and behavior
- [ ] Genetic counseling
- [ ] Drugs or devices
- [ ] Gene transfer
- [ ] Other interventions

Key Words:

- Disease(s) Prostate Cancer
- Population Males-diagnosed with prostate cancer undergoing Iodine 125 seed implant

Results routinely communicated to subjects?

- [X] No
- [ ] Yes

Research participants to be seen at:

- [X] Arizona Oncology and Southern Arizona Diagnostic Imaging
1. **Precis:** *(In 400 words or fewer, describe the study objectives, population, design, and outcome measures)*

(1) Determination of accuracy and reproducibility of two different imaging modalities. This will be accomplished by comparing pre-implant Transrectal Ultrasound (TRUS) images with pre-implant MR images. TRUS images are used by most physicians as the standard measurement of prostate volumes for pre-planning dosimetry. The MR images will be compared to the TRUS images to determine volume differences.

(2) Determination of prostate volumes by comparing post-implant CT images with post-implant MR images. These scans will be performed to determine the extent of post implant prostate volume differences between the two imaging modalities.

(3) Calculating differences in dose prescribed by the physician in the pre-planning stage to the total dose in post-implant stage based upon prostate volume differences determined in pre and post-implant imaging. Using the difference in prostate volumes between pre-implant TRUS and MR images and between CT and MR post-implant images, the dose will be calculated and compared to TRUS pre-implant dose prescribed by the physician to determine the extent of under or over dosage of the prostate and surrounding tissue.

**Population:**
The research will image approximately 10 brachytherapy patients for pre-implant and post-implant prostate volume evaluation using the MRI at Southern Arizona Diagnostic Imaging Center. The TRUS pre-implant and CT post-implant imaging will be performed at Arizona Oncology.

**Design and Outcome:**
The images obtained from TRUS, MRI, and CT will be contoured to determine differences in prostate volumes. Then, based upon these differences, the total dose the prostate received will be calculated and compared to the prescribed dose to identify if under or over-dosage of the prostate has occurred on one modality contrasted with the other.

2. **Objective and specific aims:**

The accuracy of prostate post-implant dosimetry in identifying freedom of biochemical failure is dependent upon imaging. I propose to compare our pre-implant TRUS and post-implant CT images with MR pre and post-implant images to access the quantitative and qualitative differences. From these results, physicians will be able to enhance brachytherapy procedures with the goal of better delineating dose requirements required for a successful implant. The results of this study may help determine systematic and variable differences, perhaps altering the standard of care in post-implant dosimetry.
3. **Brief Rationale and Background:**

Post-implant dosimetry analysis is crucial in brachytherapy for determining the dose the prostate and surrounding tissue received from the permanent seed implants. It also provides the physician a means of evaluating seed distribution in relation to prostate volumes for future prostate cancer patients. However, current studies indicate a lack of standard procedures or guidelines for physicians for post-implant dosimetry analysis in clinical settings (Nag et al. 2000). Currently, during the preplanning stage of Brach therapy a Transrectal Ultrasound (TRUS) is used to determine the clinical target volume (CTV). TRUS images are also used during surgery for correct seed localization and distribution and prostate delineation. For post-implant dosimetry, the imaging modality most frequently used is computed tomography (CT) since seeds cannot be well localized on ultrasound. TRUS imaging has frequency disruption and artifacts due to the metallic seed capsules. Though CT is one of the most common imaging modalities, distinguishing the prostate base and apex regions from surrounding tissue is difficult. (McLaughlin et al. 2002; Rasch et al. 1999; Potters et al. 2001; Anderson et al. 1999; Graves et al. 2001; Roach, et al. 1996). As a result of post-implant swelling and poor soft tissue resolution of CT images, prostate volumes are on the average 1.4 times larger than the volumes determined initially in ultrasound and MR images (McLaughlin et al. 2002; Parker et al. 2003; Roach et al. 1996). Therefore, if CT imaging is used as the sole means of evaluation in post-implant dosimetry, dose coverage of the prostate would be calculated to be less than what was actually prescribed in the preplanning stage due to the perceived increase in prostate volume. To overcome the limitations of CT imaging in defining prostate volume, MR imaging is proposed in pre and post-implant dosimetry.

The significance of post-implant analysis is for physicians to accurately quantify the dose delivered and then subsequently relating it to freedom of biochemical failure. Current research can support evidence to directly correlate the freedom from biochemical failure in permanent seed implants to two post-implant parameters, D90, the dose delivered to 90% of the prostate volume, and V100, the amount of prostate volume receiving 100% of the prescribed dose (Gong et al. 2002; Stock et al. 1998; Wallner et al. 2003. This research may assist in altering the standard of care in post-implant dosimetry analysis by (1) comparing prostate volumes in pre-implant TRUS images with pre-implant MR images (2) comparing prostate volumes in post-implant CT images with post-implant MR images and (3) calculating the difference in dose prescribed by the physician in pre-planning stage to the total dose in post-implant stage based upon prostate volumes determined in pre and post-implant imaging.

4. **Description of Study Population:**

4.1 Estimated number of participants, enrollment ceiling, and anticipated enrollment by year.
TRUS and MR images will be performed on 3-10 Brachytherapy patients. Only 3 pre-implant patients will have the MRI scan if a pattern appears indicating prostate volumes for pre-implant TRUS and MR images are consistent with a difference of approximately 1.07. The TRUS images will be obtained at Arizona Oncology office and the MR images will be obtained at Southern Arizona Diagnostic Imaging office. The MRI data will be transferred to Dicom where the prostate volumes will be contoured on Variseed software. Prostate volumes will be determined during the standard volume study by the physician.

The standard post-implant CT will be performed in addition to MRI scans for 10 brachytherapy patients. These scans will be performed to determine the extend of post implant prostate volume differences between the two imaging modalities. The CT images will be done at Arizona Oncology Office and the MR images will be obtained at Southern Arizona Diagnostic Imaging office.

4.2 Description of clinical inclusion/exclusion criteria.

Eligible participants will be limited to males diagnosed with prostate cancer scheduled to undergo a prostate seed implant and who are not prescribed hormone therapy to reduce prostate size nor are they receiving external beam treatment.

4.3 Location of study.

The study will be performed at Arizona Oncology office located at West Orange Grove, Building 1, Tucson, Arizona and at Southern Arizona Diagnostic Imaging, 1845 West Orange Grove, Suite 103, Tucson, Arizona.

4.4 Description of recruitment strategies

Recruitment will be done by Dr. Curtis Mack, MD at Arizona Oncology Office.

4.5 For existing sample/data sets, note whether samples were originally collected for research or clinical practice. If obtained for research, include a description of the original purpose of study and prior plans for sample storage. Was consent obtained that would be applicable to this study? (Include copy of original consent forms.)

This research study is based upon identifying differences in imaging modalities in delineation of the prostate of cancer patients in determining total dose to the organ and surrounding tissues for identifying freedom from biochemical failure. A consent form is included in the packet of forms for submittal to the IRB committee.
4.6 Description and justification of inclusion/exclusion of participants.

The objectives previously stated specifies that the participants be male, and within the standard age of men seen previously with prostate cancer. Patients undergoing hormonal treatment are excluded because the prostate volume changes under this additional source.

4.7 Description of efforts to include under-represented minorities.

Not-applicable.

4.8 Description of any financial compensation. If participant withdraws early, describe how compensation will be modified.

Since this research is based upon pre and post implant MR imaging performed during standard treatment form prostate cancer, the participant will not be financially compensated.

5. Description of procedures: (Please include a flow-sheet or chart).

5.1 Approved Drugs

Not-applicable.

5.2 Unapproved Drugs/Devices

Not-applicable.

5.3 Diagnostic studies

Not-applicable.

5.4 Biological Specimens

Not-applicable.

5.5 Medical information

Not-applicable.

5.6 Describe questionnaires or other psychological instruments and estimate how long they will take to complete, and whether they address sensitive topics

Not-applicable.

5.7 Specific results that will be given to participants or their health care providers

Not-applicable.
5.8 Genetic counseling

Not-applicable.

5.9 Description of criteria for withdrawal from study.

(1) Determination of prostate volumes by comparing pre-implant TRUS images with pre-implant MR images.
TRUS and MR images will be performed on 3-10 Brachytherapy patients.
The TRUS images will be obtained at Arizona Oncology office and the MR images will be obtained at Southern Arizona Diagnostic Imaging office.
The MRI data will be transferred to Dicom where the prostate volumes will be contoured on Variseed software. Prostate volumes will be determined during the standard volume study by the physician.

(2) Brachytherapy Iodine-125 Seed Implant Surgery.
Dr. Curtis Mack, MD will perform the Iodine-125 permanent seed implant at Northwest Medical Center. Approximate time will be 1.0 to 1.5 hours. The preplanning stage of brachytherapy uses Transrectal Ultrasound (TRUS) in the volume study to determine the clinical target volume (CTV). TRUS images are also used during surgery for correct seed localization and distribution and prostate delineation.

(3) Post-implant examination in determination of prostate volumes by comparing post implant CT images with post-implant MR images approximately 30 days after surgery.
The standard post-implant CT will be performed in addition to MRI scans for 10 brachytherapy patients. The CT images will be done at the Arizona Oncology office and the MR images will be obtained at Southern Arizona Diagnostic Imaging office. The rectal coil in post-implant MR images is not recommended due to the need to keep consistent parameters with post-implant CT images that do not require rectal coils.
Figure 14. Flow-chart of brachytherapy implantation procedures.
6. Description of statistical considerations and/or analytic plan

In pre-implant data analysis, the prostate volumes will be compared from the standard Transrectal Ultrasound (TRUS) images, contoured during the Volume Study by Dr. Curtis Mack, MD, to volumes determined in the MR images. A previous study has indicated that TRUS prostate images were comparable in size to MRI prostate images, with a difference of only 1.07. Only 3 pre-implant patients will have the MRI scan if a pattern appears indicating prostate volumes for pre-implant TRUS and MRI images are consistent with a difference of approximately 1.07.

During the post-implant data analysis, prostate volumes will be compared from the standard CT images to MR images. Both MRI and the CT images are contoured using a Variseed Software program. Since soft tissue is difficult to distinguish on CT images, contouring the prostate to determine volume for dosimetry is very subjective. Post-implant swelling and poor resolution of soft tissue results in a prostate volume larger than the TRUS volume generally used in pretreatment planning. In previous studies, CT prostate volumes were on the average, 1.4 times larger than the volumes determined initially in ultrasound or MR imaging studies.

Post-implant Brachytherapy dosimetry analysis will use the data from the pre and post implant prostate volumes to determine the dosage to the prostate and surrounding tissue.

7. Description of potential benefits of study

7.1 Direct benefits to participants (physical or psychosocial)

The MRI scans are not physically or psychosocially beneficial to the patient. The scans are performed as a means of identifying a prostate volume differences and are only an addition to the standard brachytherapy procedures.

7.2 Collateral benefit to participants (medical or genetic counseling care)

The MRI scans are not beneficial to the diagnosis or treatment of the patient. The scans are being performed in conjunction with the standard Brach therapy Transrectal Ultrasound (TRUS) and Computer Topography (CT) scans. However, additional biological and anatomical patient information obtained by another imaging modality increases the possibility of identifying any abnormalities. In the event an investigator notices an abnormality on an MRI scan, a physician will be consulted as to whether the finding merits further investigation, in which case the investigator will contact you and your primary care physician and inform you of the finding.
7.3 Benefits to society

The accuracy of prostate post-implant dosimetry in identifying freedom of biochemical failure is dependent upon imaging. This research proposes to compare standard pre-implant TRUS and post-implant CT images with MRI pre and post-implant images to access the quantitative and qualitative differences. The images obtained from TRUS, MRI, and CT will be contoured to determine differences in prostate volumes. Then, based upon these differences, the total dose the prostate received will be calculated and compared to the prescribed dose to identify if under or over-dosage of the prostate has occurred. From these results, physicians will be able to modify brachytherapy procedures with the goal of improving dose distributions perhaps increasing the life expectancy of the patients based upon improved D90 and V100 values, perhaps decreasing side effects by limiting doses.

8. Description of likelihood and seriousness of harms and how safety will be maximized

MRI Scans:
The MRI machine uses a strong magnet and radiowaves to make images of the body's interior. The scanning procedure is very much like an x-ray CT scan. You will be asked to lie on a long narrow couch for a certain amount of time (approximately 30 minutes) while the machine gathers data.

During this time you will not be exposed to x-rays, but rather a magnetic field and radiofrequency magnetic fields. You will not feel either. You will, however, hear repetitive tapping noises that arise from the MR scanner. We will provide earplugs or ear phones that you will be required to wear. The space within the large magnet in which you lie is somewhat confined, although we have taken many steps to relieve the "claustrophobic" feeling.

Risks:
Magnetic fields do not cause harmful effects at the levels used in the MRI machine. However, the MR scanner uses a very strong magnet that will attract some metals and affect some electronic devices. If you have a cardiac pacemaker or any other biomedical device in or on your body, it is very important that you tell the operator/investigator immediately. As metallic objects may experience a strong attraction to the magnet, it is also very important that you notify the operator of any metal objects (especially surgical clips), devices, or implants that are in or on your body before entering the magnet room. All such objects must be removed (if possible) before entering the magnet room. In some cases, having those devices means you should not have an MRI scan performed. In addition, watches and credit cards should also be removed as these could be damaged. You will be provided a way to secure these items. If you have any history of head or eye
injury involving metal fragments, if you have ever worked in a metal shop, or if you could be pregnant, you should notify the operator/investigator.

Subjects will be screened in the same manner as all patients having routine MR to exclude those with pacers and/or cerebral aneurysm clips. If you have had a previous reaction to Gadolinium-based contrast agents or a history of severe allergies, please notify the operator/investigator.

Some of the RF imaging coils, imaging software and devices being used in your scan are not approved by the FDA but are similar to counterparts that have been approved by the FDA. There is a small risk of heating from the cables associated with these devices. Please report any heating sensation immediately.

The scans performed in this study are for specific research purposes and are not optimized to find medical abnormalities. The investigators for this project may not be trained to perform medical diagnosis. The investigators and Arizona Oncology Office and Southern Arizona Diagnostic Imaging offices are not responsible for failure to find existing abnormalities with these MRI scans. However, on occasion the investigator may notice a finding on an MRI scan that seems abnormal. When this occurs, a physician will be consulted as to whether the finding merits further investigation, in which case the investigator will contact you and your primary care physician and inform you of the finding. The decision as to whether to proceed with further examination or treatment lies solely with you and your physician. The investigators and the consulting physician, are not responsible for any examination or treatment that you undertake based on these findings. Because the images collected in this study may not comprise a proper clinical MRI scan, these images will not be made available for diagnostic purposes.

8.1 Drugs/devices/gene transfer
   Not-applicable.

8.2 Radiation
   Not-applicable.

8.3 Sedation
   Not-applicable.

8.4 Psychological harms *(misunderstanding, anxiety, self esteem, depression)*
   Not-applicable.
8.5 Risks to family relationships

Not-applicable.

8.6 Discrimination

Not-applicable.

9. Collection, monitoring, analysis and reporting of adverse events

9.1 If this is either a natural history or limited encounter protocol, explain this to the IRB and specify the occurrences that will be excluded from adverse event reporting.

Not-applicable.

9.2 Describe plan to monitor adverse events as defined in Section 8.0 for this protocol. (anticipated and unanticipated, serious and non-serious)

Not-applicable.

9.3 Describe plan to report adverse events as defined for this protocol in accordance with NIH and NHGRI regulations. (Note that all serious adverse events as defined for this protocol must be reported in writing by mandated deadlines to the NHGRI Clinical Director, NHGRI IRB, and other agencies, if pertinent.)

Not-applicable.

9.4 Describe whether a Data Safety and Monitoring Board (DSMB) will be used.

Not-applicable.

10. Description of how privacy and confidentiality of medical information/biological specimens will be maximized

10.1 Will participant identifiers be attached to data, or will samples/data be coded or unlinked? (Even if names are removed, how likely is potential identification?)

10.2 Description of any clinical/demographic information that will be included. (age, ethnicity, sex, diagnosis, stage, treatment)

10.3 How might this information make specific individuals or families identifiable?

10.4 If research data will be coded, how will access to the “key” for the code be limited? Include description of security measures (password-protected
database, locked drawer, other). List names or positions of persons with access to the key.

10.5 Will pedigrees be published? Include description of measures to minimize the chance of identifying specific families.

10.6 Will any results be provided to participants or their health care providers? Explain.

10.7 Will personally identifiable information be released to third parties?

10.8 Under what circumstances will data/samples be shared with other researchers?

10.9 Describe any additional features to protect confidentiality.

Only team members directly involved with your care and the research will have access to information, data, and results of the study. All information and data from this study will be identified with a code number instead of your name. The key for this code will be stored in a locked file cabinet.

The pre and post iodine-125 implant MR images of the prostate that we collect from you may be shared with other researchers in the future, linked together with other information such as your age, gender, and ethnicity. If this information is shared, we will not give other researchers your name, address, or phone number. Your name and all identifying information will be removed. There will be a code to link your data with your name and other personal information.

If future research on your pre and post iodine-125 implant MR images of the prostate provides important information related to your health, we will try to contact you. If you wish to be contacted, you must let Dr. Curtis Mack, MD at Arizona Oncology know about changes in your address or phone number.

11. Description of alternatives to participation (Other clinical or research interventions that participants should consider.)

Not-applicable.

12. Assessment of significance of study (Reasonableness of risks to participants in relation to the anticipated benefits of the study.)

The reasonable risk to participants is minimal since the pre-operative Ultrasound and post-implant CT scan necessary for this study are part of the standard treatment routine for prostate cancer patients. The only addition is the MRI studies to be done pre and post implant. MR imaging is safe and non-invasive, producing images with significant boundary definition of prostate volumes. The benefits of having the same patients imaged pre and post-implant, is considerable when identifying volume differences in relation to total dose the prostate and surrounding tissue received in post-implant dosimetry analysis. If CT imaging is used as the sole means of
evaluation in post-implant dosimetry, dose coverage of the prostate will not be as accurate. Though techniques have been developed to improve CT post-implant dosimetry, we feel there is room for significant improvement.

13. Description of specific funding source and budget. (If project is funded from PI’s discretionary budget, this should just be noted without budget)

13.1 Clinical Center funds (clinical tests, nursing, in-patient days, etc.)

13.2 DIR resources (data management, statistics, non Clinical Center testing, and contracts.)

Funding for this research comes from the Northwest Medical Center.

14. Description of Consent Process

14.1 Who will obtain consent (PI, study coordinator, and primary physician)? If collaborators who are not designated as co-investigators will be obtaining consent, the consent form should be signed by both the PI and the collaborator who is obtaining consent.

14.2 Setting where consent will be obtained (location of in-person discussion, phone, mail).

14.3 What information will be provided to participants? (Include consent form and any other related material, including information about stored tissues and pedigrees).

14.4 Protections for participants who may be vulnerable to coercion or undue influences (pregnant women, fetuses, children, people with impaired decision-making ability).

14.5 Will children be studied? (Include copy of assent form).

14.6 Are there special circumstances regarding obtaining consent? (Waived consent, opt-out, verbal consent, consent with speakers of other languages and translation of materials into other languages.)

Participant’s consent will be obtained by Dr. Curtis Mack, MD, at Arizona Oncology, 1845 West Orange Grove, Building 1, 520-544-2919 during the initial volume study.

A Consent Form is included in this packet.

Participants unable to make rational decisions in regards to study participation will not be included.

(11/29/00)
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Publications


Deana Tuttle, “TWINSCAN Diagnostics”, “Production Metrology”, and “Imaging and Overlay Errors for TWINSCAN”, ASM Lithography, Veldhoven, Netherlands.

Presentations/Lectures


Radiation Therapy Seminar, 2005, Las Vegas, Nevada. “Comparison and Application of Intensely Modulated Radiation Therapy (IMRT) and Three-dimensional Conformal Radiotherapy (3D-CRT).”


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Awards

Tandy Technology Teacher of the Year, 1996

Thesis Title: Post-implant Dosimetry Analysis of Brachytherapy Patients using Pre and Post-implant MRI

Thesis Examination Committee:
Chairperson, Dr. Phillip Patton, Ph.D.
Committee Member, Dr. Steen Madsen, Ph.D.
Committee Member, Dr. Mark Rudin, Ph.D.
Committee Member, Dr. Merrill Landers, Ph.D.
Graduate Faculty Representative, Dr. James McWhorter, Ph.D.