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**A Dosimetric Study on Photon Beam Energies With and Without a  
Flattening Filter in SBRT Treatments for Prostate Cancer**

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**Medical Dosimetry Master's Program**

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## **Abstract**

**Purpose:** The role of radiation therapy in managing prostate cancer has developed and improved greatly throughout the years. The purpose of this study was to analyze a newly developing method of treatment practices with two different therapy energies.

**Methods:** This retrospective study pulled patient data from the facility's treatment planning system database who had primary prostate cancer treated to the prostate bed. Each patient was planned for the same treatment technique with two different beam energies, 6X and 6FFF (flattening filter free).

**Results:** A two-sample t-test was done to compare means of the max doses to the bladder, rectum, and femoral heads between the two energies, as well as the estimated time it would take for the treatment to be executed on the treatment machine. The means for the bladder, rectum, and max doses showed to have no difference between them but the time did show a significant difference.

**Conclusions:** There was not a dosimetric difference between treating with 6X and 6FFF energy, but a significant decrease in time, showing that it would be beneficial to treat with 6FFF. The decrease in time also decreases the chance of anatomical differences occurring between treatment set up and treatment completion.

## Introduction

Prostate cancer is the most common cancer in men. Nearly half of all newly diagnosed cases now being clinically localized asymptomatic cancers with the most common prostate cancer being adenocarcinomas. In 2014, there were 180,193 new cases diagnosed and 28,343 who died from prostate cancer just in the United States. Recently there has been a rise in the number of early diagnoses, with most recent data in 2017 showing 207,430 new cases<sup>7</sup>. This growth in the diagnosis of early-stage cancers is because of the increase of frequent testing initiatives and the escalated use of prostate specific antigen (PSA) screening since the 1990s<sup>1,2</sup>. As a result of these earlier diagnoses and a rise of localized cases from increased screening, only one in seven men will die from their cancer diagnosis. Even with the decreased mortality rates, prostate cancer is a disease with a highly variable natural history; advanced prostate cancer is a serious threat to both life expectancy and quality of life<sup>2</sup>. Due to this threat, it is important to recognize the differences in anatomy to better personalize treatment plans to each patient.

Although there will be differences in anatomy from patient to patient, it is important to understand the basic anatomy of the prostate. The prostate gland lies posterior to the pubic symphysis and lies anterior to the rectum, inferior to the bladder neck, and superior to the urogenital diaphragm. It consists of five lobes: an anterior, a posterior, a medial, and two lateral lobes. The anatomical position within the prostate consists of four zones: peripheral, central, transitional, and the anterior fibromuscular zone. An average prostate gland is between 20 and 30 cc with the peripheral zone composing two-thirds of its volume. The urethra passes centrally through the prostate gland. With treatment planning, the borders of the prostate relative to the bladder, rectum, and bony anatomy such as the femoral heads play an important role<sup>1,2</sup>. These healthy tissues of the rectum and bladder are referred to as organs at risk (OAR).

The anatomy plays an important role in treatment planning. Firstly, the physicians and dosimetrists must take into consideration the histology of the prostate cancer. A biopsy is done to take a sample of the tumor which is then analyzed in a lab to further provide information for the histology. Typically, prostate cancer is staged clinically using the tumor, nodes, metastasis system, known as TNM, with localized cancer that has not spread to distant sites or to lymph nodes being classified as T1 or T2<sup>3</sup>. Those cancers that have extended beyond the “prostate capsule” and have invaded the seminal vesicles are labeled T3. A T4 classification is for cancers that have invaded structures other than the prostate, such as the bladder or rectum, and are considered potentially metastatic. Each classification can be further divided into “a, b, or c” based on tumor involvement, localization, or even how the tumor was identified<sup>2</sup>.

Along with the determination of the histology, the physician must account for the grade of the tumor. The Gleason score (GS) is the most common method for grading. It is based on the morphologic architecture of the prostate tumor and is determined by adding the grades of the two most common histologic patterns found in the biopsy cores<sup>2</sup>. The GS is applicable to adenocarcinomas and squamous cell carcinomas but not to sarcomas or transitional cell carcinomas. Each pattern is graded from 1 (most differentiated) to 5 (least differentiated) and the overall score is the sum of these most common grades<sup>2,3</sup>. Therefore, the Gleason scores can range from 2 to 10. In modern clinical practice, the GS is broken down into three categories that can be used to describe the tumor: well-differentiated (score 2 to 6), moderately differentiated (score of 7), and poorly differentiated (score 8 to 10)<sup>2</sup>.

Finally, a patient’s PSA level is an important aspect in the staging of the tumor. The PSA level indicates the risk of a cancer, with low-risk cancer being slow growing and having a good chance of being cured. High-risk cancer is such that it is likely to recur or spread. This

screening should be discussed with men over the age of 40, for an elevated PSA may prompt a biopsy. According to S. Brawley et al, a PSA level up to 10 mcg per liter (L) reflects low-risk and very low-risk prostate cancer, 10 to 20 mcg per L reflects intermediate risk, and greater than 20 mcg per L reflects high-risk prostate cancer. However, elevated PSA levels can also result from recent ejaculation, benign prostatic hyperplasia (BPH, also called prostate gland enlargement), and prostatitis and may lead to false positive results, meaning that a biopsy was not necessary<sup>2</sup>. In summary, histology, grade, and PSA level are all useful in the clinical application for determining treatment options by case as well as identifying the risk of recurrence.

Since each patient will have varying diagnostic criteria, it is important to look at each treatment option and determine which is best for the specific case. Currently, the three most common recommendations for treatments include active surveillance, surgery, and radiation therapy<sup>1</sup>. Active surveillance is an appropriate strategy for patients who are asymptomatic and have low-risk disease. It involves routine PSA level screening and surveillance biopsies with the expectation to intervene with a more definitive treatment if disease progression is seen<sup>2</sup>. This option allows patients to wait until symptoms arise, frequently referred to as “watch and wait”.

Active surveillance offers low risk prostate cancers a passive approach while others may choose a more proactive and invasive treatment. Surgery involves a radical prostatectomy (RP) that can be performed using an open or minimally invasive approach, such as a robotic or laparoscopic surgery<sup>3</sup>. Between 40% and 50% of patients select to undergo this procedure initially. This surgery removes the prostate, the surrounding capsule, seminal vesicles, and the ampullae of the vas deferens. As with any surgery, there are risks involved including the following: urinary incontinence, trouble maintaining an erection, impotence, and a loss of

fertility<sup>2,3</sup>. Nerve sparing techniques may decrease the rates of risks of urinary incontinence and erectile dysfunction and laparoscopic techniques have decreased acute surgical morbidity, decreased blood loss, shortened hospital stays, and have more rapid postoperative recovery rates. However, patients with clinical evidence of extracapsular (T3) disease or high-risk factors, such as high GS or PSA levels, may be at an increased risk of residual disease after the nerve sparing surgery<sup>2</sup>. In cases like those, postoperative radiation therapy might be recommended.

Radiation therapy can be offered as salvage radiation post RP, or by its self as treatment to all levels of prostate cancer. Today, popular techniques include internal low dose rate (LDR) and high dose rate (HDR) brachytherapy as well as external photon and proton beam treatments. Brachytherapy is a good option as a definitive treatment of the prostate when a patient has opted out of surgery and the prostate is still intact for low-risk patients and some patients at an intermediate-risk. There are a few advantages of brachytherapy, including less treatment time, a rapid dose fall-off outside of the prostate, and less issues related to organ motion in planning and subsequent treatment delivery<sup>2</sup>. It can also be used as a boost after external beam therapy. The main disadvantage to brachy is that it is the most invasive approach to radiation and there are limitations of who can receive brachytherapy based on the volume of the prostate; these factors become void if a patient opts for the longer external beam treatment instead.

External beam radiation therapy (EBRT) is commonly used to treat patients with clinically localized or locally advanced prostate cancer over eight to nine weeks. It may be used to treat any clinical stage – T1 to T4 – with the goal of eradicating local prostate cancer before it advances or metabolizes<sup>2,3</sup>. Historically, the common practice for prostate cancer EBRT used to consist “of a 4-field box or bilateral 120-degree arcs that were delineated using bony landmarks or a single CT slice to include the prostate, seminal vesicles, and pelvic lymph nodes”<sup>2</sup>. This

three-dimensional conformal radiation therapy (3D-CRT) limited the prescription between 64 and 70 Gy because of large amount of normal tissue, including the rectum and small bowel, that was irradiated as a result. With an increase in technology in simulation, planning, and treatment execution, doses were able to increase without also increasing the toxicity.

In the mid-1990s, intensity-modulated radiation therapy (IMRT) was introduced as the newest technology to reduce normal tissue irradiation. External radiation now includes three-dimensional planning with computed tomography (CT) and magnetic resonance imaging (MRI) images, conformal treatment delivery paired with inverse planning and IMRT, and image localization utilizing cone beam CT, fiducial markers, and even ultrasound<sup>2</sup>. These new techniques improved upon the quality of radiation therapy, allowing for a safe delivery of higher radiation doses over 74 Gy while still taking into consideration of OAR dose tolerances. These higher doses then improved PSA control and overall survival, along with modest changes in toxicity and quality of life as reported by patients<sup>2</sup>. Using IMRT versus 3D-CRT allows for doctor defined treatment margins and creates better fall-off gradients between the PTV and surrounding structures such as the bladder and rectum. This led to better OAR sparing and is overall a better treatment option. There is also a more dynamic version of IMRT, volumetric modulated arc therapy (VMAT), that uses continuous beam arcs as opposed to a set number. VMAT continuously treats as the gantry rotates around the patient with the MLCs moving throughout the treatment. Either IMRT or VMAT are excellent options for treating prostate cancer and allow for conformal plans for low, intermediate, and high-risk patients.

No matter which EBRT treatment modality is used, there are multiple beam energies that can be chosen for treatment. Typically, prostate cancers are treated with a beam energy from 6 MV to 10 MV. Higher energies are not used due to neutron scatter that occurs with increasing



beam energy since we currently do not have a way to measure neutron dose in the patient. These beams are often “hardened” with a flattening filter; this filter is cone-shaped and attenuates the beam more along the central axis and less along the edges to produce a flat beam profile as seen in Figure 1. However, there is also the option of a flattening filter free (FFF) beam. It has been shown that IMRT plans developed with a FFF beam were clinically acceptable; dose distribution was similar, but the FFF plans required less monitor units (MU) since there is not a filter to attenuate the beam, decreasing the chance for leakage and scatter doses outside the treatment field<sup>4</sup>. This study by Vassiliev et al used intensity modulated radiation therapy (IMRT) and did not look at dynamic arc planning. The decrease in MU required also decreases the treatment time, lessening the amount of time the patient must be in clinic and is important regarding bladder and rectum filling during the treatment. Shorter treatments decrease the time from the daily verification films and reduce the chance of the anatomy changing over this time.

While FFF allows daily treatment time to be shortened, hypofractionation allows us to lessen the number of treatment days. Hypofractionation is considered when the daily dose is greater than 2 Gy, so the total number of treatment fractions decreases. All tissues have a radiobiological characteristic that is an indicator of sensitivity to fraction size. This is known as the  $\alpha/\beta$  ratio which ranges from 0.5 Gy to 10 or more Gy<sup>5</sup>. A tissue with a low  $\alpha/\beta$  ratio is one that resists radiation damage by DNA repair, so when the dose per fraction increases the cell death rate increases. In contrast, a tissue with a high  $\alpha/\beta$  ratio indicates a rapidly proliferating tissue, one that is less sensitive to fractionation. For prostate cancer, the  $\alpha/\beta$  ratio is low and even lower than normal tissues; therefore, hypofractionation has a radiobiologic advantage and is more efficient than conventional fractionation as shown by Hennequin et al<sup>5</sup>. In cases such as prostate cancer, hypofractionation is an effective option to also decrease treatment course length.

A treatment technique that has an extreme advantage of hypofractionation is stereotactic body radiation therapy (SBRT). This option delivers an extremely high dose of at least 500cGy per fraction of radiation in a small number of fractions. By combining this with VMAT, the arc technique allows for a more conformal dose to the treatment area in a smaller amount of time. This modality is effective and safe in both early-stage primary cancers and oligo-metastases, cancers that have spread from another part of the body<sup>6</sup>. SBRT has been studied using the FFF beams. It has been concluded that SBRT with FFF beams is a feasible option by Alongi et al but fails to look at this with a dosimetric point of view. To further their research, utilizing an autoplanning system by Pinnacle would make it more efficient to create such plans. This system allows the dosimetrist to input their desired restraints and treatment setup and then the computer attempts to create a plan based on these goals. In the end, it is up to the dosimetrist to check what has been created and then push the plan further to create the best possible treatment plan for the patient. By combining SBRT and autoplanning, not only will the doses to the OAR be better and the treatment planning to execution time will decrease, but the dose to the planning target volume (PTV) will be more conformal. With the pressure increasing from insurance companies to streamline treatment time, it will be beneficial to observe the planning of such an option. This study will analyze the planning of SBRT treatments for prostate cancer with 6X and 6FFF energies to see if there is a dosimetric difference between the two.

## **Materials and Methods**

### *Subjects*

This retrospective study used the local patient data base to pull a sample population of patients who had a diagnosis of primary cancer of the prostate. Based on the G-power program,

a minimum of 27 cases are needed for a medium effect, power of 0.8, and a p-value of 0.05 for a successful comparison of means. However, due to time restraints, a random selection of 13 patients who were treated previously with radiation for prostate cancer were selected. Cases were selected that had a prostate PTV previously contoured by the clinic's radiation oncologist. Each patient's original prescription was 7000cGy in 280cGy fractions for a total of 25 treatment fractions. The planning CT was used as well as the original contours for the PTV, femoral heads, bladder, and rectum. No identifying data was recorded, and patient files were numbered accordingly.

### ***Procedure***

For each subject, the original plan was copied without the dose so that all the contours came over. They were each planned to a prescription of 3625cGy in 725cGy fractions for five treatment fractions. Pinnacle treatment planning system version 16.2 was used, utilizing the auto planning feature with dose constraints put on the organs at risk based on the scorecard used (Table 1). Two arcs were created, treating 178 to 182 degrees counterclockwise and 182 to 178 degrees clockwise with the collimator rotated five degrees off axis. The max delivery time per beam was set to 140 seconds, which was the program's default as recommended by the Pinnacle representative. After the initial auto planning optimization, a second optimization was done with added goals set on the PTV: max dose at 105% of the dose, min DVH with 97% of the PTV getting 100% of the dose, and a uniform dose at 100% of the dose. Each plan was run so that most of the scorecard goals were met, as summarized in Table 1, that were taken from RTOG 0938. A total of two plans per patient, one at 6MV and one at 6FFF, were run for a total of 26 plans.

This model was created with the researcher's own experience in clinic and understanding how the autoplanning system could best be manipulated. After each run, optimization goals were adjusted to ensure that the OARs were spared as much as reasonably possible and that the PTV had optimum coverage, so that the CTV would receive the full prescription dose to its full volume. If multiple runs were needed, the goals were slowly pushed to decrease dose to the OARs and altering the dose distribution surrounding the PTV. Once the scorecard passed, the gradient and conformity indexes were calculated. The conformity index (CI) needed to be around 1 and the gradient less than 5. The CI was calculated by dividing the volume of the 100% isodose line by the PTV volume and the gradient by dividing the volume of the 50% isodose line by the PTV volume. Each plan met the criteria for RTOG 0938 and were clinically acceptable.

### ***Data Collection and Analysis***

After two plans for each patient were run, data was collected from Pinnacle's planning system. For each subject and each plan, the max dose for the bladder, rectum, and femoral heads were collected as well as the PTV size, bladder overlap percentage, rectum overlap percentage, and monitor units required. The max dose was collected for ease of comparison since all the other constraints were met. This data was taken directly from the treatment planning system. Data was imported to the IBM SPSS Statistics program to be cleaned and analyzed with a t-test statistical analysis. Data cleaning was done to simplify the analysis by renaming variables so that they were easily distinguished from one another, such as RECTUM\_6X and RECTUM\_6FFF. Analysis was done to compare the means of bladder max, rectum max, and femoral heads max doses between 6X and 6FFF energies.

## Results

The data collected on our sample population involved a wide range of anatomical differences. The PTV size ranged from 141.3cc to 410.6cc with a mean of 242.5cc and a standard deviation of 83.1cc. It would be beneficial to normalize contouring technique so that PTV size could be more uniform among patients but still taking into account their own unique anatomy. Bladder overlap percentages ranged from 2.8% to 65.5% with a mean of 20.5% and rectum overlap percentages from 4.1% to 14.5% with a mean of 8.5%. The overlap percentages came from the autoplanning system, where it calculates the amount of OAR volume that overlaps with PTV volume and can be the expected amount receiving the full prescription dose. The more that the PTV overlaps with an OAR, the higher dose to that OAR can be expected. For the plans run with 6X energy, the bladder max ranged from 3804cGy to 4005cGy with a mean of 3864cGy, rectum max from 3758cGy to 3906cGy with a mean of 3827cGy, femoral heads max from 1407cGy to 1612cGy with a mean of 1503cGy, and the time for the treatment to be completed ranged from 5.11 minutes to 8.11 minutes with an average time of 6.44 minutes. For the plans run with 6FFF energy, the bladder max ranged from 3779cGy to 4019cGy with a mean of 3851cGy, rectum max from 3752cGy to 3934cGy with a mean of 3844cGy, femoral heads max from 1159cGy to 1620cGy with a mean of 1463cGy, and the time for the treatment to be completed ranged from 1.42 minutes to 2.16 minutes with an average time of 1.76 minutes. This full summary with all standard deviations is shown in Table 2.

For the paired t-test, the null hypothesis was “There is no difference in means between 6X and 6FFF energies.” The alternative hypothesis was “There is a difference in means between 6X and 6FFF energies.” The tests were run to compare the mean max doses to the OARs between the two treatment energy modalities. If there was not a mean difference, the test

statistic would be very close to zero with a high p-value. The analysis showed that only the mean time differed between the two energies with significance of  $p < 0.001$  and showed that it was significant, so we reject the null and can conclude that the average treatment time differs between 6X and 6FFF energy plans. The means of the bladder max doses ( $p = 0.175$ ), the rectum max doses ( $p = 0.285$ ), and the femoral head max doses ( $p = 0.122$ ) failed to reject the null with a significance of  $p < 0.05$  and concluded that the means were similar. The output of this statistics t-test is shown in Table 3.

Overall, this analysis shows that the plans were dosimetrically similar, with no average differences in max doses to the OARs. There is a greater advantage when it relates to time to complete the treatment, with 6FFF treatments averaging 4.68 minutes faster than those run with a flattening filter of 6X energy.

## **Discussion**

With these results, we have shown that there is no difference dosimetrically in treating with 6X versus 6FFF in an SBRT setting of 3625cGy in five fractions when it comes to max doses to the organs at risk while considering that all mean and volumetric dose constraints were met. We did see a difference in treatment time, which would be a benefit to the patient; they would not have to lay on the treatment table for as long, decreasing the likelihood of anatomical differences occurring between setup films and treatment completion. In addition, the shortened treatment times can allow for a clinic to treat more patients in the day, making the insurance companies happy and bringing more money into the clinic.

This study showed that it was possible to create a viable treatment plan using an SBRT treatment schematic planned with Pinnacle's autoplanning software. This allows for multiple

plans to be run at once and gives a more conformal treatment to the prostate PTV. While autoplanning can take multiple hours to run, Pinnacle has the ability to run many plans at once so the dosimetrist can be more productive even if there is an increase in SBRT, and even VMAT, treatments.

### ***Limitations and Future Research***

Due to time restraints, we were not able to run plans on the recommended number of patients to achieve the strength of results we were hoping for. In the future, it would be beneficial to continue to run these plans to see if the same results occur. In addition, after discussion with the clinic's radiation oncologist, it was discussed that it would be beneficial to have a uniform method of contouring the PTV since it did vary among the different plans. Having guidelines to follow for such a research project could ensure that there were no confounding variables impacting the dosimetric view of this planning technique. With the wide ranges of PTV sizes, bladder overlap, and rectum overlap percentages, it is also concerning to have these conclusions based on a small sample size. By increasing the sample size, the distribution of these volumes would become more normal, and the standard deviation would decrease.

If there was not such a time constraint for this project, it would have been beneficial to expand the cases to include patients whose lymphatics were also being treated, such as those being treated with a simultaneous integrated boost. Prostate treatments vary greatly among patients, so to have more data and separate them based on full pathology and treatment technique. Another topic would be to expand upon the differences in PTV size among patients and compare that to the doses that the OARs receive as well as difficulty in covering the CTV to

ensure tumor control. With prostate cancer being so prevalent in men in the United States, further research can only benefit patients and decrease complications.

Another limitation is that we did not collect the volumetric doses for the OARs, such as the bladder and rectum, in each plan. Max doses are not the only dosimetric criteria that impacts the quality of a plan, but the mean doses and volumetric doses are a vital part of the plan evaluation process<sup>10</sup>. While each plan met the overall constraints, this research study fails to analyze if 6FFF could have been better at every metric, not just that the max doses were the same and that the time per treatment was much less for 6FFF than 6X. Meeting constraints does not imply that the two plans per patient were the same in terms of quality. Expanding upon our research, this would be an excellent addition to further evaluate the differences between 6X and 6FFF energies in SBRT prostate treatments.

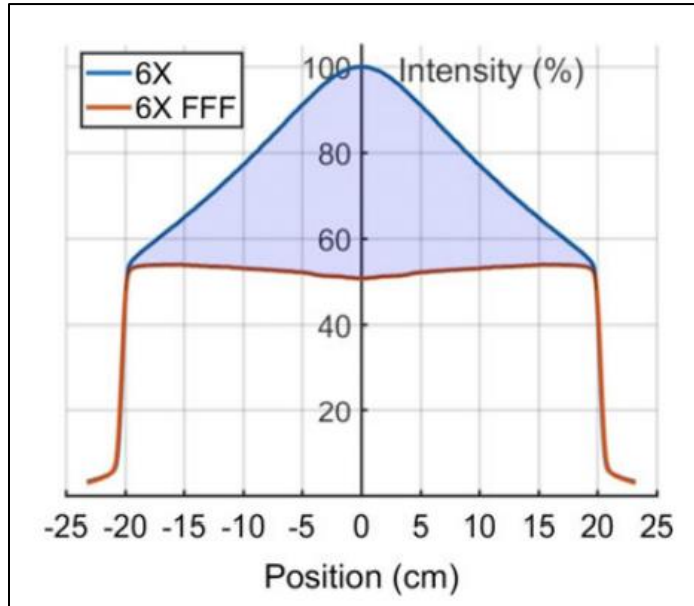


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## Appendix

**Figure 1:** Profiles of 6X and 6X FFF beams



**Table 1:** Scorecard Used for plan evaluation.

<b>ROI</b>	<b>Type</b>	<b>Dose (cGy)</b>	<b>Volume</b>
<i>PTV</i>	Min DVH	3625	95%
<i>PTV</i>	Max DVH	3988	0.030cc
<i>Bladder</i>	Max Dose	3800	-
<i>Bladder</i>	Max DVH	1830	15cc
<i>Femoral Heads</i>	Max DVH	3000	10cc
<i>Penile Bulb</i>	Max Dose	5000	-
<i>Rectum</i>	Max Dose	3800	-
<i>Rectum</i>	Max DVH	2500	20cc
<i>Bowel</i>	Max Dose	3200	-

**Table 2:** Descriptive Statistics on the data collected.

	Minimum	Maximum	Mean	Std. Deviation
<i>PTV SIZE C^3</i>	141.318	410.597	242.534	83.134
<i>BLADDER OVERLAP %</i>	2.785	65.486	20.456	20.161
<i>RECTUM OVERLAP %</i>	4.117	15.449	8.490	3.143
<i>BLADDER_6X CGY</i>	3804.3	4005	3863.6	58.1
<i>RECTUM_6X CGY</i>	3757.7	3905.6	3826.9	38.9
<i>FEMORAL HEADS_6X CGY</i>	1407.4	1611.8	1503.8	60.7
<i>TIME_6X MINUTES</i>	5.11	8.11	6.44	0.89
<i>BLADDER_6FFF CGY</i>	3778.8	4019	3850.9	68.7
<i>RECTUM_6FFF CGY</i>	3752.2	3934.2	3844.3	50.9
<i>FEMORAL HEADS_6FFF CGY</i>	1158.6	1619.7	1462.9	120
<i>TIME_6FFF MINUTES</i>	1.42	2.16	1.76	0.23

**Table 3:** A paired samples t-test showing the paired differences.

		95% Confidence Interval of Difference						
		Mean	SD	Std Error Mean	Lower	Upper	t	Sig (2- tailed)
<b>Pair 1</b>	<i>Bladder_6X</i>	12.7	31.7	8.8	-6.5	31.9	1.442	0.175
	<i>Bladder 6FFF</i>							
<b>Pair 2</b>	<i>Rectum_6X</i>	-17.4	56.1	15.6	-51.3	16.5	-1.119	0.285
	<i>Rectum_6FFF</i>							
<b>Pair 3</b>	<i>Femoral Heads_6X</i>	40.9	88.6	24.6	-12.6	94.4	1.664	0.122
	<i>Femoral Heads_6FFF</i>							
<b>Pair 4</b>	<i>Time_6X</i>	4.7	0.7	0.19	4.3	5.1	24.2	0.000
	<i>Time_6FFF</i>							