Oregon Health & Science University
School of Medicine

Scholarly Projects Final Report

Title *(Must match poster title; include key words in the title to improve electronic search capabilities.)*

Assessment of Mid-Treatment Imaging on Shifts during Stereotactic Body Radiotherapy for Prostate Adenocarcinoma

Student Investigator's Name

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3/15/2023

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Project Course *(Indicate whether the project was conducted in the Scholarly Projects Curriculum; Physician Scientist Experience; Combined Degree Program [MD/MPH, MD/PhD]; or other course.)*

Scholarly Projects Curriculum

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Project/Research Question

- How does time between pre-treatment and mid-treatment CT relates to application of shifts and magnitude of shifts on the treatment table?
- How does SpaceOAR rectal gel affect application and magnitude of shifts?

Type of Project *(Best description of your project; e.g., research study, quality improvement project, engineering project, etc.)*

Retrospective research study

Key words *(4-10 words describing key aspects of your project)*

Prostate cancer, stereotactic body radiation, intrafraction motion, SpaceOAR

Meeting Presentations
If your project was presented at a meeting besides the OHSU Capstone, please provide the meeting(s) name, location, date, and presentation format below (poster vs. podium presentation or other).

N/A

Publications *(Abstract, article, other)*
If your project was published, please provide reference(s) below in JAMA style.

N/A

Submission to Archive
Final reports will be archived in a central library to benefit other students and colleagues. Describe any restrictions below (e.g., hold until publication of article on a specific date).

No restrictions

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Next Steps

What are possible next steps that would build upon the results of this project? Could any data or tools resulting from the project have the potential to be used to answer new research questions by future medical students?

Yes, this data could be used to answer new research questions. It would be interesting to increase the power of this study and analyze more patients, and then to evaluate how well OHSU planned treatment volumes (PTVs) correlate with average magnitude of translational/rotational shifts observed. It would also be helpful to have more timing information (e.g. total treatment time, as opposed to just the timing of the initial CT and mid-treatment CT. Additionally could evaluate if other factors like BMI have an impact on magnitude or type of shift observed.

Please follow the link below and complete the archival process for your Project in addition to submitting your final report.

https://ohsu.ca1.qualtrics.com/jfe/form/SV_3ls2z8V0goKiHZP

Student's Signature/Date *(Electronic signatures on this form are acceptable.)*
This report describes work that I conducted in the Scholarly Projects Curriculum or alternative academic program at the OHSU School of Medicine. By typing my signature below, I attest to its authenticity and originality and agree to submit it to the Archive.

3/16/2023

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Report: *Information in the report should be consistent with the poster, but could include additional material. Insert text in the following sections targeting 1500-3000 words overall; include key figures and tables. Use Calibri 11-point font, single spaced and 1-inch margin; follow JAMA style conventions as detailed in the full instructions.*

Introduction *(≥250 words)*

It is estimated that there will be over 240,000 new cases of prostate cancer in 2021, and greater than 34,000 deaths. [1] Prostate cancer currently represents 13.1% of all new cancer cases diagnosed annually in the U.S. and is the most commonly diagnosed cancer in men.[2] Additionally, prostate cancer is the second leading cause of cancer death in U.S. men.[3] At the time of diagnosis, 74% of men have localized disease, confined to the prostate.[2] The high incidence of curable disease warrants further research into treatments that can be both efficient and efficacious.

Stereotactic body radiotherapy (SBRT) is delivered in much fewer fractions and higher doses than conventional EBRT, thus it is imperative that the treatment is both accurate and precise to ensure treatment of the prostate as well as minimization of radiation to surrounding organs at risk (OAR).[1] Given the possibility for intrafraction motion during SBRT treatment, it is important to monitor for it. One study using intraprostatic fiducial markers demonstrated that there is a 10% chance of prostate displacement >/=5 mm after 18 minutes.[4] A mid-treatment image with correction as needed could be a simple alternative to continuous real-time imaging, and that will be the focus of this study. If this were proven to be true, it would presumably make it easier for more radiation programs to start their own SBRT program since they would not need to purchase a real-time tracking device or robotic-based radiosurgery system for tracking fiducial marker. [5]

Studies have shown that continuous monitoring of prostate position and intervention during treatment is important due to shifts outside of planned prostate position that necessitate corrective interventions. The amount of time between initial pre-treatment and mid-treatment CT can vary for multiple reasons, and thus it would be helpful to understand the relationship between intrafraction prostate motion and time. The objective of this study is to assess how time between pre-treatment and mid-treatment CT relates to application of shifts and magnitude of shifts. An additional objective is to assess how SpaceOARar rectal gel (allows separation of rectal wall from prostate) could affect application and magnitude of shifts.

Methods *(≥250 words)*

This study is a retrospective review of 93 patients that were treated with prostate SBRT between 2018 and 2022. Mosaiq database which contains imaging shift data and the electronic medical record EPIC were utilized for data collection. All patients were treated with the same protocol, head in, supine, arms across chest, and straight legs with full-moderately full bladder. A Vac-Lok™ Cushion was used for immobilization, with pants off and alignment conducted by 3 point pelvis tattoo. The majority of patients also had three gold fiducials implanted in the prostate which allowed for prostate alignment. Pretreatment cone beam CTs (CBCTs) were used to position patients. Mid-treatment CBCTs were utilized to ensure proper positioning of prostate, and allow for repositioning of the patient if the prostate was outside of treatment margins. The

prescription dose was 36.25 Gy divided over 5 fractions.

A total of 415 treatment fractions were analyzed. Inclusion criteria for this study was that patients had to have biopsy-proven prostatic adenocarcinoma that was localized to the prostate, >18 years old, and ADT therapy was allowed.

Exclusion criteria included salvage SBRT (receiving radiation after surgical removal of prostate). Individual fractions were excluded from analysis if Mosaiq recorded two dates for one fraction, making it unclear which set of corrective shifts were applied on that date. Due to repeated measures (each patient receives 5 treatment fractions) most analyses were performed by comparing each of the 1st fractions of each patient to each other, and so on. Descriptive statistics summarize study sample characteristics. Outcomes were assessed using independent t-test and Pearson chi squared test as well as Pearson correlation coefficient.

IBM SPSS Version 28 software utilized for data analysis and statistics.

Results *(≥500 words)*

The study population included 93 patients with median age of 70 years old at time of treatment, with age range from 50-84 years old. The median weight of patients was 205lbs, with a range from 146-321lbs. The average treatment time for all patients was 6 minutes 55 seconds ± 2 min 59 seconds, median time being 6 min 13 seconds, and the range of treatment time from 4 minutes 21 seconds to 41 minutes 7 seconds. Notably, 95% of fractions had a treatment time of <10 minutes. The majority of patients were clinical T stage CT1 (65%), followed by CT2 (32%) and then CT3 (3%). Out of the 93 patients, 89 had gold fiducial markers in place (96% of patients).

There were a total of 415 fractions included in the analysis with 303 fractions without SpaceOAR, and 112 fractions with SpaceOAR. Out of the 415 fractions, there were 203 fractions where a shift was applied (49%), and 212 shifts with no shift applied (51%). In evaluating all patients to see if there was a difference in whether a shift was applied or not for fraction 1-5, there was no statistically significant difference (p=0.525). In a comparison of patients that have SpaceOAR rectal gel to patients without SpaceOAR rectal gel, there was no significant difference in whether a shift was applied (p-value for fraction 1-5 ranged from 0.384 to 0.897).

In comparing the average magnitude of translational shifts (superior/inferior, anterior/posterior, right/left) for fraction 1 the average shift for patients with SpaceOAR was 0.93 ± 1.44 mm, and for patients without SpaceOAR was 1.07 ± 1.57 mm (p = 0.385). In a comparison of all fractions (112 without SpaceOAR, 303 with SpaceOAR), the average shift magnitude for SpaceOAR was 1.44 ± 2.3 mm and for patients without SpaceOAR was 1.23 ± 1.82 mm (p = 0.170).

In evaluating the correlation between magnitude of the three translational shifts and seconds between initial CBCT and mid-treatment CBCT (fraction 1, 74 patients), the r value was 0.115 with a p-value of 0.330 (Figure 1). Individual analysis of all five fractions returns a similar r value, but two out of five have a p-value of <0.05. In cumulative analysis of all 415 fractions and the relationship between magnitude and time the r value was 0.175 and the p value was <0.001.

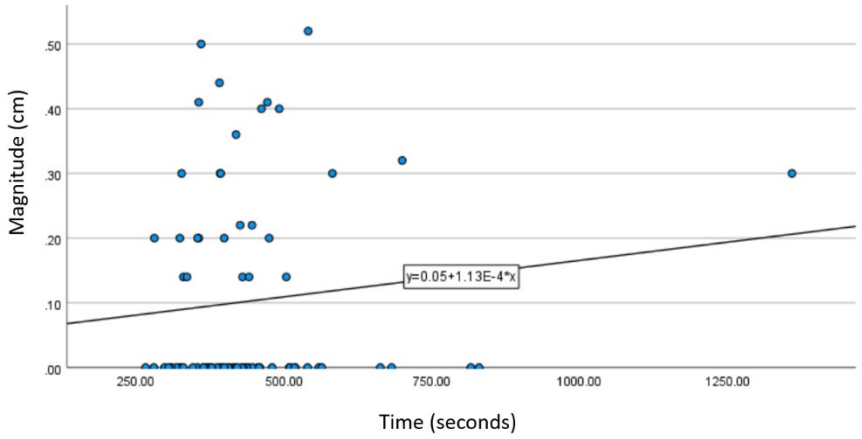

Fig. 1– Correlation between magnitude of the three translational shifts and seconds between initial CBCT and mid-treatment CBCT (fraction 1, n=74).

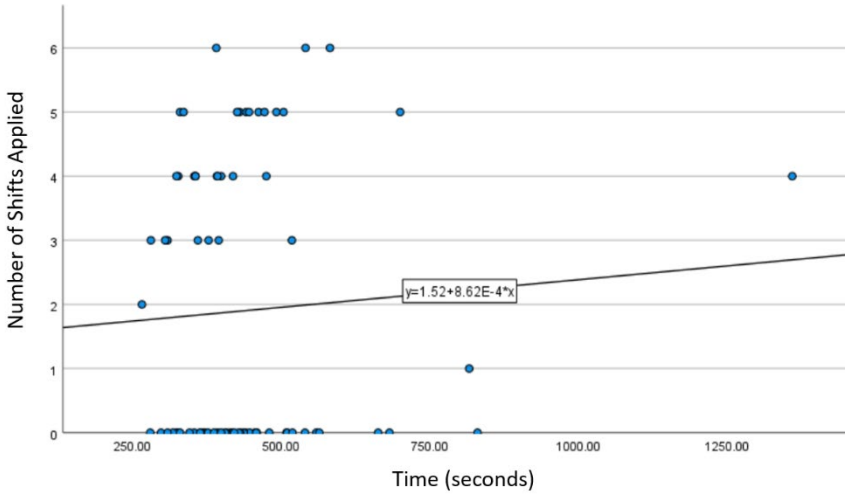

Fig. 2– Correlation between number of translational and rotational shifts applied and seconds between initial CBCT and mid-treatment CBCT (fraction 1, n=74).

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Additionally, the correlation between the number of shifts applied and seconds between initial CBCT and mid-treatment CBCT was evaluated. Shifts were not differentiated in this calculation, and the maximum number of shifts per fraction is 6. In comparison of fraction 1 (74 individual fractions) to time between initial CBCT and mid-treatment CBCT the r-value was 0.061 with a p-value of 0.61 (Figure 2). Individual analysis of all five fractions returns a similar r value, and no p-values are significant. In cumulative analysis of all 415 fractions and the relationship between the number of shifts and seconds between initial CBCT and mid-treatment CBCT the r value was 0.093 and p value was 0.059.

The average magnitude of the shift for superior/inferior was 0.32 ± 1.66 mm (favor superior). The average magnitude of shift for left/right was -0.02 ± 0.87 (favor left). The average magnitude of shift for anterior/posterior was -0.05 ± 1.38mm (favor posterior), the average shift for coronal was -0.02 ± 0.44 degrees (favor CCW). The average shift for sagittal was -0.38 ± 1.29 degrees (favor CCW). The average shift for transverse was -0.06 ± 0.58 degrees (favor CCW).

Discussion *(≥500 words)*

Previous studies of intrafraction motion of the prostate have shown that the probability of motion increases with time.[6] However, to our knowledge, have not looked at the correlational relationship between magnitude of prostate motion and time. It is important to note that other studies have elucidated that prostate motion typically occurs in certain patterns, with the logical argument of bladder filling during treatment to explain posterior and inferior drift, necessitating anterior and superior corrective shifts, respectively.[6,7] This serves as one example of a factor that can affect prostate positioning with time. In averaging superior/inferior shifts (+0.32 ± 1.66 mm, favor superior) and anterior/posterior (-0.05 ± 1.38mm, favor posterior) shifts of this study, the trend was not as clear, but is not denied by our findings.

First, there was also no significant difference in whether a shift was applied in fraction 1 versus 2, 3, 4, or 5 (p=0.525). Though protocol is the same for each fraction, this analysis is further reassuring that there is not some variable related to different treatment session that affects intrafraction prostate motion.

In this study, there was a weak correlation (r=0.115) between magnitude of shifts applied and time between pre-treatment and mid-treatment CT (figure 1), indicating that length of time by itself is likely not a strong contributor to intrafraction prostate motion. With inclusion of all 415 fractions in the analysis, the strength of the relationship increased (r=0.175), but despite statistical significance this is still a weak correlation. Arguably, the weak correlation between time and intrafraction prostate motion is in support of mid-treatment CT over continuous monitoring of prostate motion.

There is no or weak correlation between time between pre-treatment and mid-treatment CT and number of shifts applied (figure 2), which again suggests that intrafraction prostate motion is not strongly associated with time.

Patients with SpaceOAR rectal gel do not appear to have different translational intrafraction motion of the prostate compared to patients without SpaceOAR, indicating that the rectal gel does not significantly mitigate or alter prostate motion. This finding is supported by smaller studies. A small 2020 study found

significance only in the sagittal rotational axis, but notably, this study only had 20 patients.[8] In another study published in August 2020, this one evaluating the effect of hydrogel spacer on intrafractional prostate motion during CyberKnife treatment, they did not find any significant effect on hydrogel space on intrafractional prostate motion in the translational axes.[9]

There are many possible future directions for work related to this project. It remains unclear what factors influence intrafraction prostate motion and would be beneficial to investigate how other variables (prostate size as example) could alter motion, such that treatment-related imaging could be tailored to patient specific factors. In a 2015 study of continuous monitoring of the prostate, 10% of patients would not achieve PTV D95 (the minimum dose planned to 95% of the target volume) due to prostate shifts during treatment.[6] Given this it would be beneficial to further elucidate the relationship between prostate intrafraction motion and time. Specifically, what is the average treatment time at which the intrafraction motion of the prostate brings the prostate out of the planned treatment volume (PTV), as this is information that could help with timing intrafraction CTs for positioning, as opposed to implementing a continuous monitoring system which as discussed before, is expensive.

One of the limitations to also consider for this project is the sample size. This is proven by the fact that a significant correlation was not detected when comparing each fractions time between pre-treatment and mid-treatment CBCT to magnitude, but was clearly seen when all fractions were analyzed together.

Another limitation of this study is that we did not have total treatment time, because the two times we were able to collect from the Mosaiq database were the time of the initial CBCT and the mid-treatment CBCT. In order to collect other times, someone would need to manually record them (e.g., total beam on time, time between initial CBCT and beam on time). This could be helpful if a study is able to determine the time threshold at which prostate motion would bring the prostate outside of PTV, and thus, mid-treatment CTs could be coordinated to happen in anticipation of significant motion.

Conclusions *(2-3 summary sentences)*

Ultimately, this study does not reveal a strong correlation between time and intrafraction prostate motion that would support the need for continuous monitoring of intrafraction prostate motion. Additionally, the SpaceOAR rectal gel does not have appear to have a significant influence on intrafraction prostate motion.

References *(JAMA style format)*

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