Experimental evaluation of the dosimetric impact of intrafraction prostate rotation using film measurement with a 6DoF robotic arm

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Abstract

Purpose:

Tumor motion during radiotherapy can cause a reduction in target dose coverage and an increase in healthy tissue exposure. Tumor motion is not strictly translational and often exhibits complex six degree-of-freedom (6DoF) translational and rotational motion. Although the dosimetric impact of prostate tumor translational motion is well investigated, the dosimetric impact of 6DoF motion has only been studied with simulations or dose reconstruction. The present study aims to experimentally quantify the dose error caused by 6DoF motion. The experiment was designed to test the hypothesis that 6DoF motion would cause larger dose errors than translational motion alone through gamma analyses of 2D film measurements.

Methods:

Four patient-measured intrafraction prostate motion traces and four VMAT 7.25Gy/Fx SBRT treatment plans were selected for the experiment. The traces represented typical motion patterns, including small-angle rotations (<4°), transient movement, persistent excursion and erratic rotations (>6°). Gafchromic film was placed inside a custom-designed phantom, held by a high precision 6DoF robotic arm for dose measurements in the coronal plane during treatment delivery. For each combination of the motion trace and treatment plan, two film measurements were made, one with 6DoF motion and the other with the 3D translation components of the same trace. A gamma pass rate criteria of 2% relative dose/2 mm distance-to-agreement was used in this study and evaluated for each measurement with respect to the static reference film. Two test thresholds, 90% and 50% of the reference dose, were applied to investigate the difference in dose coverage for the PTV region and surrounding areas, respectively. The hypothesis was tested using a Wilcoxon signed-rank test.

Results:

For each of the sixteen plan and motion trace pairs, a reduction of the gamma pass rate was observed for 6DoF motion compared with 3D translational motion. With 90% gamma-test threshold, the reduction was 5.8% ± 7.1% ($p<0.01$). With 50% gamma-test threshold, the reduction was 4.1% ± 4.8%($p<0.01$).

Conclusion:

For the first time, the dosimetric impact of intrafraction prostate rotation during SBRT treatment was measured experimentally. The experimental results support the hypothesis that 6DoF tumor motion causes higher dose error than translation motion alone.

1. Introduction

The range and distribution of intrafraction prostate motion observed in patients has been reported in a number of studies.[1-3] An analysis of prostate intrafraction translational motion in 427 patients found that displacement >2mm occurred in 66% of fractions while 28% of fractions had >3mm displacement.[4] In addition to translational motion, the prostate motion also includes rotation. Prostate intrafraction rotations were reported to be small in most cases.[5-7] The most dominant rotations were observed to be around the left-right (LR) axis.[1,8] Intrafraction rotations of 2.5º(±2.3º) around the LR axis were reported in a study on 39 prostate cancer patients.[3] However, in extreme cases, the rotational motion can reach beyond 10º.[6,8]

Simulation studies suggest that the dosimetric effect of prostate intrafraction rotational motion is significant. A simulation study on 548 prostate motion trajectories[9] showed that rotational corrections up to 5º were required to achieve 98% Clinical Target Volume (CTV) coverage in 98% of the treatments. In addition, it was found that a 3 mm CTV to Planning Target Volume (PTV) margin was only sufficient for adequate CTV D_{95} coverage in 65% of the 26 patients.[6] Rijkhorst et al [10] suggested an additional 4 mm margin was needed to account for tumor rotation.

To date, the dosimetric effect of intrafraction prostate rotation was studied only through simulation or retrospective dose reconstruction. The majority of studies used averaged rotation displacement to quantify the effect of intrafraction rotation. In this paper, we describe an experimental evaluation of the dosimetric impact of intrafraction 6DoFmotion on prostate SBRT treatment. The experiment was designed to test the hypothesis that intrafraction 6DoF motion would cause a larger dosimetric error compared with translational motion only, and to quantify the magnitude of this difference.

2. Materials and Methods

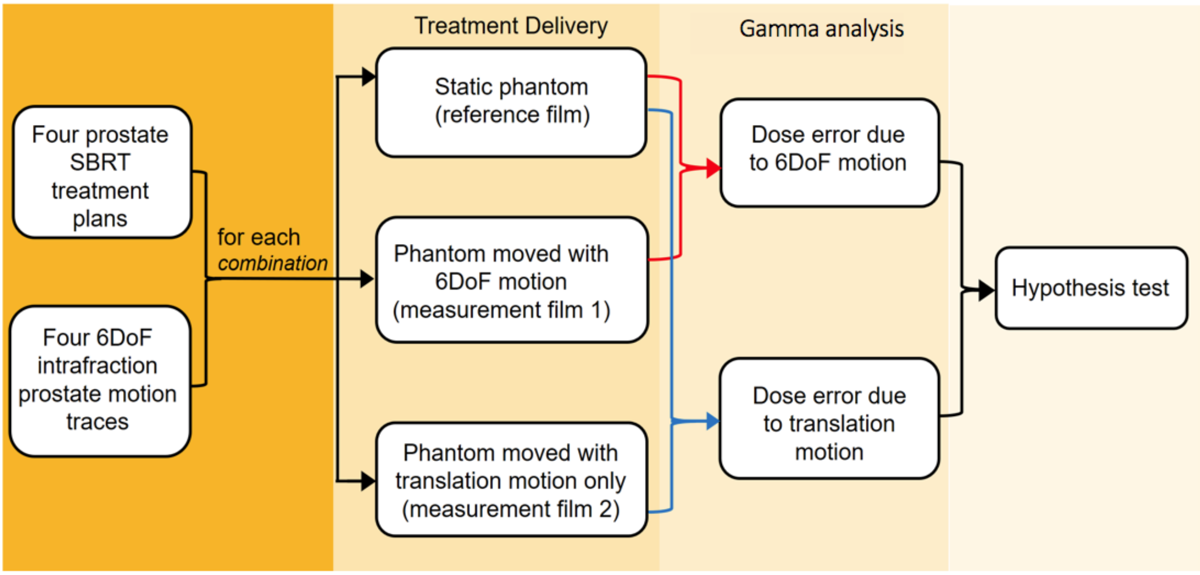

Figure 1: Process chart for the experiment.

2.1 Experimental Setup

The experiment was designed to measure coronal plane dose distributions of prostate SBRT treatment plans using film. The phantom holding the film was positioned at isocenter and moved by a programmable robotic arm according to measured patient 6DoF motion trajectories. The experimental process is illustrated in Figure 1 and the experimental setup is shown in Figure 2.

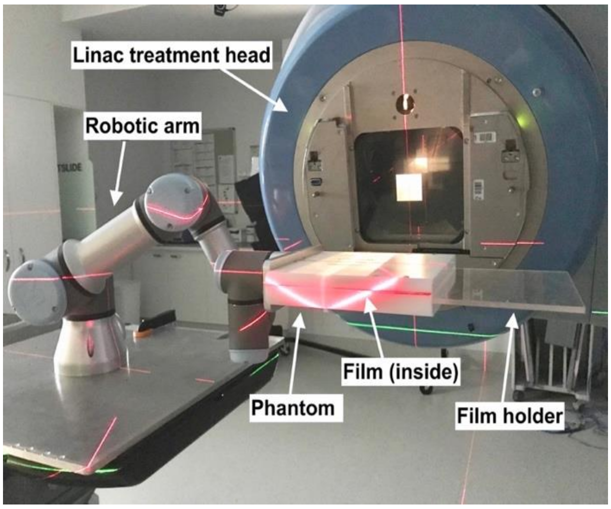

Figure 2: The experimental setup: a plastic phantom containing film was attached to a programmable 6DoF robot. The robot was used to replicate patient-measured prostate motion during treatment delivery.

2.2 6DoF robotic arm

A programmable 6DoF robotic arm (UR3 robot, Universal Robots, Odense Denmark) was chosen for its wide range of movement and high localization accuracy. The six rotating joints, each with a 360° range, and 500 mm reach enable the robot to reproduce translational or rotational organ movement.[a] In-house software was used to interface with the robot. The dynamic localization accuracy of the robotic arm in reproducing motion traces is <0.2 mm and <0.2° for translation and rotation, respectively.[11]

2.3 Phantom and film

The phantom was made of polyoxymethylene acetal (density=1.4 g/cm^3) with outer dimensions 213 × 200 × 40 mm^3. Its inner structure was an exact fit to the transparent film holder to allow easy slide-in and fixation. The film holder comprised a two-layer structure made of Polymethyl methacrylate (PMMA, density=1.16 g/cm^3) with a thin layer of hollow space (120 ×170 mm^2) for the film to fit (Figure 3).

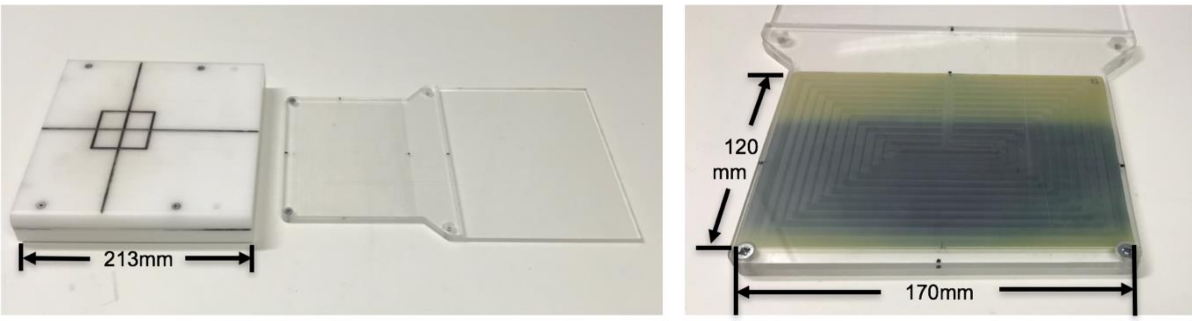

Figure 3: Left, custom-designed polyoxymethylene phantom and plastic PMMA film holder. Right, post-irradiation film inside the film holder.

The film used in the experiment was Gafchromic™ EBT3 dosimetry film (Ashland Advanced Materials, New York, USA). The EBT3 film was selected as the dosimeter for these experiments as it has a surface spatial resolution of ≤25 μm and a dynamic range of 0.1 Gy to 20 Gy.[b]

2.4 Motion traces

The motion traces (Figure 4) used in the experiment were acquired during SBRT treatments of prostate cancer patients enrolled in the TROG15.01 SPARK (Stereotactic Prostate Adaptive Radiotherapy utilizing Kilovoltage Intrafraction Monitoring) trial.[12] The motion monitoring method, Kilovoltage Intrafraction Monitoring (KIM), reconstructed the real-time 3D positions of gold fiducial markers inside the prostate based on their 2D X-ray projections,[13] and then computed 6DoF translation and rotation around the center-of-mass of the fiducial markers using an iterative closest point (ICP) algorithm.[7,14] Four traces representing four typical types of observed prostate intrafraction rotation were selected.

As shown in Figure 4, the first trace (Figure 4.a) consisted of continuous small-angle (<4°) rotations around all three axes, which represented the most prevalent pattern found in published studies: a mean motion magnitude below 3°.[3,5,7,15] The second trace (Figure 4.b) included a transient large-angle deflection that went beyond 10°, an example of extreme motion.[6,8] In the third trace (Figure 4.c), there was a persistent rotational excursion (average 4.5°) about the LR axis while the rotation about the other two axes was small, corresponding to the dominance of rotations about the LR axis in most patients.[1,8] In all but the third trace, the translation motion was small (<3 mm). In the third trace, the translation motion exhibited a slow drift pattern in the SI and AP direction. The fourth trace (Figure 4.d) was selected to study the impact of large-angle (>6°) and high-frequency erratic behaviors of tumor rotation. As the experiment delivery duration exceeded the duration of the second and fourth traces, these traces were repeated. A low-pass filter was applied to each trace to eliminate measurement noise.

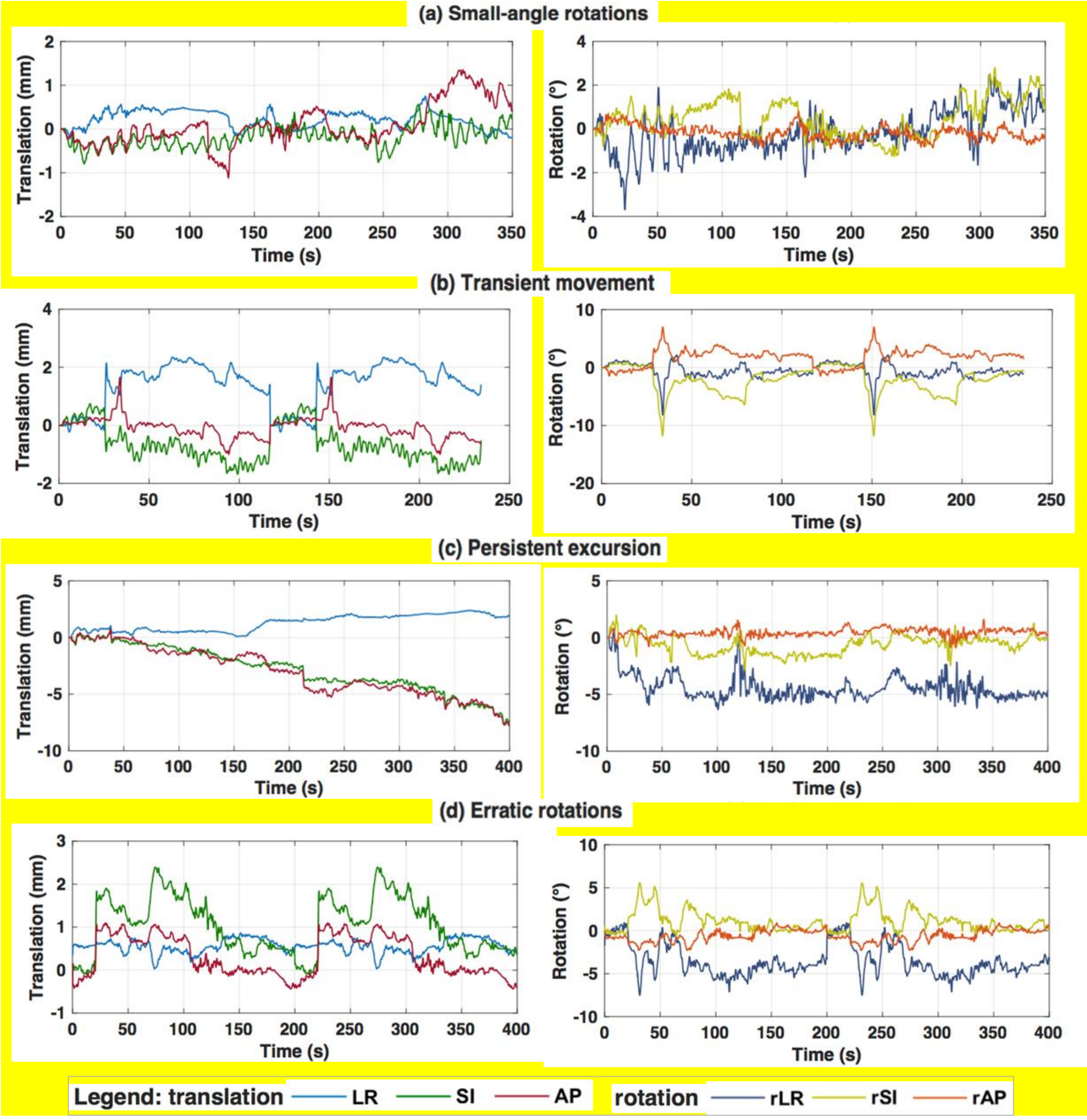

Figure 4: The four selected clinical prostate motion traces used in the study. Plots show translation (mm) in the left-right (LR), superior-inferior (SI) and anterior-posterior (AP) directions and rotation (degrees) about the three corresponding axes (rLR, rSI and rAP).

2.5 Treatment plans

Four VMAT 6MV treatment plans, designed to deliver 7.25Gy per fractions in two arcs (240º to 120º and 120º to 240 º), from the SPARK trial were used for investigation in the experiment. Details on the planning constraints can be found in Keall et. al (2015).[16] The PTV cross-section of the plans differed in shape, ranging from relatively circular to wedge-shaped, as can be seen in the dose distributions of the reference film measurement for each plan (Figure 5).

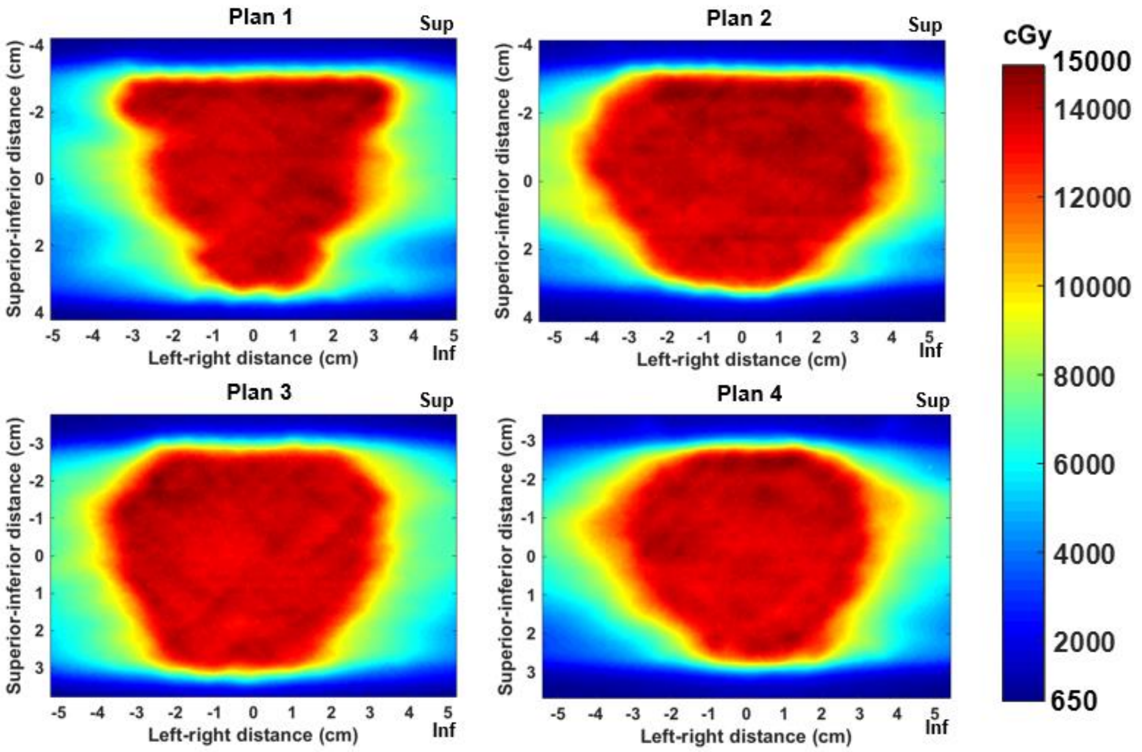

Figure 5: Measured coronal reference dose distributions for the four prostate SBRT treatment plans. There was no phantom motion for these reference scans.

For each treatment plan, one static coronal film measurement of the dose delivery at isocenter was obtained first to serve as the reference film. After that, for each motion trace, two film measurements were made while the robot replicated full 6DoF motion and 3D translation only, respectively.

2.6 Film processing

All the film pieces were scanned at 75 dpi by a 48-bit flatbed RGB color scanner (EPSON Expression 12000XL, Seiko Epson Corporation, Nagano, Japan). Each piece of measurement film was scanned before and after radiation exposure to calculate the net change in optical density (OD) with 2D uniformity correction applied using DoseLab (version 6.80, Varian Medical System). The net OD was converted to dose with accuracy of 0.1 cGy, following AAPM TG-69.[17]

Each measurement film was registered to the reference film manually. Following film registration, a gamma test[18] using a criteria of 2% relative dose/2 mm distance-to-agreement (DTA) between the measured film and the reference film was performed. The test criteria were stricter than 3%/3 mm as suggested for IMRT commissioning in AAPM TG-119[19]. The reference dose in each test was the D_{max} of the reference (static measurement). Two test thresholds, 90% and 50% of the reference dose, were applied to investigate the difference in dose coverage for the PTV region and surrounding areas, respectively.

To evaluate whether the pass rate difference was statistically significant, a Wilcoxon signed-rank test was performed on the two groups of gamma pass rate data for 6DoF motion and 3D translation. This test was chosen based on the small sample size and the unknown population distribution.

3. Results

A summary of the gamma pass rates with 90% test threshold is plotted in Figure 6 (top). Including rotation caused a reduction of the gamma pass rate in all cases compared with translation alone (Figure 6, bottom). The mean reduction was 5.8% with a standard deviation of 7.1% (range: [0.2%, 25.8%]). The reduction in gamma pass rates in the film's PTV region due to added rotation was statistically significant ($p<0.01$).

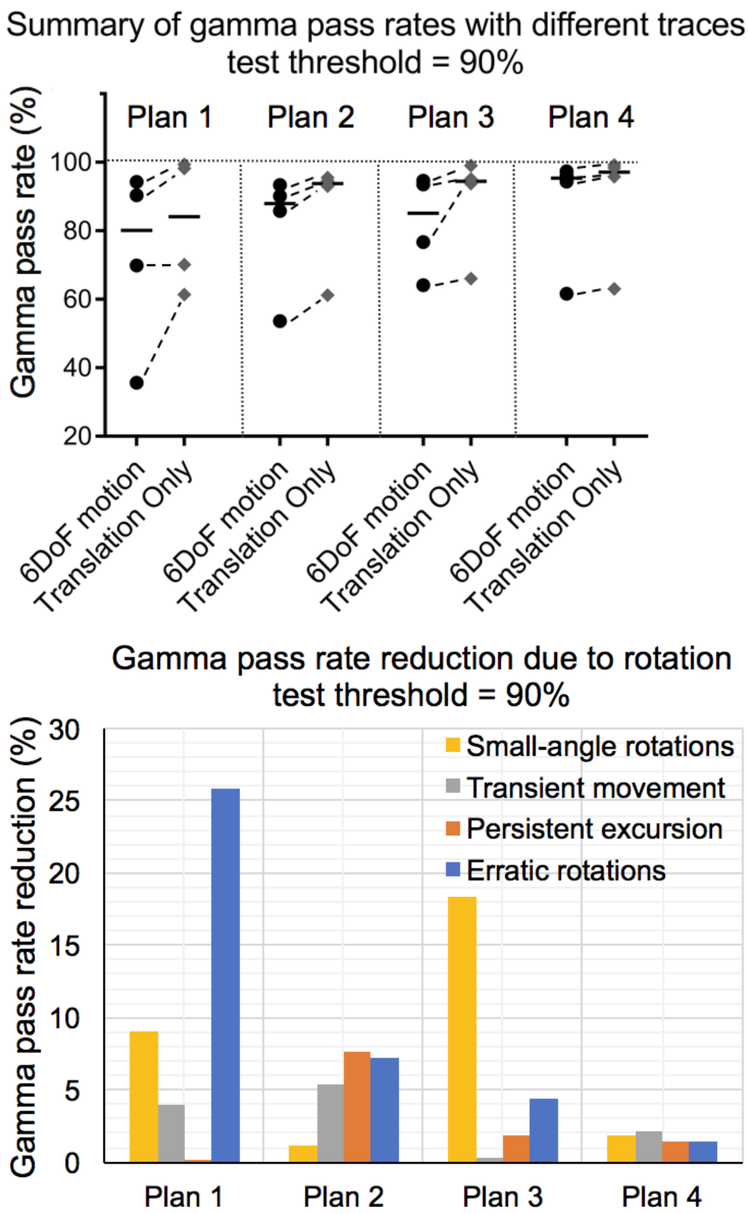

Figure 6: Gamma pass rate data for a 90% test threshold of the reference dose. Top, summary of the gamma pass rates for each plan, with a dashed line connecting trace pair results and the median bar for results from the same trace. Bottom, summary of the reduction in pass rates caused by rotation for each tested prostate trace.

Results for a test threshold of 50% of the PTV dose are summarized in Figure 7. In this case the mean gamma pass rate reduction due to rotation was 4.1% with a standard deviation of 4.8% (range: [-0.7%, 19%]. The reduction was also statistically significant ($p < 0.01$).

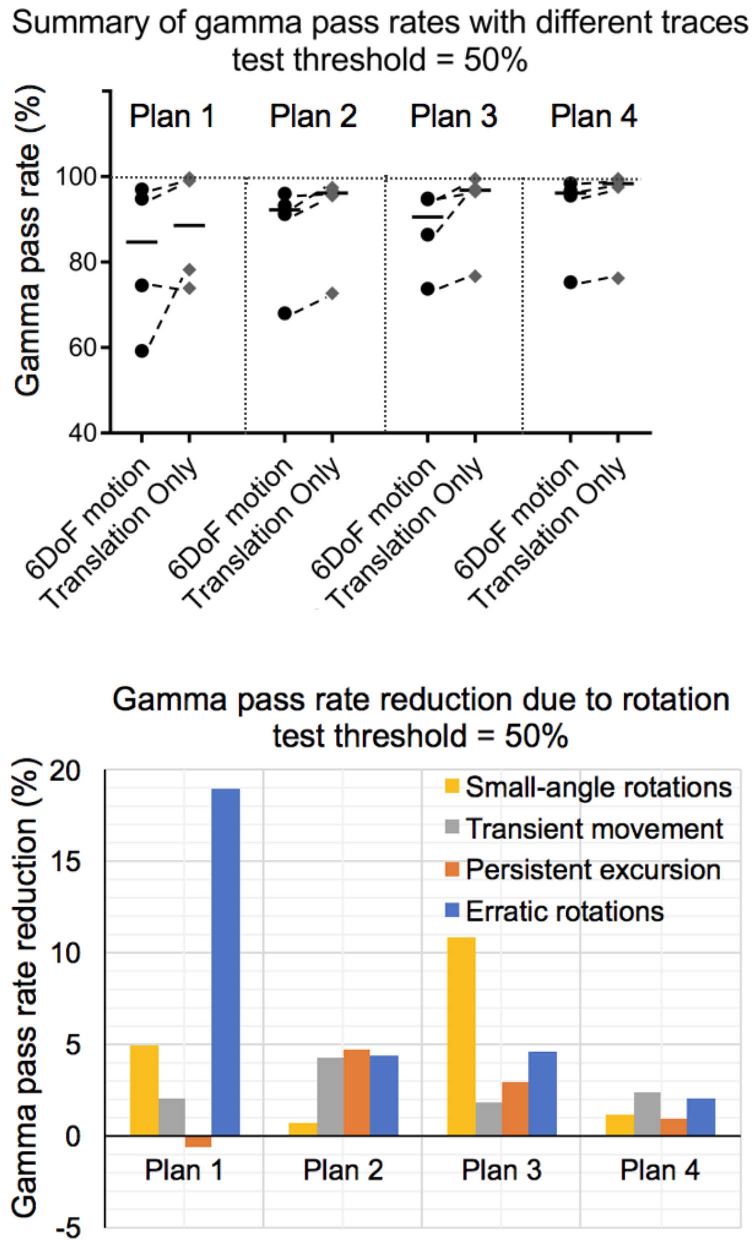

Figure 7: Gamma pass rate data for a 50% test threshold of the reference dose. Top, summary of the gamma pass rates for each plan, with a dashed line connecting trace pair results and the median bar for results from the same trace. Bottom, summary of the reduction in pass rates caused by rotation.

The difference in dose contours and gamma function values between the reference film and the measurement involving 6DoF motion is shown in Figure 8. Two examples using a 90% test threshold are exhibited, one as a typical case (90.1% pass rate) and the other as an extreme case (35.6% pass rate). In the typical case, the pass rate difference between 6DoF motion and translation only was 5.4%, while in the extreme case the pass rate difference reached 25.8%.

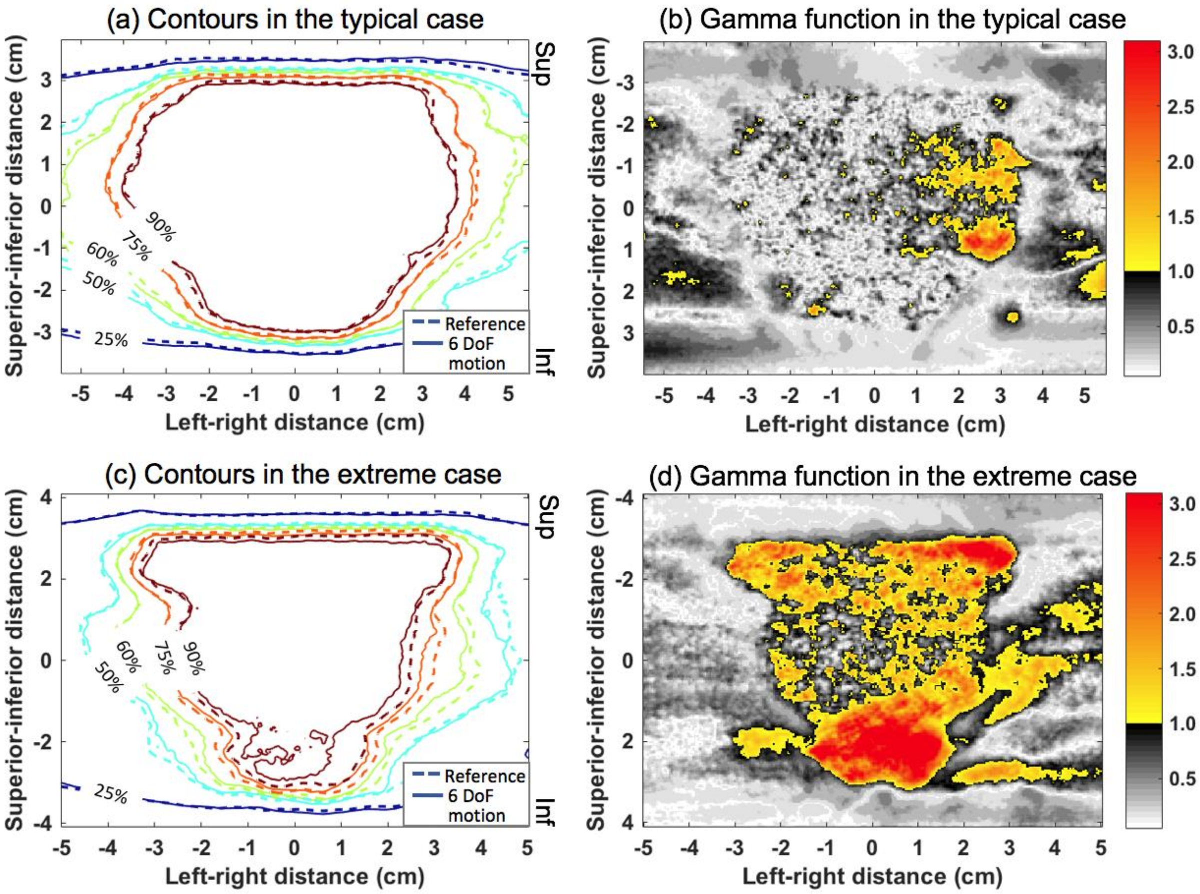

Figure 8: Dosimetric effects of 6DoF motion in a typical case((a)&(b), 90.1% pass rate) and an extreme case((c)&(d), 35.6% pass rate). (a)/(c) Dose contours presented as percentage of the reference dose(1334.0 cGy) for the measurement with 6DoF motion and the reference film. (b)/(d) Corresponding gamma function values of each pixel in the reference film.

4. Discussion

Film-based dose measurements in a robotically controlled phantom were performed to experimentally investigate whether prostate intrafraction rotation results in influential differences to the delivered dose during treatment. The results showed that a statistically significant dose distribution mismatch beyond the tolerance level of 2%/2 mm could be attributed to intrafraction rotation, degrading target tumor dose coverage and increasing normal tissue exposure. The results are consistent with previous simulation studies reporting decreased CTV/PTV coverage due to prostate rotation.[6-9]

The gamma pass rate reduction due to 6DoF motion on the high dose region (90% max dose) was 5.8% (±7.1%) while the gamma pass rate reduction on medium to high dose region (50% max dose) was 4.1% (±4.8%). We evaluated the gamma failure rate with two different thresholds in order to evaluate the effect of rotational motion outside of the PTV (high dose). To this end, we found the dose error caused by rotation were mainly within the PTV in the plane of measurement, the coronal plane. For rotational motion around the Superior-Inferior and Left-Right axes (roll and tilt) such as the test motion with persistent excursion (Trace 3) and erratic rotation (Trace 4), measurements in the sagittal or axial planes would be better suited to measure the dosimetric error.

In the present study, prostate patient plans with different levels of sphericity were included. A regular shaped prostate (plans 3 and 4) that is almost spherical would be less sensitive to rotation than an irregularly shaped prostate such as plan 1 and to a lesser extent, plan 2. Our result indeed showed that plans 3 and 4 were more forgiving than plan 1. These results agree with the modelling study by Wolf et al. (2019).[20 Increasing the sphericity of the prostate at the contouring stage to ensure a spherical target is potentially a strategy to minimize the effect of unpredictable intrafraction prostate 6DoF motion. However, this strategy can increase the overlap volumes between the PTV and the surrounding organs, which needs careful consideration, especially in the context of SBRT treatments.

The results also showed dose failures inside and outside the nominal PTV region. The dependency of dosimetric error on both the motion trace and the geometry of the treatment plan suggests interplay effect between intrafraction 6DoF motion and multi-leaf collimator (MLC) movement during VMAT-based SBRT treatment, as reported by several authors on respiratory motion.[21-23] Instead of adding extra margins to mitigate the potentially considerable interplay effect,[24] it could be reduced by measuring motion and correcting for it in real-time. MLC tracking has been experimentally demonstrated to correct translation and in-plane rotation[25,26] and could be expanded to account for out-of-plane rotation. Similarly, 6DoF couches could be used to correct 6DoF target motion, such as a modified HexaPOD couch[27] where the couch control is linked to the 6DoF target position output. More recently, a parallel kinematics robotic stage was developed for 6DoF head motion compensation during stereotactic radiosurgery.[28,29] An experiment performed with this robotic stage showed an average increase of 6.8% of the gamma pass rate (1%/1mm criteria) when using 6DoF head motion compensation compared with no correction.[30]

Several procedures during the experiment and analysis process may introduce geometric and thus dosimetric uncertainties. The accuracy and precision of Kilovoltage Intrafraction Monitoring algorithm used to obtain the 6 DoF prostate motion trace was 0.2±1.3º and 0.1±0.5 mm for rotation and translation.[31] The robotic arm has a reproducibility of 0.1 mm and 0.2º for translational and rotational motion, respectively. With a triple-channel scanner and recommended film dosimetry protocols the film's measurement accuracy was under 5% and the optical density to dose conversion was accurate to 0.1 cGy.[32] For image registration quality inside DoseLab, the image's rotational accuracy was controlled below ± 0.1º using markers drawn on four edges of the film using ImageJ (Version 1.52e, Public domain). The image translational accuracy was within ± 0.7 mm (two pixels) based on dose profiles' comparison. These geometric uncertainties need to be taken into account when interpreting the resulting gamma pass rates of each film and the reproducibility of this study.

Although our results point to the likelihood of significant dose degradation effects due to prostate intrafraction rotation, our experimental design had several limitations. The phantom and film holder were not anthropomorphic, thus the radiation transport process would differ from that in the human body. Further, we performed indirect 2D dose distribution comparisons using gamma tests instead of 3D CTV/PTV coverage analysis. To overcome these limitations, future experimental work with anthropomorphic phantoms or polymer gel dosimetry could be conducted.

5. Conclusions

For the first time, the dosimetric impact of intrafraction prostate rotation was evaluated experimentally using clinical VMAT prostate treatment plans and patient-measured motion traces executed by a 6DoF robotic arm. The experimental results support the hypothesis that 6DoF tumor motion causes significantly larger dose error than translation motion alone.

Acknowledgement

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Footnotes

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