# Investigation of Rotational Deviations on Single Fiducial Tumor Tracking with Simulated Respiratory Motion using Synchrony® Respiratory Motion Tracking for Cyberknife® Treatment

by

Zachary A. Christ

A Thesis submitted to the Faculty of

The Charles E. Schmidt College of Science

In Partial Fulfillment of the Requirements for the Degree of

Professional Science Master

Florida Atlantic University

Boca Raton, FL

May 2018

Copyright 2018 by Zachary Christ

**Investigation of Rotational Deviations on Single Fiducial Tumor Tracking with Simulated Respiratory Motion using Synchrony® Respiratory Motion Tracking for Cyberknife® Treatment**

by

Zachary Christ

This thesis was prepared under the direction of the candidate's thesis co-advisors, Dr. Charles Shang and Dr. Theodora Leventouri, Department of Physics, and has been approved by the members of his supervisory committee. It was submitted to the faculty of the Charles E. Schmidt College of Science and was accepted in partial fulfillment of the requirements for the degree of Professional Science Master.

SUPERVISORY COMMITTEE:

Charles Shang, B.Med, MS, DABR, FAAPM
Thesis Co-Advisor

Theodora Leventouri, Ph.D
Thesis Co-Advisor

Silvia Pella, Ph.D., DABR

Luc Wille, Ph.D.
Chair, Department of Physics

Ata Sarajedini, Ph.D.
Dean, Charles E. Schmidt College of Science

Khaled Sobhan, Ph.D.
Interim Dean, Graduate College

April 27, 2018
Date

## Acknowledgements

I would like to acknowledge the help and assistance of Dr. Charles Shang. He spent many hours assisting me with the formulation, theory, and writing of this thesis.

I would also like to thank Dr. Theodora Leventouri and Dr. Silvia Pella for their time and effort in this endeavor.

I would also like to thank Dr. Jeanne Christ, my mother. She taught me how to write and guided my process throughout this thesis.

I would also like to thank Olivia Christ, my sister. Thank you for your thorough review of this thesis and guiding comments.

**Abstract**

Author: Zachary A Christ

Title: Investigation of Rotational Deviations on Single Fiducial Tumor Tracking with Simulated Respiratory Motion using Synchrony® Respiratory Motion Tracking for Cyberknife® Treatment

Institution: Florida Atlantic University

Thesis Advisor: Charles Shang

Thesis Co-Advisor: Dr. Theodora Leventouri

Degree: Professional Science Master

Year: 2018

It is hypothesized that the uncertainty of the Synchrony® model from the rotation of a geometrically asymmetrical single fiducial shall be non-zero during the motion tracking. To validate this hypothesis, the uncertainty was measured for a Synchrony® model built for a respiratory motion phantom oriented at different yaw angles on a Cyberknife® treatment table.

A Mini-ball Cube with three cylindrical GoldMark™ (1mmx5mm Au) numbered fiducials was placed inside a respiratory phantom and used for all tests. The fiducial with the least artifact interference was selected for the motion tracking. A 2cm periodic, longitudinal, linear motion of the Mini-ball cube was executed and tested for yaw rotational angles, 0° – 90°. The test was repeated over 3 nonconsecutive days. The uncertainty increased with the yaw angle with the most noticeable changes seen between20° and 60° yaw, where uncertainty increased from 23.5% to 57.9%. A similar

test was performed using a spherical Gold Anchor™ fiducial. The uncertainties found when using the Gold Anchor™ were statistically lower than those found when using the GoldMark™ fiducial for all angles of rotation.

For the first time, it is found that Synchrony® model uncertainty depends on fiducial geometry. In addition, this research has shown that tracking target rotation using a single fiducial can be accomplished with the Synchrony® model uncertainty as it is displayed on the treatment console.

The results of this research could lead to decreased acute toxicity effects related to multiple fiducials.

**Investigation of Rotational Deviations on Single Fiducial Tumor Tracking with Simulated Respiratory Motion using Synchrony® Respiratory Motion Tracking for Cyberknife® Treatment**

## List of Tables

## List of Figures

## Introduction

Lung cancer is the uncontrolled growth of abnormal cells beginning in the lungs or airways. Cancer cells rapidly divide and form tumors in the body. Malignant tumors may spread aggressively or metastasize throughout the body resulting in death[1].

Lung cancer accounts for more deaths by cancer than all other sites[2]; 87,200 men and 71,570 women died in 2014 from cancer in the lung or bronchus region[2]. Surgical tumor resection is an option for lung tumor treatment, but patients are sometimes deemed inoperable. For these non-surgical candidates, the option of radiotherapy is available[3]. This method involves delivering highly-conformal – accurately targeted on tumor while sparing surrounding normal tissue – radiation to the tumor. Stereotactic body radiation therapy (SBRT) is an external beam treatment technique designed to deliver an extremely high dose of radiation precisely to a tumor in fewer treatments (fractions) than conventional fractionation[4]. Local tumor control rates with SBRT rival those from surgical resection[5,6]. In lung cancer SBRT, target tracking offers maximum dose sparing for the surrounding critical organs while further escalating radiation dose to the tumor, which often translates to better local tumor control.

Lung tumor motion during respiration can reach up to 2.5cm in the superior/inferior direction[7]. This makes targeting the tumor with a conformal radiation dose a primary concern for physicians and physicists alike. The Cyberknife® is a linear accelerator with real-time tumor tracking capability, which makes it an optimal choice for highly conformal lung SBRT. The Cyberknife® consists of a small 6-MV linac mounted on a computer-controlled robotic arm capable of moving with six degrees of freedom, two orthogonally placed X-ray imaging systems and optical tracking system for real-time tumor tracking[8]. Real-time tumor tracking is a method of dynamically moving the focal point of the radiation beam to correspond with the position of the tumor target[8]. The Cyberknife® in conjunction with the Synchrony® Respiratory Tracking system creates a breathing cycle model based on the lung tumor motion and tracking fiducials implanted inside the tumor. The compact linear accelerator adjusts its position to follow the motion of the tumor. The Synchrony® Tracking system has thresholds for movement set at 3cm superior/inferior direction, 2cm anterior/posterior direction, and ± 3cm laterally to account for lung tumor motion. It can follow 3° of rotation.

The Cyberknife® M6 is capable of treating a moving target using two real-time tumor tracking methods: Synchrony® Respiratory Motion Tracking System with fiducials and Xsight Lung Tracking System (XLTS) without fiducials. Accuracy for both methods is reported as sub 1.5mm RMS[9]. Both of these methods are used in lung tumor radiotherapy treatments by the Cyberknife® M6 at the Lynn Cancer Institute of Boca Raton, pictured in Figure 1.

**Figure 1**. Cyberknife® M6™ with InCise™ MLC, Lynn Cancer Institute, Boca Raton Regional Hospital. Courtesy of Accuray Inc.

The Synchrony® Respiratory Tracking system is a 6D real-time tumor tracking method that uses radiopaque fiducials within the target and fiber optic light emitting diodes (LEDs) on the patient's breast plate. Orthogonal X-rays – user controlled ionizing energy of 40-120 kVp – delivered by sources A and B are received by paired imaging detectors to visualize the target and record its 6D position throughout the patient's breathing cycle. Meanwhile, the LEDs on the patient's chest wall continuously (>25Hz) send signals to a camera inside the treatment room indicating their positions. Using these two information sets, a correlation model between the target position images and the LED position on the chest wall is generated by the Synchrony® Respiratory Tracking system. The model is fit using linear, curvilinear and bi-curvilinear forms to minimize overall correlation error[9]. Figures 2-5 depict Synchrony® equipment and correlation model generation process.


**Figure 2**. Synchrony Vest with three fiberoptic LED markers


**Figure 3**. Live orthogonal X-ray images of respiratory phantom overlaid onto DRRs from planning CT for fiducial alignment.

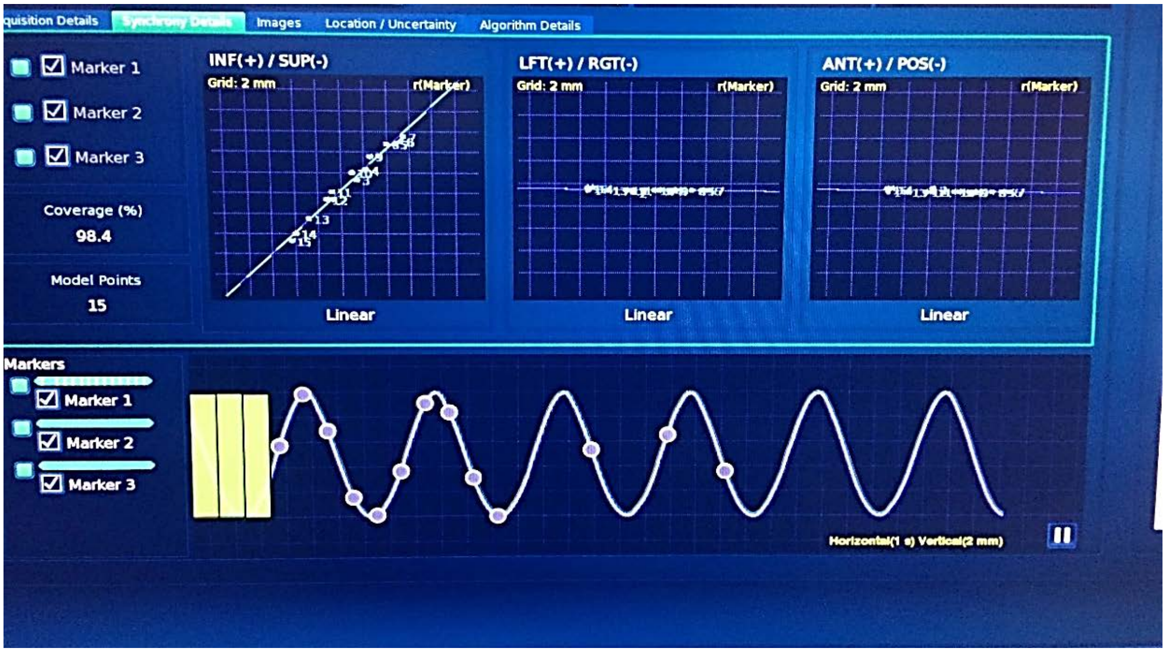


**Figure 4**. Synchrony Model. Sine-like wave depicts LED marker motion. The points on the wave represent times that two X-ray images were taken.

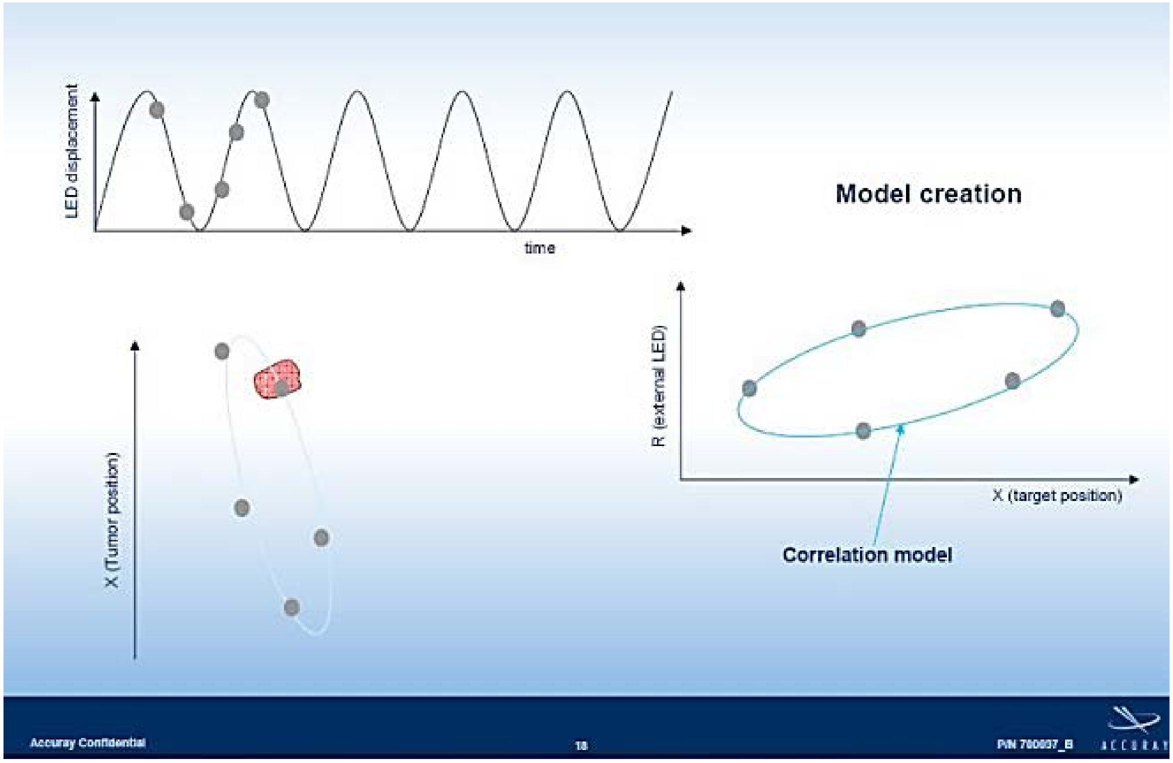


**Figure 5.** Depiction of correlation model linking LED motion to tumor position during respiration.

The Synchrony® model is based on minimizing correlation error between LED position on patient's chest wall and implanted fiducial positions. Synchrony® uses the 15 most recent X-ray images and the LED signals to build the correlation model. The Cyberknife® is able to adjust to changes in the patient's breathing pattern and tumor motion throughout treatment by updating its correlation model with bursts of three new X-rays, taken at user-defined intervals (20s – 150s), which will replace the oldest X-ray images. A minimum of one fiducial is required to use Synchrony® Respiratory tracking system, but this limits tracking and correction capability to 3D translational tracking. Three fiducials within the target are required for automatic corrections involving rotation. The major disadvantage of the three-fiducial Synchrony® tracking method is the implantation of multiple fiducials. Fiducial placement requires an interventional radiologist to surgically implant a radiopaque marker into the target inside the patient. One advantage of radiation therapy over surgical resection as a method of tumor treatment is its non-invasive nature; implantation of 3 fiducials in the target negates this advantage. A high risk for implantation complications exists. Complications include pneumothorax and pulmonary hemorrhage[10, 11]. Pneumothorax, or collapsed lung, occurs when air enters the chest and the pressure collapses the lung. A 2009 study showed pneumothoraxes in 20 of 44 (60%) lung fiducial implantations[11]. The health risks from implantation of at least three fiducials near the tumor target pose challenges for this tumor tracking method.

A similar method developed by Accuray® and used with the Cyberknife® is the Xsight Lung Tracking System (XLTS). Instead of using implanted fiducials to track the target, the Xsight system, shown in Figure 6, takes advantage of the density difference between lung tumor tissue and surrounding healthy tissue to visualize the target. Orthogonal X-rays reveal dense tumor target tissue with a higher intensity (brighter) than the surrounding, less dense lung tissue (see Figure 7). The tumor is imaged repeatedly at different times throughout the breathing cycle, and its position is correlated to the position of LED markers on the patient's chest wall. Synchrony® generates a model of respiratory motion minimizing this correlation error.

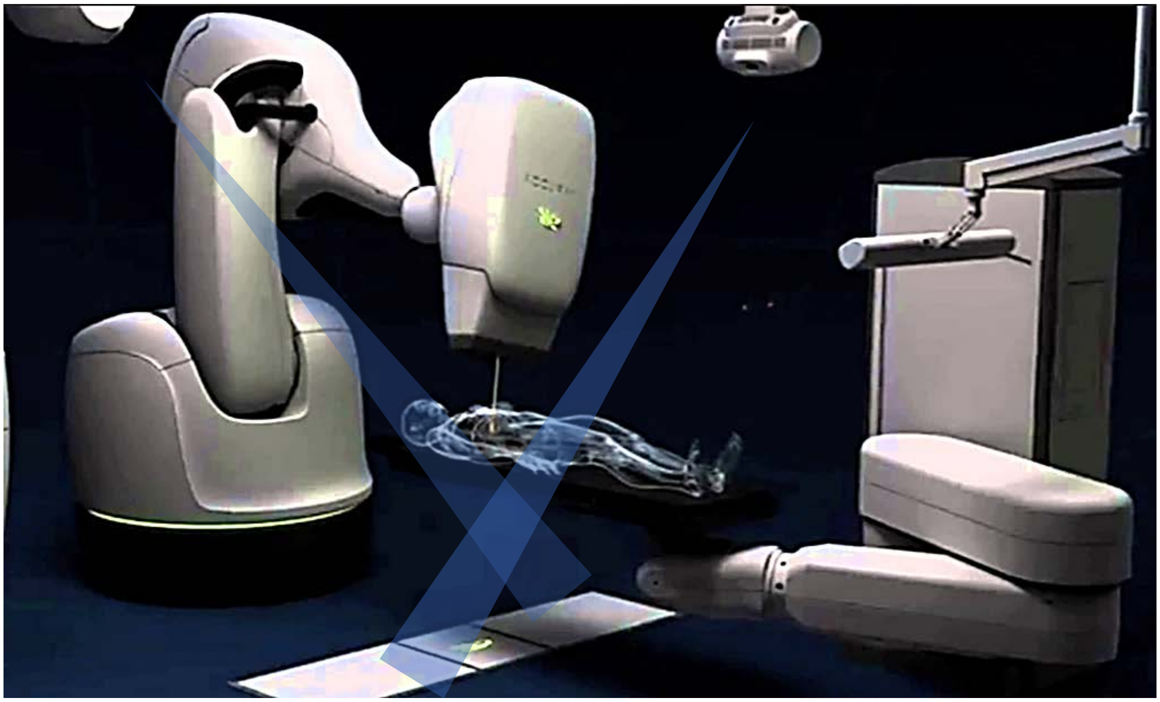

**Figure 6**. Patient set up for Xsight Lung Tracking.


**Figure 7**. Tumor tracking with Xsight Lung Tracking System.

Xsight alleviates the need for fiducial implantation while retaining beneficial real-time tumor tracking techniques. However, Accuray® limits tumor eligibility to tumors that meet the following criteria: >15mm in all directions, located in peripheral lung region, visible in both live X-ray images and in both DRRs[9]. In clinical practice, even tumors that satisfy these criteria are difficult to track. There is a low level of confidence in this method for visualizing the target using tissue density differences alone. Lung tissue, lung tumor tissue, rib bone, and air appear in close proximity to one another, causing difficulty in accurate visualization of the target tumor using *in-vivo* X-ray images and the DRRs. Similarly, the respiratory motion causes the target to move in and out from behind the high-density rib bone regions, making the target very difficult to visualize during those intervals of the breathing cycle[12].

An interesting technique that sidesteps the challenges of both Synchrony® Respiratory Tracking system with three fiducials and the Xsight Lung tracking system is *single fiducial tracking* with Synchrony®. A single fiducial dramatically enhances the target visualization compared to the Xsight system using tissue density differences. Radiopaque fiducials cause unmistakable, high-intensity pixels on the DRRs and real-time X-ray images throughout the breathing cycle. Limiting the number of fiducials to one also reduces the risk of adverse side effects related to fiducial implantation. In fact, a clinical procedure where the interventional radiologist implants fiducial synchronously during diagnostic biopsy eliminates the need for repeated invasive procedures[12].

A parameter called *uncertainty* is used as one measure of the Synchrony® correlation model. When the target is imaged on the Cyberknife® treatment table, a 21x21 pixel array framing the fiducial on the X-ray image is compared to a 21x21 pixel array containing the fiducial on the DRR from the planning CT scan. Uncertainty is displayed as a percentage. The uncertainty is generated automatically, and it is easily viewed from the treatment console.

A large percentage uncertainty is indicative of a poor match in fiducial position. The default threshold for acceptable uncertainty to proceed with treatment provided by Accuray® is 40%. Any uncertainty greater than this value would pause treatment due to poor target alignment. It is possible to continue to treat with uncertainty higher than 40% by manually overriding the interlock from the treatment console. The uncertainty parameter is available for use with any number of fiducials.

The purpose of this research is to investigate the uncertainty parameter response to target rotation with a single asymmetrical fiducial when tracking the target. It is hypothesized that the uncertainty of a Synchrony® correlation model will increase with target rotation in the yaw direction. It is further hypothesized that the uncertainty parameter's dependence on target rotation is affected by the geometry of the fiducial; if the fiducial is asymmetric, uncertainty will be more dependent on target rotation than if the fiducial is isotropic.

## Materials and Methods

Part 1

The purpose of part 1 is to establish the presence of the possibility for target miss due to target rotation using signal fiducial tracking. To do this, a planned radiation dose was delivered to a target aligned at 0° (control) and to 40° yaw rotation. A schematic 2D diagram is shown in Figure 8.

Equipment and Materials:

- Cyberknife® M6 with Synchrony® Respiratory Tracking System
- QUASAR™ Respiratory Motion Phantom
- Mini-ball Cube with three 1mm x 5mm GoldMark™ fiducials
- Gafchromic™ $EBT^3$ film
- MultiPlan CyberKnife® treatment planning software

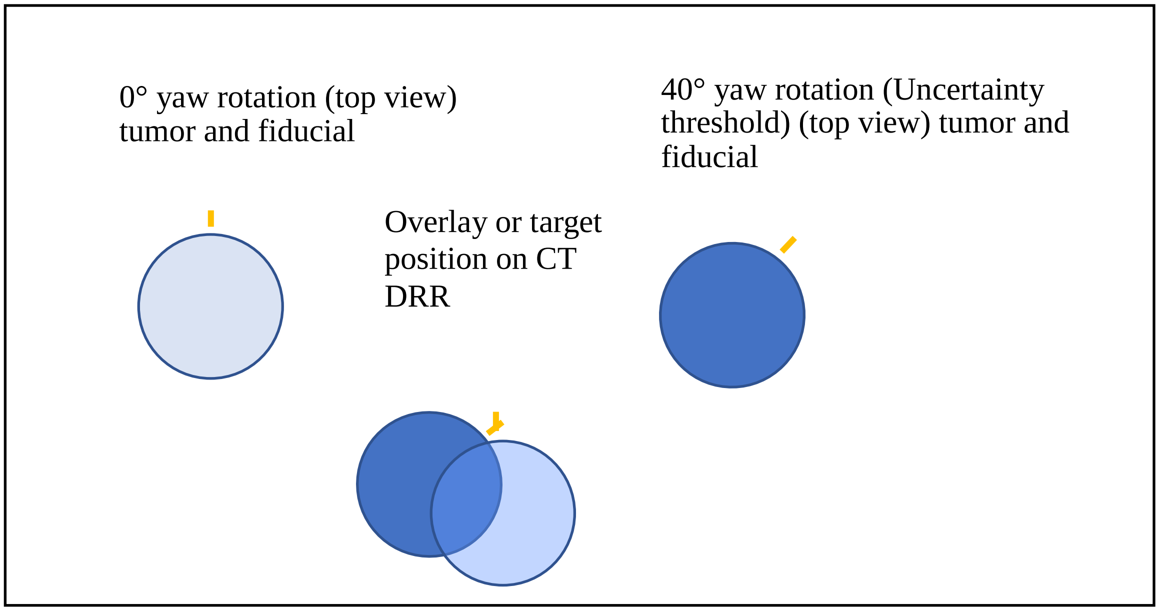


**Figure 8**. Light blue circle with small rectangle above represents tumor target and GoldMark™ fiducial on planned CT (DRR). Dark blue circle represents target rotated 40° in yaw direction around the fiducial.

First, a CT scan of the QUASAR™ Respiratory Motion Phantom with Split Cedar Insert with Mini-ball Cube with three, numbered GoldMark™ fiducials. (See Figures 9-11). This CT scan (Figure 13) was exported to Accuray® treatment planning software, Multiplan, to generate the DRRs. The Mini-ball Cube was chosen as a target, and spherical dose centered on the Mini-ball Cube was prescribed 480cGy to the 70% isodose line (Figure 14). Fiducial tracking was selected on the Multiplan software to establish 21x21-pixel arrays centered on the fiducials. Next, film was placed inside the Mini-ball cube to record dose delivery in the sagittal and transverse planes. The phantom was placed on the treatment table, set into ±1cm linear respiratory motion, and aligned using three fiducials (to ensure 0° alignment) with the Synchrony® Respiratory tracking system. The full dose was delivered to the target, and the film was removed for analysis. The phantom was then rotated 40° in the clockwise yaw direction (using graph paper and protractor) and aligned and tracked using a single fiducial Synchrony® method (see Figure 12). A model for the respiratory motion was built, and the same dose was delivered to the target. The films were scanned and analyzed by pixel intensity by an end-to-end software package to determine the accuracy of dose delivery. Accuracy of dose delivery is given as distance between the center of the dose delivered, defined by the a 70% isodose line, and the center of target.

**Figure 9.** Mini-ball Cube with 1mmx5mm GoldMark™ fiducials.

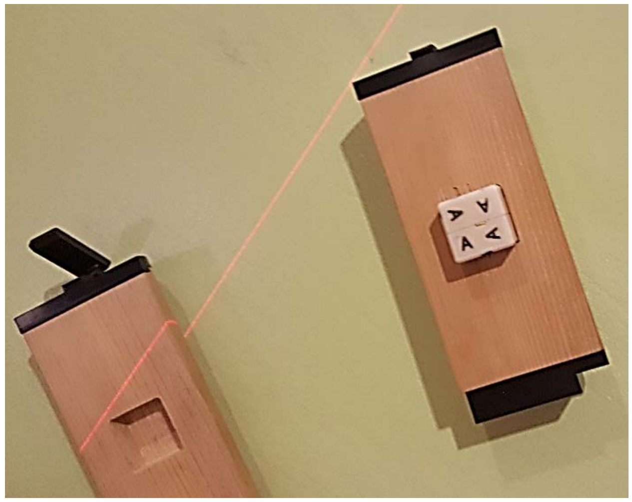

**Figure 10**. Split-Cedar insert with Mini-ball Cube.

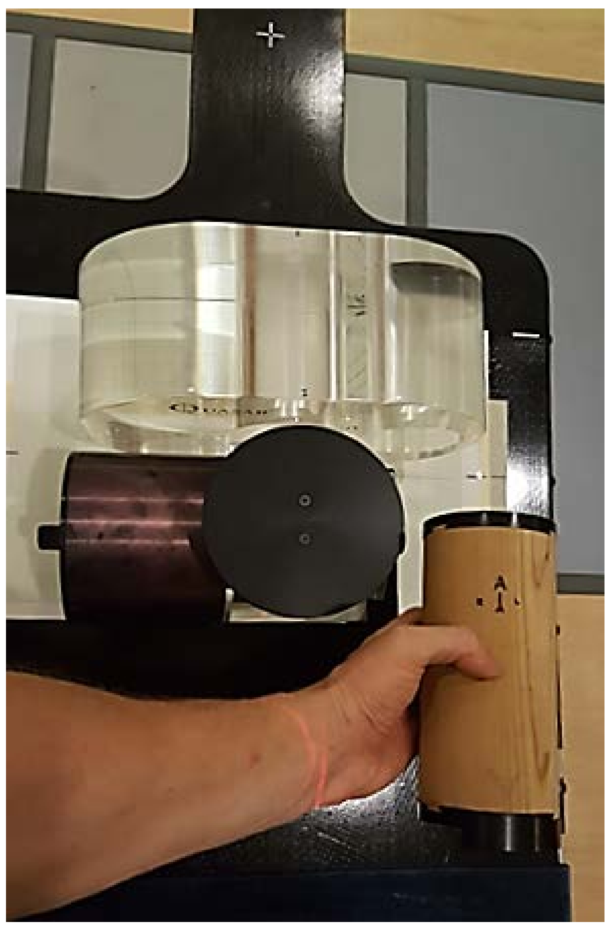

**Figure 11**. QUASAR™ Respiratory motion phantom aligned at 0°.

**Figure 12**. QUASAR™ Respiratory Motion phantom on treatment table with LEDs aligned at 40°.

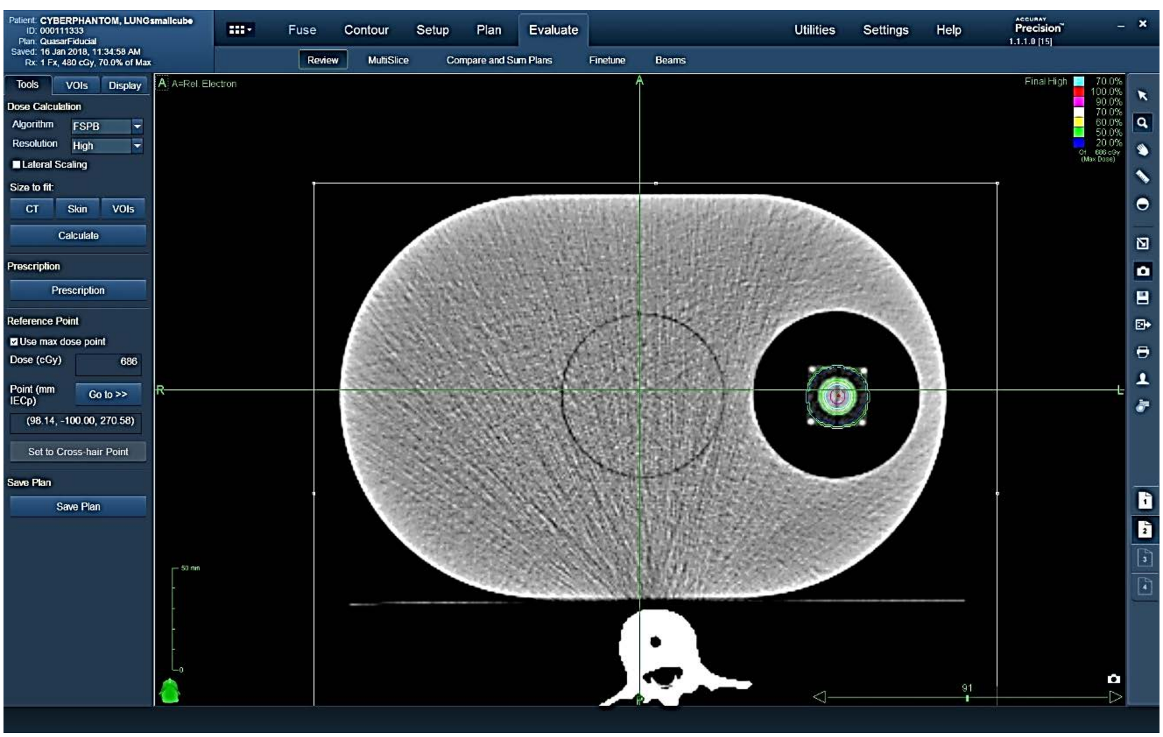


**Figure 13.** Imported CT with treatment plan for phantom.

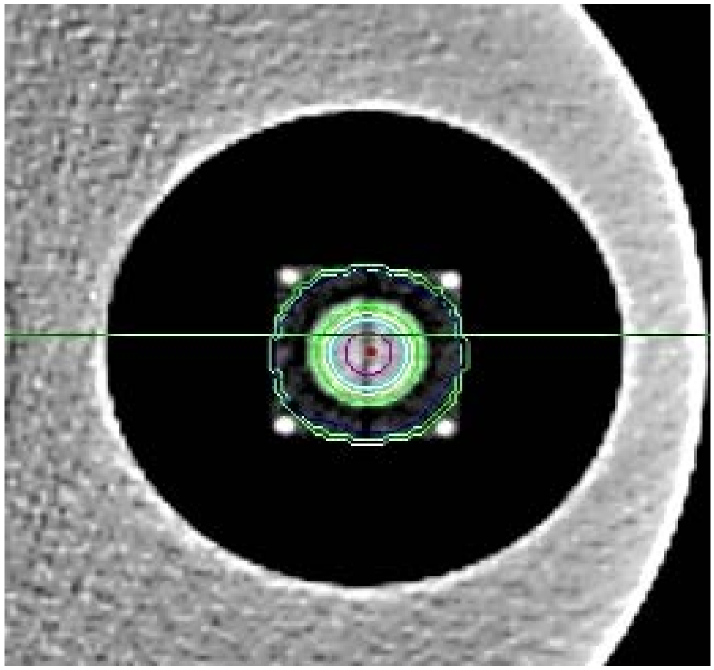

**Figure 14.** Close up of treatment plan.

Part 2

Measuring the uncertainty in Synchrony® Tracking System model for different yaw rotational angles to establish dependence of uncertainty on target rotation.

Equipment and Materials:

- Cyberknife® M6 with SYNCHRONY® Respiratory motion tracking
- QUASAR™ Respiratory Motion Phantom
- Mini-ball Cube with three 1mm x 5mm GoldMark fiducials
- MultiPlan CyberKnife® treatment planning software

For the second experiment, the QUASAR™ Respiratory Motion Phantom with Split-Cedar insert and Mini-ball cube with GoldMark™ fiducials were placed on the treatment table, set into ±1cm respiratory motion, and aligned using three, numbered fiducials. Alignment with three fiducials ensured the starting position of the phantom was at 0° yaw rotation relative to planning CT. Next, a single fiducial was chosen and tracking of the other two fiducials was turned off. Using less than three fiducials automatically turns off rotational corrections of the Synchrony® system. Synchrony® Respiratory Tracking system created a correlation model between the motion of the LEDs on the chest plate of the phantom and the internal motion of the mini-ball cube by taking 15 X-ray images with each orthogonal X-ray tube, Camera A and Camera B. The maximum uncertainty from either camera for each image was chosen, and an average of these uncertainties was recorded as the uncertainty for 0° yaw rotation.

Using the graph paper marked with different angles of yaw rotation, the QUASAR™ Respiratory Motion phantom was manually rotated 10° in the clockwise yaw direction. The process of recording uncertainty was repeated for all yaw rotations in 10° intervals from 0°-90°.

Part 3

Comparing uncertainty response for geometrically different fiducials.

Equipment and Materials:

- Cyberknife® M6 with Synchrony® Respiratory motion tracking
- QUASAR™ Respiratory Motion Phantom
- Mini-ball Cube with three 1mm x 5mm GoldMark™ fiducials
- MultiPlan CyberKnife® treatment planning software
- GoldAnchor™ fiducial
- Tissue-equivalent bolus

Phantom with GoldMark™ fiducial, CT, and dose plan from part 1 were used. GoldAnchor™ was implanted into rectangular 2cmx5cm tissue-equivalent bolus to form a small cluster. (See Figure 15-16).

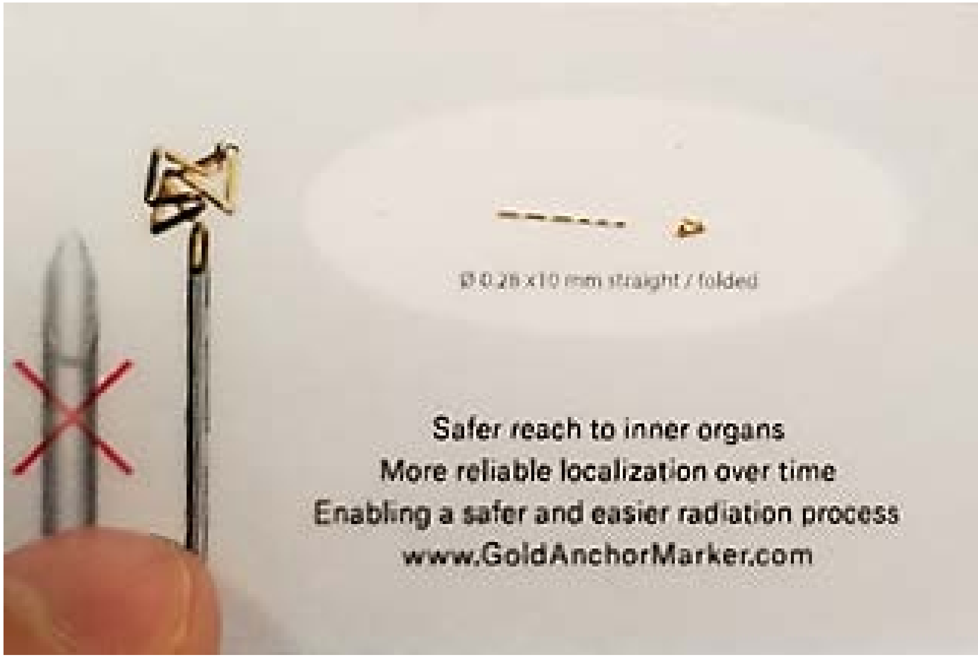


**Figure 15.** GoldAnchor™ fiducial.

**Figure 16.** GoldAnchor™ fiducial inserted as cluster into 2cm x 5cm tissue-equivalent bolus.

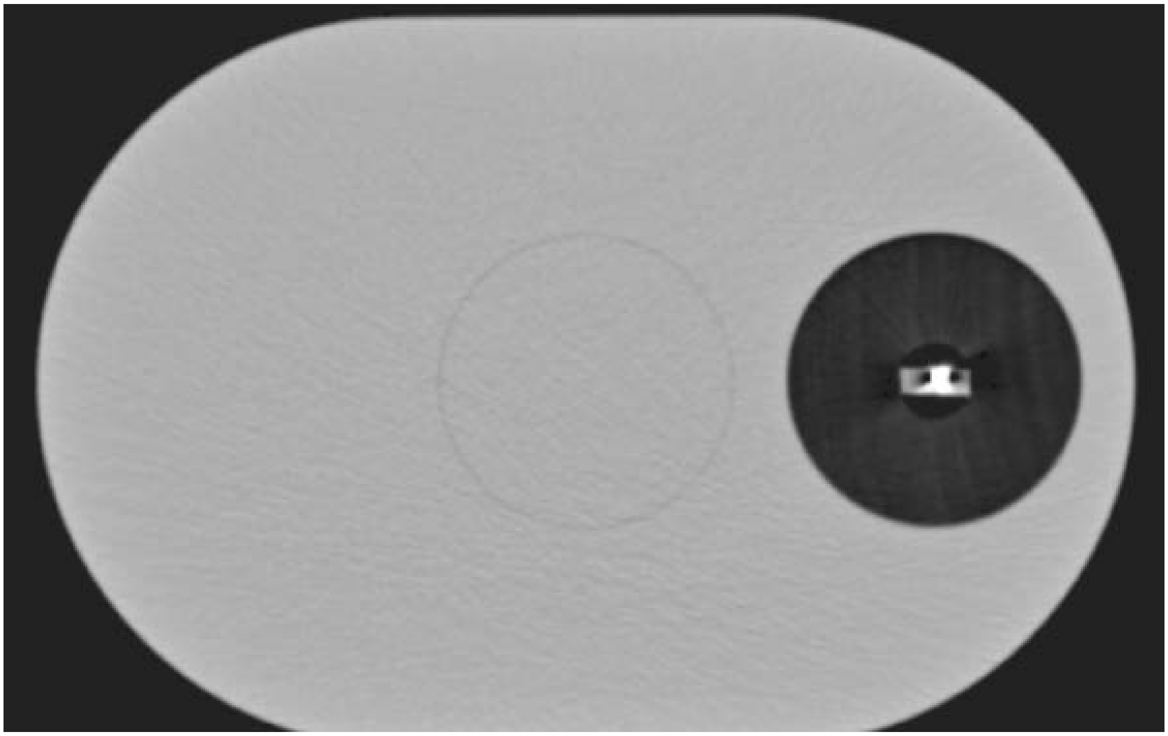

**Figure 17**. Bolus with GoldAnchor™ fiducial. High-Z material streak artifact showing on CT.

The Gold Anchor™ fiducial was implanted into bolus of dimensions 2cm x 5cm and placed securely into second Split Cedar Insert within QUASAR™ Respiratory Motion Phantom and marked to maintain orientation throughout experiment. This bolus was wedged into a second Split-Cedar insert and placed inside the QUASAR™ phantom. After a CT scan, a similar dose plan was created for the phantom with the Gold Anchor™ as was delivered for the phantom with the GoldMark™ fiducials. A plan was necessary in order to generate the DRRs for phantom alignment and Synchrony® model creation. The phantom was placed on the treatment table and aligned using 1 fiducial at 0°. A Synchrony® model was created, and the uncertainty was recorded by averaging the uncertainties in the individual images that make up the full respiratory motion model. Afterwards, the phantom was rotated by 10° in the clockwise yaw direction, and a similar process was used to record the uncertainty corresponding to a target rotation of 10°. The

QUASAR™ phantom with the GoldMark™ insert was used first for all uncertainty measurements and then the experiment was repeated using the insert with the GoldAnchor™. Twice this method was used with both phantoms for all angles in 10° intervals from 0° - 60°.

Statistical Methods

The uncertainty for each angle is an average of 30 uncertainties generated for that angle. These 30 generated uncertainties for each angle for each phantom were analyzed for mean difference using a matched pair t-test.

## Results

Part 1

The irradiated Gafchromic™ $EBT^3$ films are shown in Figure 18, darkened by radiation dose. The results from the end-to-end analysis of the films indicated accurate delivery to the target when the phantom was aligned using 3 fiducials (0° yaw rotation). There was a significant target miss when the target was rotated by 40° and aligned using 1 fiducial (see Figures 19-20). Targeting errors for the two dose deliveries were .61mm and 2.49mm. Less than 1mm targeting error is acceptable clinically with >1mm being a cause for concern on these end-to-end tests[9, 12]. The results indicated that single fiducial tracking leaves the possibility for a large target miss resulting from a lack of rotational information. However, the uncertainty during the alignment of the phantom at 40° was very high (~40%). Although this was the default uncertainty percent threshold, ~40% represents a high practical value during routine treatment. This abnormally large uncertainty may indicate misalignment, so its cause should be investigated prior to dose delivery in a clinical setting.

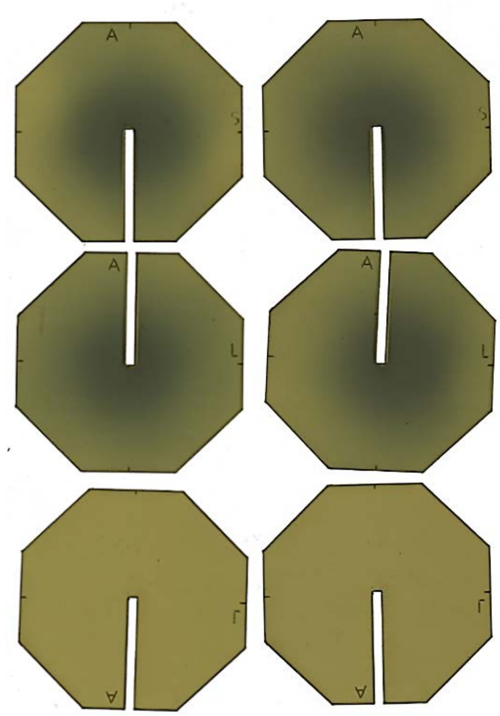

**Figure 18**. Gafchromic EBT3 film after dose delivery. Phantom was aligned at 0° yaw rotation during dose delivery (left). Phantom aligned 40° yaw rotation during dose delivery (right).

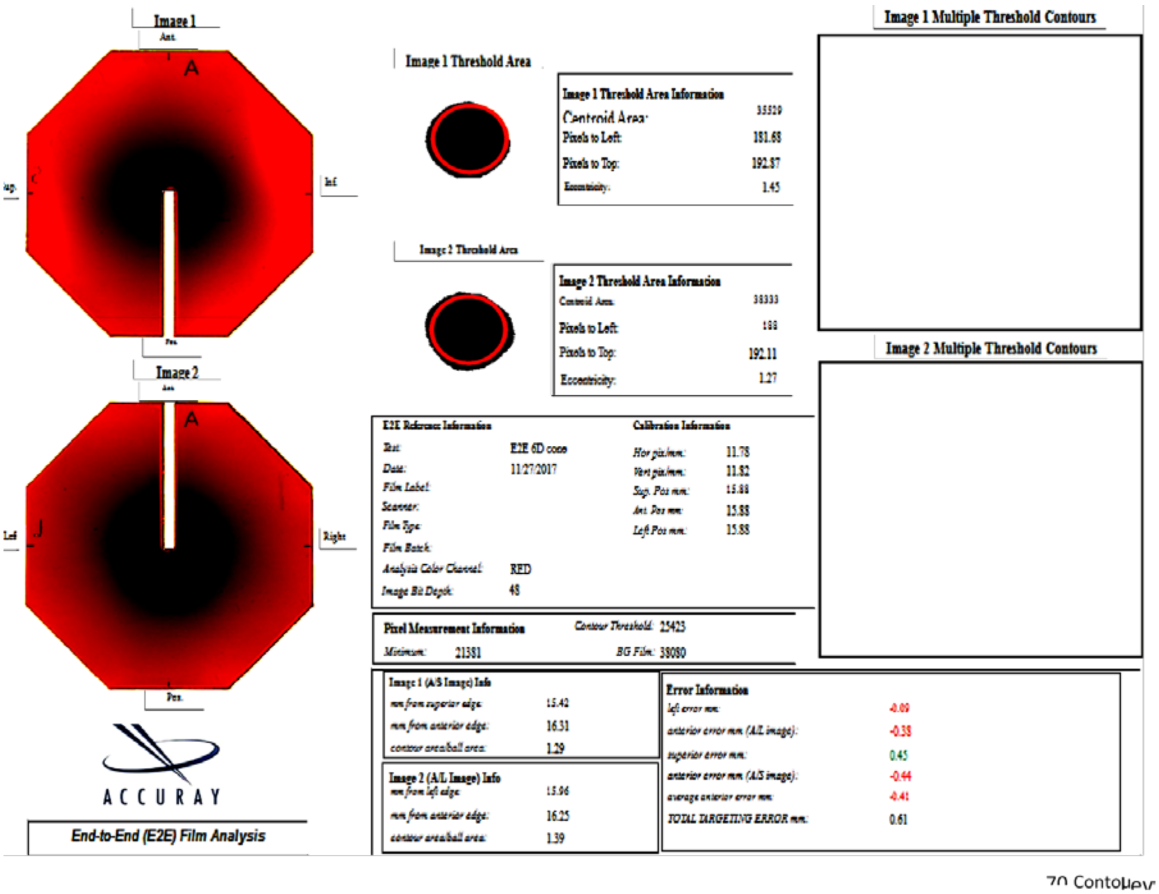


**Figure 19**. Film analysis using End-to-End program for dose delivery with phantom aligned at 0°. The total targeting error is .61mm.

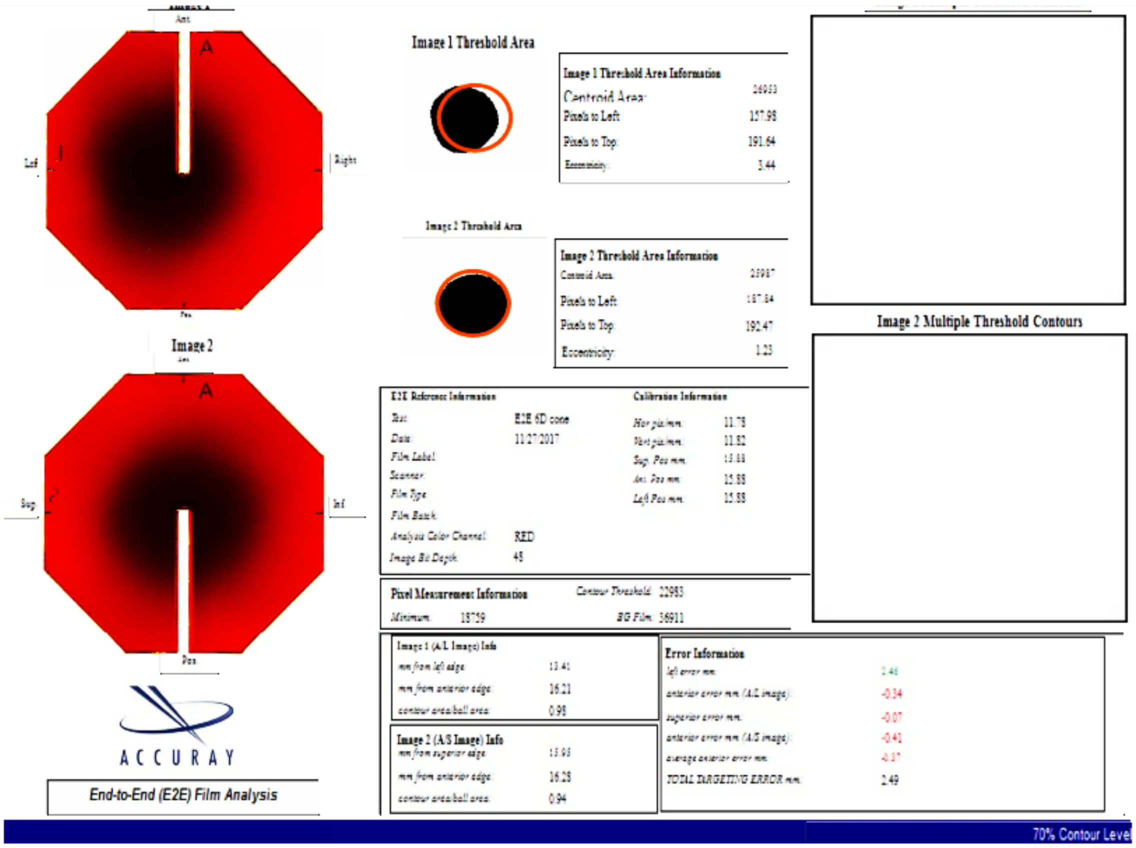


**Figure 20.** Film analysis using End-to-End program for dose delivery with phantom aligned at 0°. The total targeting error is 2.49mm.

Part 2

Table 1 and Figure 21 show the increase in uncertainty as the target is rotated from 0° to 90°. Zero degrees alignment results in uncertainty of 18%. The maximum uncertainty occurs when the target rotates to 80° at 64.1%. There is a sharp increase in uncertainty from 23.5% to 57.9% when the target rotates from 20° to 60°. The uncertainty, plotted as a function of the target's yaw angle, can be fit with a 3rd degree polynomial, $R^2$ = .998. This indicates a dependence of uncertainty on fiducial (and target) rotation. This confirmed the research hypothesis that the uncertainty parameter is dependent on target rotation.

**Table 1**. Yaw Angle, uncertainty (%), and standard deviation in Synchrony® system using GoldMark™ fiducial.

| Yaw Angle (degrees) | Synchrony Uncertainty (%) | Std. Dev. |
|---|---|---|
| 0 | 18.9 | 0.66 |
| 10 | 19.4 | 0.46 |
| 20 | 23.5 | 1.87 |
| 30 | 30.3 | 0.35 |
| 40 | 40.6 | 0.85 |
| 45 | 45.2 | 0.64 |
| 50 | 50.6 | 0.86 |
| 60 | 57.9 | 0.12 |
| 70 | 62.5 | 0.26 |
| 80 | 64.1 | 0.55 |
| 90 | 63.9 | 0.61 |

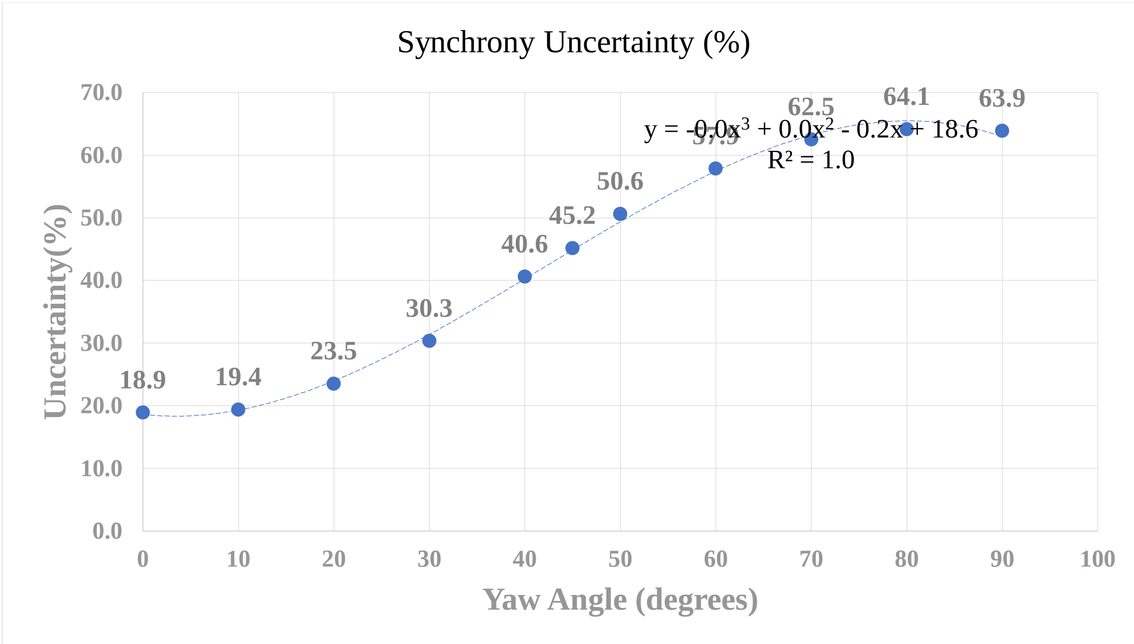


**Figure 21**. Uncertainty as a function of the target yaw angle using GoldMark™ fiducial implant. The error bars are of similar size to markers.

Part 3

Table 2 and Figure 22 show statistically significant ($p<.001$) differences between the uncertainties when using two differently shaped fiducials. Uncertainties using both the GoldMark™ and the GoldAnchor™ increased as target yaw angle increased. However, uncertainties when using the GoldAnchor™ fiducial grew from 17.0% at 0° to 25.7% at 60° target yaw rotation while uncertainties rose from 18.5% to 57.7% when the GoldMark™ fiducial for similar target rotations. All variables except fiducial type were kept constant between measurements: phantom, orientation, and tracking method. Thus, the difference in uncertainty was directly related to differently shaped fiducials. This indicated a dependence of uncertainty on fiducial geometry.

**Table 2.** Average Uncertainty, standard deviation, and yaw angle for GoldMark™ and GoldAnchor™

| Yaw Angle (°) | Uncertainty (%) GoldMark™ | Std. Dev. GoldMark™ | Uncertainty (%) GoldAnchor™ | Std. Dev. GoldAnchor™ | Paired Sample t-test P-value |
|---|---|---|---|---|---|
| 0 | 18.5 | 0.31 | 17.0 | 1.01 | <.001 |
| 10 | 19.6 | 0.82 | 17.7 | 0.51 | <.001 |
| 20 | 23.7 | 0.67 | 19.2 | 0.74 | <.001 |
| 30 | 30.8 | 0.64 | 21.8 | 0.60 | <.001 |
| 40 | 39.5 | 0.46 | 23.9 | 0.47 | <.001 |
| 45 | 44.6 | 0.48 | 24.6 | 0.80 | <.001 |
| 50 | 49.7 | 0.38 | 24.9 | 0.59 | <.001 |
| 60 | 57.7 | 0.35 | 25.7 | 0.57 | <.001 |

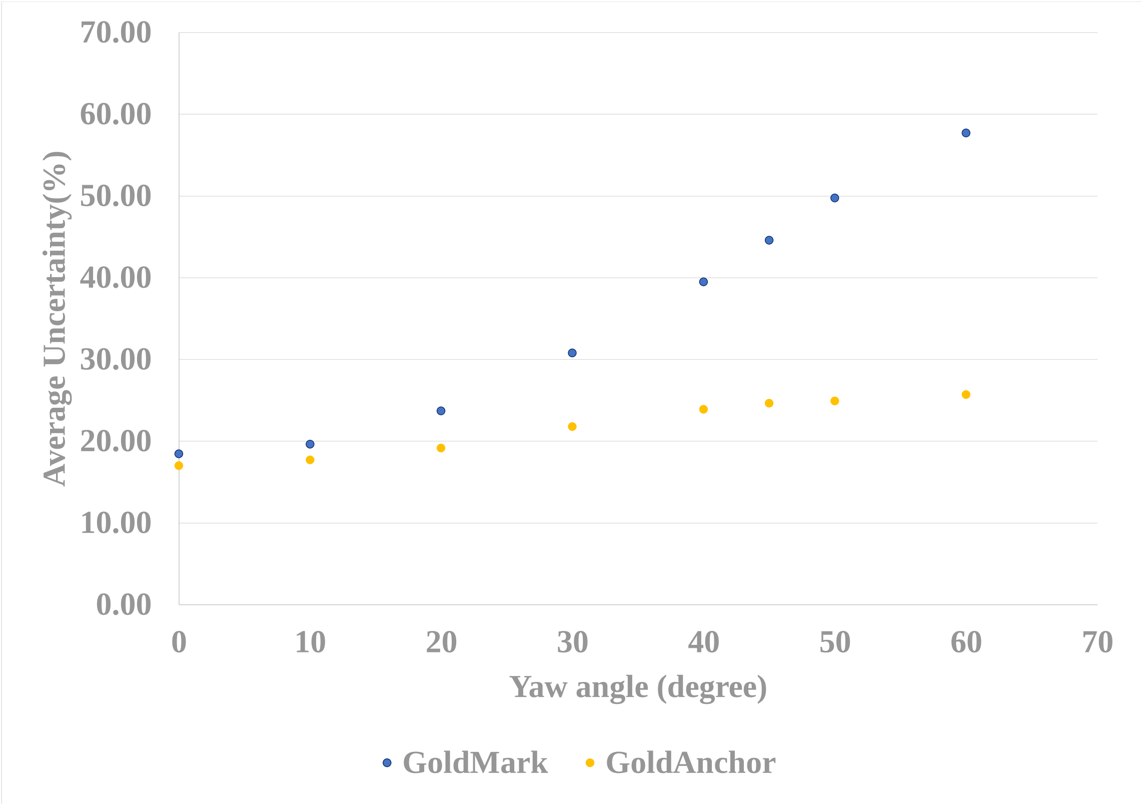


**Figure 22.** Uncertainty as a function of the target yaw angle.

## Discussion

Excessive toxicity is a major concern when using SBRT as a method of cancer treatment[5,6]. However, local control rates of lung tumors using Cyberknife and SBRT are comparable to local control rates of tumors treated with surgical resection[5, 6, 7]. The main acute-toxicity encountered during Cyberknife stereotactic ablative lung surgery (SABR) of lung-tumors is implantation-related pnuemothorax[3]. Placement of a single fiducial during diagnostic biopsy could dramatically reduce this toxicity.

A limitation of employing single fiducial Synchrony® Respiratory Tracking system is the lack of target rotational information. This limits the real-time correction capability of the Cyberknife® only to 3D tracking. When using single fiducial tracking, the Synchrony® tracking system aligns to the fiducial, ideally in the center of the target. Otherwise, in a majority of cases, the rotation of the fiducial-target system may result in a drifted Synchrony® tracking and less accurate dose delivery. However, the results from this investigation suggest that such a possibility of misguided tumor tracking using a single fiducial-based Synchrony® model can be indicated by the uncertainty value of the model displayed on the treatment console. Hence, the single-fiducial tracking with Synchrony® provides an opportunity for decreased risk of pneumothorax while maintaining confidence of fiducial tracking systems. The results of this study can be clinically implemented. Some factors to be considered include fiducial asymmetry, geometric fiducial placement within tumor, and fiducial artifacts.

Fiducial asymmetry refers to the appearance of the fiducial on orthogonal X-rays. The orientation of a cylindrical fiducial like the GoldMark™ will partly determine the asymmetry when projected onto a 2D image. For instance, if the longitudinal axis of the cylinder is parallel to the incoming X-rays, the projected image on the detectors will be a circle. This creates a rotationally symmetric image, which may not provide a detectable increase in uncertainty in the Synchrony® model when target rotation is introduced. Similarly, a cylinder situated parallel to the normal vector of the treatment couch (taken as a flat, horizontal plane) will not appear different on X-ray images when subjected to yaw rotation. However, pitch and roll rotation would alter its projected image. These considerations warrant further study of optimal shape, placement, and orientation of asymmetric fiducials when used with Synchrony® single-fiducial tracking. Synchrony® dependence on pitch and roll rotation should be investigated.

Similarly, geometric position within tumor would alter the accuracy of dose delivered to a rotated target. Rotation around a fiducial located centrally in a spherically symmetric target would result in no loss of dose to the target. However, rotation around a fiducial located in the periphery of the tumor may result in inaccuracies as seen in Figures 19-20. Also, high-Z material fiducials cause streak artifacts on patient CT scans (see Figure 17). These artifacts result in higher uncertainty values when the CT scans are matched to live-image X-rays. Evidence of this effect can be seen when the phantom was aligned at 0° yaw rotation and uncertainty values were statistically lower when using the GoldAnchor™ fiducial than those for the GoldMark™ (Table 2). The higher values in uncertainty could be attributed to the thickness of the fiducials; a thinner GoldAnchor™

caused less artifact than a thicker GoldMark™ fiducial. Uncertainty dependence on this factor should also be explored.

## Conclusion

The hypothesis of this study was verified by the results. A correlation is demonstrated between the displayed uncertainty of a moving target tracking model and the degree of target rotation when using the single fiducial-based Synchrony® Respiratory Tracking system. This uncertainty depends on the fiducial asymmetricity projected on the paired X-ray localization images of a Cyberknife® robotic radiotherapy system. To our knowledge, detection of target rotation by uncertainty is a novel use of this parameter. Ultimately, if single fiducial tracking is used as a method of real-time tumor tracking, it is envisioned that the uncertainty parameter can overcome the limitation of tracking target rotation. Single fiducial tracking will enhance treatment of lung tumors by reducing the chance of pneumothorax and other implantation complications.

## References


1. https://www.medicalnewstoday.com/info/lung-cancer
2. Siegel, R., Ma, J., Zou, Z. and Jemal, A., "Cancer statistics", A Cancer Journal for Clinicians, 2018
3. Iris C. Gibbs, M.D. Billy W. Loo, Jr., M.D., Ph.D, "CyberKnife Stereotactic Ablative Radiotherapy for Lung Tumors", Technology in Cancer Research and Treatment, 2010.
4. M. Patricia Rivera, Atul C. Mehta, "Initial diagnosis of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition)". Chest®, 2007.
5. Robert Timmerman, Ronald McGarry, Constantin Yiannoutsos, Lech Papiez, Kathy Tudor, Jill DeLuca, Marvene Ewing, Ramzi Abdulrahman, Colleen DesRosiers, Mark Williams, and James Fletcher "Excessive Toxicity When Treating Central Tumors in a Phase II Study of Stereotactic Body Radiation Therapy for Medically Inoperable Early-Stage Lung Cancer"
6. Videtic, Gregory M.M. et al., "Stereotactic body radiation therapy for early-stage non-small cell lung cancer: Executive Summary of an ASTRO Evidence-Based Guideline". Practical Radiation Oncology, Septendber-October, 2017.
7. Mageras GS[1], Pevsner A, Yorke ED, Rosenzweig KE, Ford EC, Hertanto A, Larson SM, Lovelock DM, Erdi YE, Nehmeh SA, Humm JL, Ling CC. "Measurement of lung tumor motion using respiration-correlated CT." International Journal of Radiation Oncology Biological Physics, 2004.

8. Saloomeh Vahdat, Eric K Oermann, Sean P Collins, Xia Yu, Malak Abedalthagafi, Pedro DeBrito, Simeng Suy, Shadi Yousefi, Constanza J Gutierrez, Thomas Chang, Filip Banovac, Eric D Anderson, Giuseppe Esposito and Brian T Collins, "CyberKnife radiosurgery for inoperable stage IA non-small cell lung cancer: 18F-fluorodeoxyglucose positron emission tomography/computed tomography serial tumor response assessment", Journal of Hematology & Oncology, 2010.

9. Accuray, "Equipment Specifications", 2009.

10. Yousefi S, Collins BT, Reichner CA, Anderson ED, Jamis-Dow C, Gagnon G, Malik S, Marshall B, Chang T, Banovac F. "Complications of thoracic computed tomography-guided fiducial placement for the purpose of stereotactic body radiation therapy". Clinical Lung Cancer. 2007.

11. Kothary N, Heit JJ, Louie JD, Kuo WT, Loo BW, Jr., Koong A, Chang DT, Hovsepian D, Sze DY, Hofmann LV. "Safety and efficacy of percutaneous fiducial marker implantation for image-guided radiation therapy". Journal of vascular and interventional radiology. Feb, 2009.

12. C. Shang, Chief Physicist, Lynn Cancer Institute, 2018

13. Christian Plathow et al. "Analysis of intrathoracic tumor mobility during whole breathing cycle by dynamic MRI". International Journal of Radiation Oncology. Jul, 2004.

14. Sebastian Sarudis, Anna Karlsson Hauer, Jan Nyman & Anna Bäck, "Systematic evaluation of lung tumor motion using four-dimensional computed tomography". Acta Oncologica. Jan, 2017.

15. Ingmar Lax,Vanessa Panettieri,Berit Wennberg,Maria Amor Duch,Ingemar Näslund,Pia Baumann, “Dose distributions in SBRT of lung tumors: Comparison between two different treatment planning algorithms and Monte-Carlo simulation including breathing motions”. Acta Oncologica. Jul, 2009

16. Yvette Seppenwoolde M.Sc., HirokiShirato M.D., Ph.D., KeiKitamuraM.D., Ph.D., Shinichi Shimizu M.D., Ph.D. Marcelvan Herk Ph.D.∗Joos V.Lebesque M.D., Ph.D., Kazuo Miyasaka M.D., Ph.D. “Precise and real-time measurement of 3D tumor motion in lung due to breathing and heartbeat, measured during radiotherapy”. International Journal of Radiation Oncology.” Jul, 2002.

17. Jeremy D.P.Hoisak M.S., Katharina Sixel Ph.D., Romeo Tirona B.S., Patrick C.F. Cheung M.D. Jean-Philippe Pignol Ph.D, “Correlation of lung tumor motion with external surrogate indicators of respiration”. International Journal of Radiation Oncology, Nov, 2004.