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Interfraction variability of breathing amplitude of patients undergoing SBRT lung treatment and the potential impact on dosimetry

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Abstract

Introduction

The study investigated the consistency of free breathing planning margins for fractionated SBRT treatment in the lung. The study compared breathing motion from the average CT (AVE CT) scan to the Cone Beam Computed Tomography (CBCT) from each treatment session. Various breathing techniques were also discussed, including deep inspiration breath hold (DIBH), gated breathing, abdominal compression (AC), and free breathing (FB). Free-breathing may lead to overdosing on surrounding healthy tissue if significant changes in breathing amplitude occur. Abdominal compression or breath hold may reduce abnormal breathing movement if erratic breathing occurs. The study's aim was to ensure the accuracy of radiation therapy by accurately matching the patient's position to the AVE CT.

Methods

The study collected retrospective cohort data to analyze the consistency of free breathing planning margins for SBRT lung treatment. The study included ten patients diagnosed with malignant neoplasm of the lung and compared breathing motion from the AVE CT scan to the CBCT from each treatment session. The study emphasized the importance of careful monitoring during treatment to ensure the accuracy of radiation therapy. The study's data comparison may reveal a correlation between diaphragm-PTV distance and tumor motion during breathing. A paired sample test assesses the significance of diaphragm movement and PTV-diaphragm distance. Distribution and probability plots identify any anomalies that correlate to the tumor motion.

Results

The study found that careful monitoring during treatment is essential to ensure accurate treatment. The paired sample test showed no significant difference in diaphragm movement between CBCT and AVE CT. The PTV-diaphragm distance showed a correlation with tumor motion during breathing. The study identified an outlier, subject 10, significantly impacting the correlation between PTV-diaphragm and tumor motion. Overall, the study emphasizes the importance of monitoring and adjusting for accurate radiation therapy.

Conclusion

SBRT patients undergoing treatment with a PTV margin of ITV + 5mm received minimal impact on the surrounding healthy tissue. Patients with irregular breathing patterns significantly changed the average of their diaphragm distance during CBCT, which can impact the treatment. Deep or shallow breathing can also significantly affect the treatment of the patient. The closer the target is to the diaphragm, the more pertinent the proper repetition of normal breaths becomes. Overall, the study emphasizes the importance of careful monitoring and adjustment during treatment to ensure the accuracy of radiation therapy.

Keywords

sbrt, interfractional, intrafractional, average ct, sign test, signed rank test, diaphragm movement, ptv to diaphragm, tumor motion, lung sbrt, half arc, vmat, imrt, malignant neoplasm

Introduction

Stereotactic body radiation therapy (SBRT), also known as Stereotactic ablative radiotherapy (SABR), developed in the early 1990s to be a hypofractionated treatment technique where a high dose irradiates the targeted site and a low dose irradiates to the healthy tissue (1). Compared to conventional 3D techniques, SBRT only requires one to five fractions or sessions to complete the treatment (2). With more conformal isodose lines (IDL) than 3D planning and fewer fractionations needed to complete the prescribed radiation, SBRT lung cancer studies showed significant healthy tissue sparing, including adjacent critical structures (3). The SBRT planning algorithm can calculate plans for complicated targets near critical structures or organs at risk (OARs) with significantly better conformity index (CI), gradient index (GI), conformity number (CN), and mean lung dose (MLD) (3). Beam homogeneity in SBRT is improved through more monitor units (MU) in Volumetric Arc Therapy (VMAT) than in conventional (3).

Volumetric Arc Therapy (VMAT) shortens radiation delivery time with incredible precision and speed compared to traditional radiation therapies (4). VMAT uses a rotating gantry to deliver radiation from multiple angles while changing the beam's intensity to conform to the shape of the target (4). As the shape of the beam conforms to the tumor, the conformality index approaches 1.0, creating a steep isodose line (IDL) gradient outside of the target during lung SBRT treatment planning (3). The steep gradient minimizes a low-dose spill damaging the surrounding healthy tissue as opposed to conventional lung treatment that irradiates more outside the target (3). The increased CI, steep gradient dose fall-off and faster delivery time decreases the chance of intrafractional tumor motion during lung SBRT treatment.

A factor in all radiation treatment plans and more urgent in lung SBRT is the interfractional and intrafraction motion of the patient during treatment (5). Interfractional motion is the movement of the tumor or surrounding organs between radiation treatments, while intrafractional motion is movement during treatment. Both types of motion can affect the accuracy of radiation therapy by underdosing the target (5). The patient's motion requires careful monitoring and adjustment during treatment. Four-dimensional CT (4DCT) technique is a way to create multiple images of the same area of the body from a normal expiration to the everyday inspiration of the patient's lungs to collect a complete video of the movement of the tumor and surrounding organ motion (5). 4DCT is an ingenious technique to correctly identify the tumor's motion and manage intrafractional motion during treatment (5). To ensure the target is irradiated accurately, the average CT (AVE CT) scan is compared to the cone beam CT taken before a treatment session begins to accurately match the patient's position to the AVE CT (6). For lung SBRT, tumor motion is managed by various breathing techniques which include deep inspiration breath hold (DIBH), gated breathing, abdominal compression (AC), and free breathing (FB) (5). DIBH involves the patient holding their breath briefly while the radiation is delivered (7). Gated breathing involves a respiratory gating system to monitor the patient's breathing and only provide the radiation when the tumor is in the desired position (7). Abdominal compression involves an abdominal compression system that applies pressure to the abdomen to reduce the tumor's motion due to breathing (5). Free breathing allows the patient to breathe normally for the treatment session; however, due to FB, the patient may risk overdosing on the surrounding healthy tissue (8). Significant changes in breathing amplitude may lead to underdosing the total dose to the target and overdosing surrounding healthy tissue (8). If erratic breathing occurs, abdominal compression or breath hold may reduce abnormal breathing movement (5).

The study aims to investigate the consistency of free breathing planning margins for fractionated SBRT treatment in the lung. Comparisons of breathing motion from the average CT (AVE CT) scan to the Cone Beam Computed Tomography (CBCT) from each treatment session.

Literature Review

In a previous study on the interfraction variation for lung tumor motion that moves greater than 8 mm for lung SBRT treatment, the authors compared the difference in treatment between 30 patients treated with an AC and those without one to determine the difference between AC and FB (9). Cone beam computed tomography (CBCT) and average intensity projection images were collected to compare the magnitude of the interfraction variation between patients with AC and those without (9). The study concluded that AC was an effective tool for reducing the breathing amplitude of the tumor's motion by the mean, standard deviation (SD) (9). Without AC, the longitudinal motion amplitude was 19.9 ± 7.3 mm, and with AC, motion was reduced to 12.4 ± 5.8 mm (9).

A study was completed on the intrafractional and interfractional SBRT treatment of the liver and lung tumor motion while undergoing active breathing control (ABC) (10). ABC coordinates the radiation delivery according to the patient's breathing pattern to ensure the tumor is irradiated in the same phase of the breathing cycle each time to decrease the radiation exposure to the surrounding healthy tissue (10). Of the 19 patients with liver cancer and the 15 patients with lung cancer, intrafractional systematic/random error at the medial to lateral, anterior to posterior, and superior to inferior concluded there was a 26.3% in liver and 46.7% significant motion greater than 3 mm respectively (10).

A study of interfraction and intrafraction tumor motion in lung SBRT using respiration-correlated CBCT changes in breathing patterns during treatment for Stage I non–small-cell lung cancer (NSCLC) was conducted (11). The study found that changes in breathing patterns were small. Still, patients who received abdominal compression had a significant difference of $p < 0.05$ in the variance of the changes in tumor motion amplitude (ΔM) in the superior-inferior direction that were >2 mm compared to the initial respiration-correlated CBCT (rcCBCT) (11). However, it was observed that a majority of these patients experienced a decrease in tumor motion over the course of their treatment (11). The study suggests that SBRT is an effective treatment for medically inoperable Stage I non–small-cell lung cancer. However, care must be taken to minimize the effects of changes in breathing patterns during treatment (11).

In the study of the effects of different breathing patterns for the same patient during SABR treatment for primary renal cell carcinoma (RCC), the case emphasized the need for motion management strategies in SABR for primary RCC targets (12). The author measured the kidney to identify if there was a significant change in location from where the planned site originally was (12). The authors tested FB, BH & AC breathing techniques to ensure all techniques were reviewed (12). The study showed that a change in patient breathing amplitude could significantly impact dosimetry to organs at risk and target structures (12). The importance of tools to verify breathing motion before treatment delivery was highlighted, and 4D image-guided radiation therapy verification strategies should focus on ascertaining ITV margin coverage and the effect on the surrounding organs at risk (12).

In our study, we will focus on diaphragm movement and tumor motion with treatment to the upper and lower lobes, where free breathing motion should have a more significant impact. The results would determine if the change in breathing is significant when comparing CBCT and AVE CT. If the results show a significant increase or decrease from a regular breathing pattern, the study may suggest patients could become more anxious or calmer during treatment. Protocols for the assessment for patients who would qualify for FB technique may need to be addressed to continue to provide the highest level of care for patients who undergo lung SBRT treatment. If the results are insignificant, then the current protocol for patients who qualify for free breathing that undergo lung SBRT treatment are correctly treated.

Method

Patient Selection

The study conducted is a retrospective cohort data collection to analyze the consistency of free breathing planning margins for SBRT treatment in the lungs from a Western cancer institution. All subjects selected have been diagnosed with malignant neoplasm of the lung.

All treatment were set up with a Sim Freedom Couch overlay (SBRT-B1 & SBRT-B2), head support B, CDR 3 indexable module for the leg, knees, feet, and arms up in the back position, and a blue sponge under the knees. The localization of the compression bridge configuration was customized to conform to the patient's dimensions and mitigate any potential tumor-related respiratory distress such as labored breathing. Six of the ten patients were diagnosed with malignancy of the lower lobe, while four out of ten were diagnosed with the upper lobe. All patients are prescribed 5000 cGy over five fractions. Primary photon energy was 6X, Flattening filter free (FFF). No patient was previously treated in the region of interest (ROI) for SBRT lung treatment.

Institutional Review Board (IRB)

A request was made to a Western Institution for Eligibility Authorization to conduct retrospective research on human subjects. Upon review, it was determined that the study met the human subject research criteria that required IRB approval. An application was submitted for an exempt review category and was ultimately approved. The required courses completed through Collaborative Institutional Training Initiative (CITI) were Human Research, CITI Good Clinical Practice, and Conflict of Interest mini-course. Finally, Grand Valley State University (GVSU) IRB gave the study the green light.

Planning

Subjects were scanned on Siemens CT with 4DCT to measure the breathing pattern of the tumor within the subjects to create the ITV and PTV structures. Breathing motion, tumor motion, and OARs can be assessed, delineated, and prepared for planning. All subjects underwent three half-arcs, each with unique gantry and collimator pathways taken for optimal dose distribution to the ITV and PTV.

The contour workspace tab's pixel density profile tool was utilized to obtain measurements of the gray scale from the CT scans, which allowed us to discern the movement of the diaphragm in the subjects. The AVE CT was superimposed with each of the five fractions of CBCT via the registration link to compare the breathing pattern profile graph quantitatively. Diaphragm movement is measured when compared from the AVE CT to the CBCT. The shaded HU distortion between the diaphragm and the lung will be measured to conclude how much diaphragm movement occurs during treatment (Fig. 1).

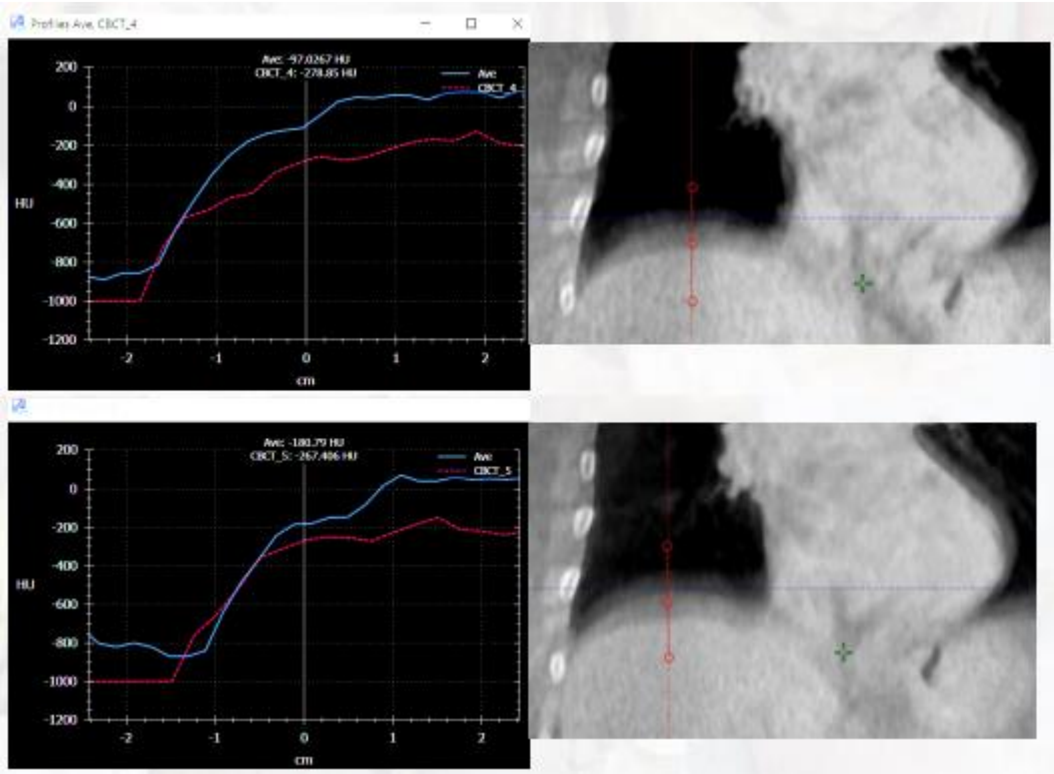

Figure 1: Pixel density profile tool measuring diaphragm movement.

If the difference is significant, it may significantly impact the proper treatment of the patient and interfraction variability during treatment.

Additionally, breathing motion would be assessed and quantified from each subject's fractions minus the AVE CT. The average of the five fractions per subject will produce an average difference between all ten subjects. For each subject's coronal/frontal view, a straight line is measured from the PTV to the diaphragm for every patient's AVE CT to compare with the tumor motion with the 4DCT phase 0% and 50%, inspiration, and exhalation. The data comparison may reveal a correlation between diaphragm-PTV distance and tumor motion during breathing.

Finally, a paired sample test, a signed rank test, for diaphragm movement was used to identify if the p-value was significant enough to be at the 5% significance level. For diaphragm- PTV distance, a paired sample test, a signed test, was used to assess if the p-value uncovered revealed any significance at the 5% significance level. Distribution and probability plots were used to identify any anomalies for diaphragm movement and PTV-diaphragm distance that correlates to the tumor motion.

Results

The study aimed to investigate the consistency of free breathing planning margins for fractionated SBRT treatment in the lung. The age of the subjects ranged between the ages of 59 to 85 years. Table 2, diaphragm movement, compares the average CT (AVE CT) to the average of all five CBCT scans from each subject to deduce the averages of both AVE CT and average fractions. For the ten subjects, the AVE CT diaphragm movement were 12.8 mm, 13.9 mm, 18.4 mm, 14.2 mm, 25.6 mm, 28.2 mm, 16.1mm, 21.1 mm, 12.1 mm, and 24.21 mm with an average of 18.7 mm. For the ten subjects, the diaphragm movement average fraction were 16.02 mm, 11.62 mm, 10.5 mm, 21.7 mm, 16.02 mm, 16.78 mm, 14.5 mm, 16.86 mm, 14.64 mm, and 26.36 mm with an average of the average fraction calculated to be 16.5 mm. The difference between the AVE CT and the average of the average fraction was 2.2 mm meaning the average motion of the diaphragm was less during treatment than during simulation by 2.2 mm. Paired sample test, the signed-rank test was used for the diaphragm movement since the distribution was symmetric (Fig. 3). A p-value of 0.4316 was generated by the signed rank test for diaphragm movement. The signed rank test p-value showed there was no significant difference of diaphragm movement in CBCT compared to AVE CT at the 5% significance level (<0.05). As for the normality test on Figure 3, no significant deviation from the normal distribution was uncovered. A summary of the diaphragm movement is seen in Table 1, 2 & 4 under diaphragm movement and breathing motion. To further solidify the calculations of diaphragm movement, the breathing motion average was calculated for the difference between each fraction and the AVE CT. On Table 3 for subject 1, the five fractions minus the AVE CT were 4.9 mm, 2.2 mm, 7.1 mm, -0.3 mm and 2.2 mm with an average of 3.22 mm. The average of all ten subjects were 3.22 mm, -2.28 mm, -7.9 mm 7.5 mm, -9.58 mm, -11.42, -1.6 mm, -4.24 mm, 2.54 mm, and 2.15 mm with an absolute average difference 2.161 mm. Also, the PTV adds an extra 5 mm range for potential setup errors that cover the ITV. The absolute average breathing difference was calculated to double-check the work completed for diaphragm motion.

PTV-diaphragm paired sample test; sign test was used since the distribution was skewed due to an outlier, subject 10 (13). Aside from subject 10, the significance of the motion of the tumors for all subjects correlated with the distance between PTV-diaphragm. Subjects 1, 2, 3, 4, 5, and 7 had an AVE CT PTV-diaphragm distance of 40.1 mm to 71.3 mm with minimal tumor motion of less than 5.5 mm. Patients 6, 8, and 9 had significant tumor motion since the distance between the tumor and the diaphragm was less than 35.4 mm. The difference between subjects is revealed in the distribution and probability plot. Subject 10 had the most significant impact on the correlation between PTV-diaphragm and tumor motion. A summary of the test for normality is seen in Table 7 and Figure 5 under PTV-diaphragm & tumor motion.

Discussion

The study aimed to investigate the consistency of free breathing planning margins for fractionated SBRT treatment in the lung. Based on the data collected and the results from Tables 1-7 & Figures 2, 3 and 5, ITV + 5mm for PTV for free breathing (FB) technique is an adequate margin for most patients undergoing lung SBRT. For breathing motion, subject 6 had the most considerable average difference of 11.42 mm from the fractionated CBCT to the AVE CT compared to the other subjects in the study. Patient 6 was one of the unique cases where the patient breathed deeply during the CT simulation, then during the five treatment sessions, the CBCT scans showed the patient's breathing pattern changed significantly. Patient 6 may have been breathing deeply during simulation but relaxed during treatment, effectively over-irradiating the lung for each fraction while in treatment, skewing the treatment plan and results from the data collection. For patient 6, diaphragm movement on the bar graph showed the AVE CT for every fraction over-irradiated the healthy tissue surrounding the tumor, which could lead to a greater risk for pulmonary toxicity following radiation treatment (14).

The method of measuring the diaphragm helps to understand the indirect impact it has on tumor motion when the tumor is closer or further away from the diaphragm. Tumor motion in all subjects vary in relation to the vertical distance from the diaphragm. There is no 1:1 correlation between tumor motion and diaphragm motion. Subjects 1, 2, 3, 4, 5, and 7 had an AVE CT PTV-diaphragm distance of 40.1 mm to 71.3 mm with minimal tumor motion of less than 5.5 mm. Patients 6, 8, and 9 had significant tumor motion since the distance between the tumor and the diaphragm was less than 35.4 mm. The tumor for patient 9 abuts the diaphragm, which had a significant impact on the target. Although the breathing pattern for patient 9 was consistent, the physicians at the Western institution increased the PTV margin by an extra 20 mm on top of the 5 mm margin placed for all patients.

The PTV-diaphragm and tumor motion data suggest that the closer the tumor is to the diaphragm, the greater the movement of the tumor becomes. Based on the data collected, if patients cannot control their breathing pattern to meet the diaphragm movement difference, then gated or DIBH would be a preferred method for the patient's safety to eliminate over-irradiation.

One limitation of the study was that it was a retrospective cohort, and there needed to be a way to verify the data collected was correctly documented. Additionally, the sample size of the cohort was relatively small, which could have a significant impact on the results if one or more subjects had a different breathing pattern than the rest of the group. Another potential factor is that the compression bridge may not have been placed in the exact location as before, which could significantly affect the patient's breathing pattern. Lastly, changes in the patient's weight could also impact the comparison between the CBCT scan and the AVE CT. These factors should be taken into consideration while interpreting the results of the study.

To optimize the efficacy of our study, we may consider grouping patients based on age and ensuring uniformity in preparation and planning through a comprehensive review of CT simulations. Additionally, we could explore the potential impact of reminding patients to maintain standard breathing patterns before simulation and treatment to assess the influence on breathing patterns and tumor movement during and between treatments. Furthermore, maintaining a consistent distance of up to 5 mm between the PTV and diaphragm for all patients with similar tumor conditions would allow for a more accurate assessment of the impact of the tumor. These considerations could enhance our treatment outcomes and improve patient care.

A prior study examined patients who utilized either an abdominal compression (AC) or free breathing (FB) technique and discovered that AC increased the longitudinal interfractional variation in tumor position, despite reducing lung tumor motion (9, 11). However, our study has demonstrated that the longitudinal tumor motion of all subjects (Table 6) collected from the 4DCT 0% to 50% phase had little impact on the tumor since the AC device mitigates labored breathing patterns. Another study on the effects of different breathing patterns during SBRT treatment revealed that any breathing alteration may impede treatment delivery to the target (12). For instance, Subject 6 was overexposed to radiation during treatment due to their irregular breathing pattern. Based on the tables, bar graphs, distribution plots collected, and the tumor's location for each subject, observed that the farther the cancer is from the diaphragm, the less tumor motion produced. Ultimately, the closer the target is to the diaphragm, the more critical it is to adhere to standard breathing patterns.

Conclusion

The results of these patients undergoing SBRT treatment showed that most patients with a PTV margin of ITV + 5 mm are correctly treated. In contrast, few patients are overtreated, affecting the surrounding healthy tissue. There were a few outliers where on one day, the patient was breathing deeply compared to other sessions. Patients with irregular breathing patterns significantly changed the average of their diaphragm distance during CBCT. Deep or shallow breathing can significantly impact the treatment of the patient. Overall, the study emphasizes the importance of careful monitoring and adjustment during treatment to ensure the accuracy of radiation therapy.

Conflict of interest

The author declared no conflict of interest.

Role of funding source

No funds were provided for the research.

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Reference:

1. Tipton KN, Sullivan N, Bruening W, et al. (2011, May). *Stereotactic Body Radiation Therapy - NCBI bookshelf.* Agency for Healthcare Research and Quality (US). (Comparative Effectiveness Technical Briefs, No. 6.) Executive Summary. https://www.ncbi.nlm.nih.gov/books/NBK55717/
2. Staff, M. C. (2019, April 27). *Stereotactic Radiosurgery*. Mayo Clinic. https://www.mayoclinic.org/tests-procedures/sbrt/pyc-20446794
3. Zhang, G. G., Ku, L., Dilling, T. J., Stevens, C. W., Zhang, R. R., Li, W., & Feygelman, V. (2011, November 9). *Volumetric modulated arc planning for lung stereotactic body radiotherapy using conventional and unflattened photon beams: A dosimetric comparison with 3D technique - radiation oncology*. BioMed Central. https://ro-journal.biomedcentral.com/articles/10.1186/1748-717X-6-152
4. Professional, C. C. medical. (2022, November 16). *Volumetric modulated arc therapy (VMAT)*. Cleveland Clinic.

https://my.clevelandclinic.org/health/treatments/17626-volumetric- modulated-arc-therapy-vmat

5. Thomas, D., Santhanam, A., Kishan, A., & Cao, M. (2018, January 22). *Initial clinical observations of intra- and interfractional motion variation in MR-guided lung SBRT*. The British Institute of Radiology. https://www.birpublications.org/doi/full/10.1259/bjr.20170522
6. Abboud, M., Wahl, G., Orentlicher, G., & Calvo-Guirado, J. (2013). *Comparison of the accuracy of cone beam computed tomography and medical computed tomography: Implications for clinical diagnostics with guided surgery*. The International journal of oral & maxillofacial implants. https://pubmed.ncbi.nlm.nih.gov/23527357/#:~:text=The%20measurement%20errors
7. *Respiratory gating and Deep Inspiration Breath Hold (DIBH)*. Stony Brook Cancer Center. (n.d.). https://cancer.stonybrookmedicine.edu/diagnosis-treatment/radiation-oncology/treatment-technology/respiratory-gating#:~:text=What%20is%20respiratory%20gating%3F,is%20in%20the%20treatment%20field
8. Prunaretty, J., Boisselier, P., Aillères, N., Riou, O., Simeon, S., Bedos, L., Azria, D., & Fenoglietto, P. (2018, November 24). *Tracking, gating, free-breathing, which technique to use for lung stereotactic treatments? A dosimetric comparison*. Reports of Practical Oncology and Radiotherapy: Journal of Great Poland Cancer Center in Poznan and Polish Society of Radiation Oncology. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6261085/
9. Mampuya, W., Nakamura, M., Matsuo, Y., & Ueki, N. (2013, September 3). *Interfraction variation in lung tumor position with abdominal compression*

during stereotactic body radiotherapy. American Association of Physicists in Medicine. https://aapm.onlinelibrary.wiley.com/doi/full/10.1118/1.4819940

10. Lu, L., Diaconu, C., Djemil, T., & Videtic, G. (2017, November 20). *Intra- and inter-fractional liver and lung.* American Association of Physicists in Medicine. https://aapm.onlinelibrary.wiley.com/doi/full/10.1002/acm2.12220
11. Bissonnette Ph.D., J., Franks M.D., K., Purdie Ph.D., T., & Moseley Ph.D., D. (2009, November 1). *Quantifying interfraction and intrafraction tumor Motion in Lung Stereotactic Body Radiotherapy Using Respiration-Correlated Cone Beam Computed Tomography*. Science Direct. https://www.sciencedirect.com/science/article/pii/S0360301609001941
12. Pham, D., Kron, T., Foroudi, F., & Siva, S. (2013). Effect of different breathing patterns in the same patient on stereotactic ablative body radiotherapy dosimetry for primary renal cell carcinoma: A case study. *Medical Dosimetry*, *38*(3), 304–308. https://doi.org/10.1016/j.meddos.2013.03.001
13. *Normality Test.* Datatab. (n.d.). https://datatab.net/tutorial/test-of-normality
14. Beach, T. A., Groves, A. M., Williams, J. P., & Finkelstein, J. N. (2018, October 25). *Modeling radiation-induced lung injury: Lessons learned from whole thorax irradiation*. International journal of radiation biology. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6483900/
15. D. Palma, S. S. (2010, November 22). *Stereotactic radiation therapy: Changing treatment paradigms for stage I nonsmall cell lung cancer*. Current opinion in oncology. https://pubmed.ncbi.nlm.nih.gov/21107257/

Tables and Figures

Diaphragm Movement & Breathing Motion

How data was collected:

Figure 1: Pixel Density Profile Tool

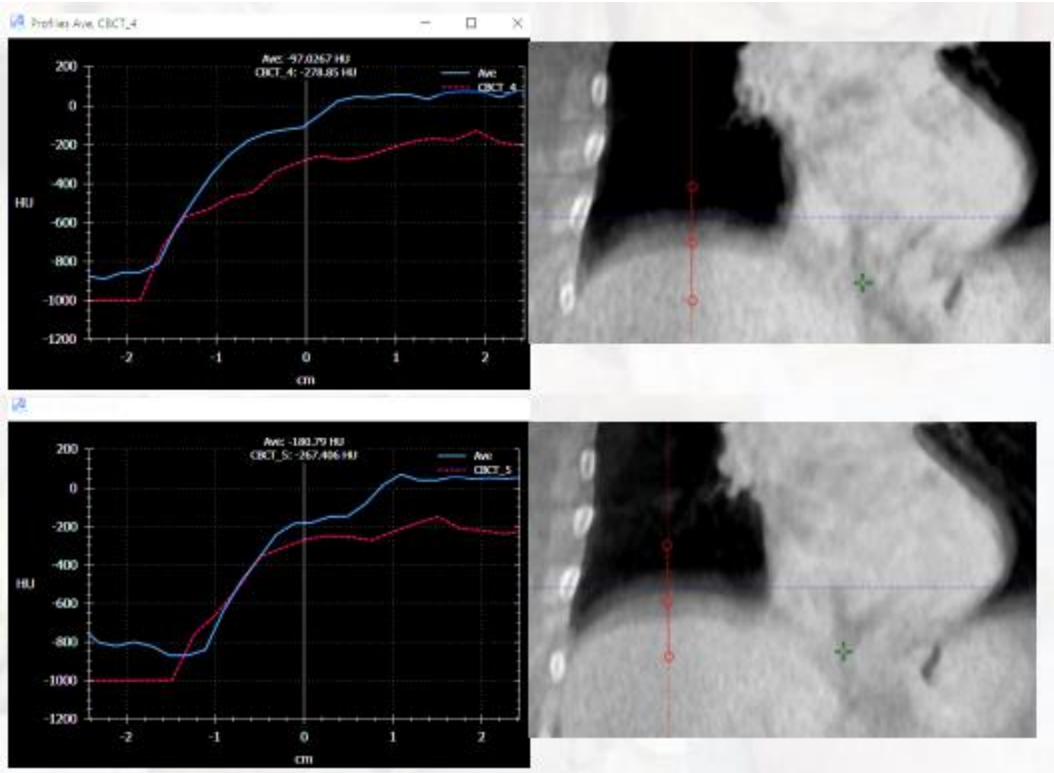
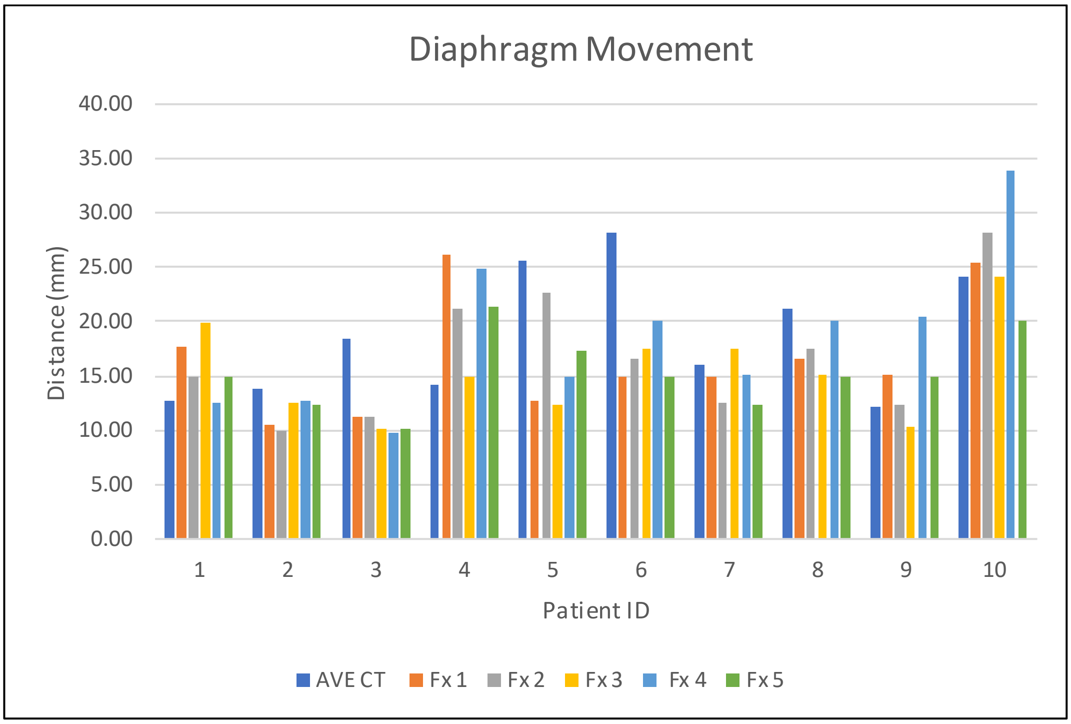


Table 1: Diaphragm Movement

Data collected for diaphragm movement:

	Diaphragm Movement						
	distance (mm)	distance (mm)	distance (mm)	distance (mm)	distance (mm)	distance (mm)	Average (mm)
	SBRT						
Patient ID	AVE CT	Fx 1	Fx 2	Fx 3	Fx 4	Fx 5	Average Fx
1	12.8	17.7	15	19.9	12.5	15	16.02
2	13.9	10.5	10	12.5	12.7	12.4	11.62
3	18.4	11.3	11.2	10.1	9.8	10.1	10.5
4	14.2	26.2	21.1	14.9	24.9	21.4	21.7
5	25.6	12.7	22.7	12.4	15	17.3	16.02
6	28.2	14.9	16.5	17.5	20.1	14.9	16.78
7	16.1	14.9	12.5	17.5	15.2	12.4	14.5
8	21.1	16.5	17.5	15.2	20.1	15	16.86
9	12.1	15.1	12.4	10.3	20.5	14.9	14.64
10	24.21	25.5	28.1	24.2	33.9	20.1	26.36

Figure 2: Diaphragm Movement



In summary,

Table 2

Subject	AVE CT (mm)	Average Fx (mm)
1	12.8	16.02
2	13.9	11.62
3	18.4	10.5
4	14.2	21.7
5	25.6	16.02
6	28.2	16.78
7	16.1	14.5
8	21.1	16.86
9	12.1	14.64
10	24.21	26.36
Average	18.7 mm	16.5 mm
Difference	**2.2 mm**	

Table 3: Breathing Motion

Data calculated for breathing motion:

Subject	Fx1-AVE CT (mm)	Fx2-AVE CT (mm)	Fx3-AVE CT (mm)	Fx4-AVE CT (mm)	Fx5-AVE CT (mm)	Average (mm)
1	4.9	2.2	7.1	-0.3	2.2	3.22
2	-3.4	-3.9	-1.4	-1.2	-1.5	-2.28
3	-7.1	-7.2	-8.3	-8.6	-8.3	-7.9
4	12	6.9	0.7	10.7	7.2	7.5
5	-12.9	-2.9	-13.2	-10.6	-8.3	-9.58
6	-13.3	-11.7	-10.7	-8.1	-13.3	-11.42
7	-1.2	-3.6	1.4	-0.9	-3.7	-1.6
8	-4.6	-3.6	-5.9	-1	-6.1	-4.24
9	3	0.3	-1.8	8.4	2.8	2.54
10	1.29	3.89	-0.01	9.69	-4.11	2.15
				Average Difference		**|2.161 mm|**

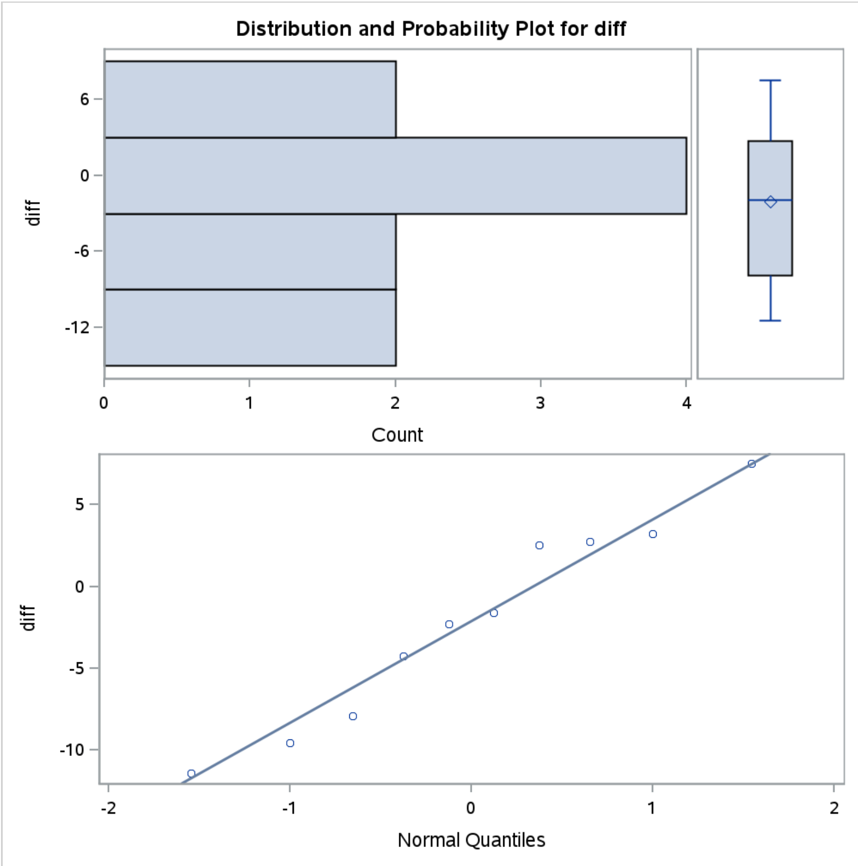
Table 4: Paired Sample Test, Signed Rank Test

Basic Statistical Measures			
Location		**Variability**	
Mean	-2.10400	**Std Deviation**	6.20519
Median	-1.94000	**Variance**	38.50434
Mode	.	**Range**	18.92000
		Interquartile Range	10.62000

Tests for Location: Mu0=0				
Test	**Statistic**		**p Value**	
Student's t	**t**	-1.07224	**Pr > |t|**	0.3115
Sign	**M**	-1	**Pr >= |M|**	0.7539
Signed Rank	**S**	-8.5	**Pr >= |S|**	0.4316

Tests for Normality				
Test	**Statistic**		**p Value**	
Shapiro-Wilk	**W**	0.956027	**Pr < W**	0.7398
Kolmogorov-Smirnov	**D**	0.172892	**Pr > D**	>0.1500
Cramer-von Mises	**W-Sq**	0.035824	**Pr > W-Sq**	>0.2500
Anderson-Darling	**A-Sq**	0.236124	**Pr > A-Sq**	>0.2500

Figure 3: Distribution and Probability Plot for difference



PTV-Diaphragm & Tumor Motion

How data was collected:

Figure 4: PTV-Diaphragm Distance

Table 5: PTV to Diaphragm Distance

	Distance PTV to diaphragm						
	distance (mm)	distance (mm)	distance (mm)	distance (mm)	distance (mm)	distance (mm)	Average (mm)
	SBRT						
Patient ID	AVE CT	Fx 1	Fx 2	Fx 3	Fx 4	Fx 5	Average Fx
1	40.1	33.4	36.9	35.9	40.6	40.2	37.4
2	71.3	64.3	63.2	70.3	72	65.4	67.04
3	56	56.8	54	53.5	58.7	57.4	56.08
4	50.4	48.3	45.5	41.1	45.5	49.1	45.9
5	55.9	54.1	52.3	53.7	53	56.2	53.86
6	30.3	33.3	28	28.8	28.2	29.9	29.64
7	70.3	69.8	67.3	68.3	69.5	71.9	69.36
8	35.4	39.6	34.7	33.2	33.3	40.3	36.22
9	0.4	0	0	0	0	0	0
10	28.8	37.1	41.1	37	40.8	33.8	37.96

Table 6: Tumor Motion

In summary, average AVE CT collected from PTV-diaphragm distance and Tumor motion collected from 4DCT 0% and 50% phase:

Subject	AVE CT (mm)	Tumor motion (mm)
1	40.1	5.3
2	71.3	4.6
3	56	2
4	50.4	5.5
5	55.9	3.7
6	30.3	19.4
7	70.3	4.4
8	35.4	11.1
9	0.4	18.4
10	28.8	8.3

Table 7: Test for Normality

Basic Statistical Measures			
Location		Variability	
Mean	-0.54400	Std Deviation	3.84351
Median	-0.80000	Variance	14.77260
Mode	.	Range	13.66000
		Interquartile Range	2.78000

Tests for Location: Mu0=0				
Test	Statistic		p Value	
Student's t	t	-0.44758	Pr > |t|	0.6650
Sign	M	-2	Pr >= |M|	0.3438
Signed Rank	S	-12.5	Pr >= |S|	0.2324

Tests for Normality				
Test	Statistic		p Value	
Shapiro-Wilk	W	0.800523	Pr < W	0.0147
Kolmogorov-Smirnov	D	0.261338	Pr > D	0.0506
Cramer-von Mises	W-Sq	0.12356	Pr > W-Sq	0.0458
Anderson-Darling	A-Sq	0.780014	Pr > A-Sq	0.0285

Figure 5: Distribution and Probability Plot for difference

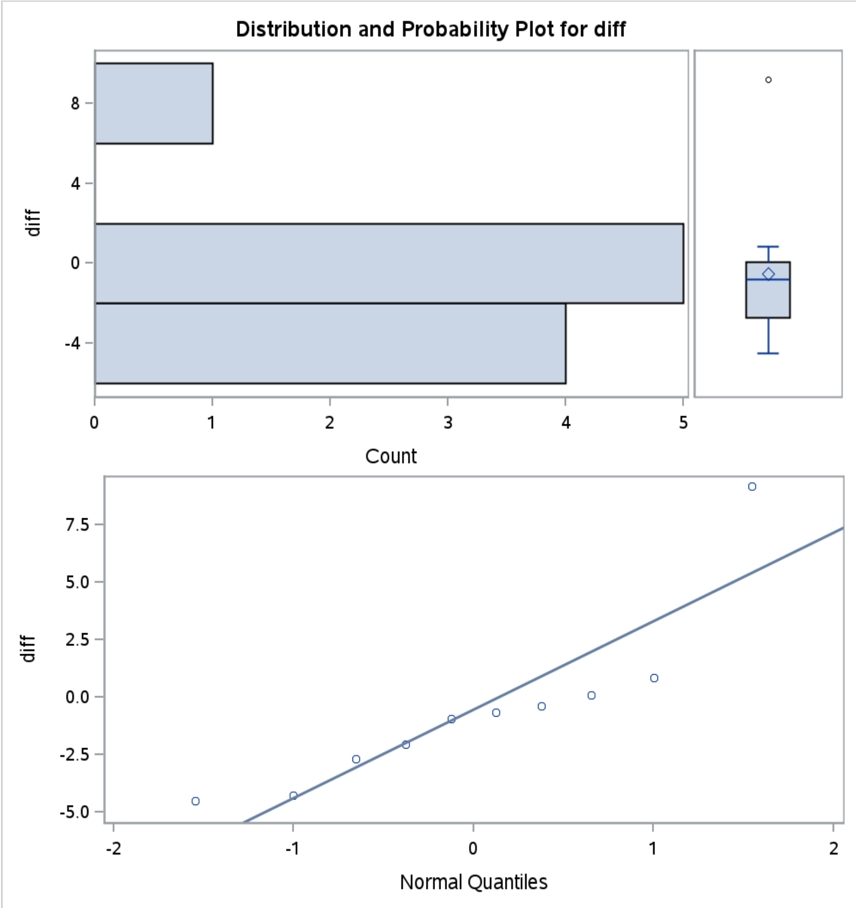
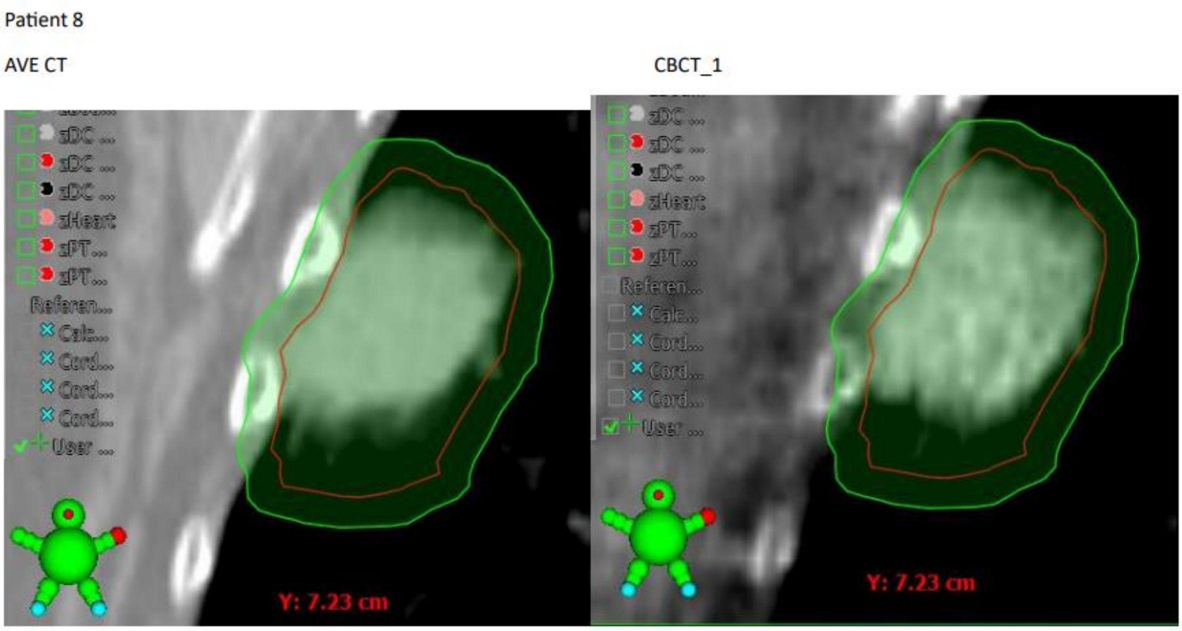


Figure 6: Examples of Tumor Movement Images

Subject 8:



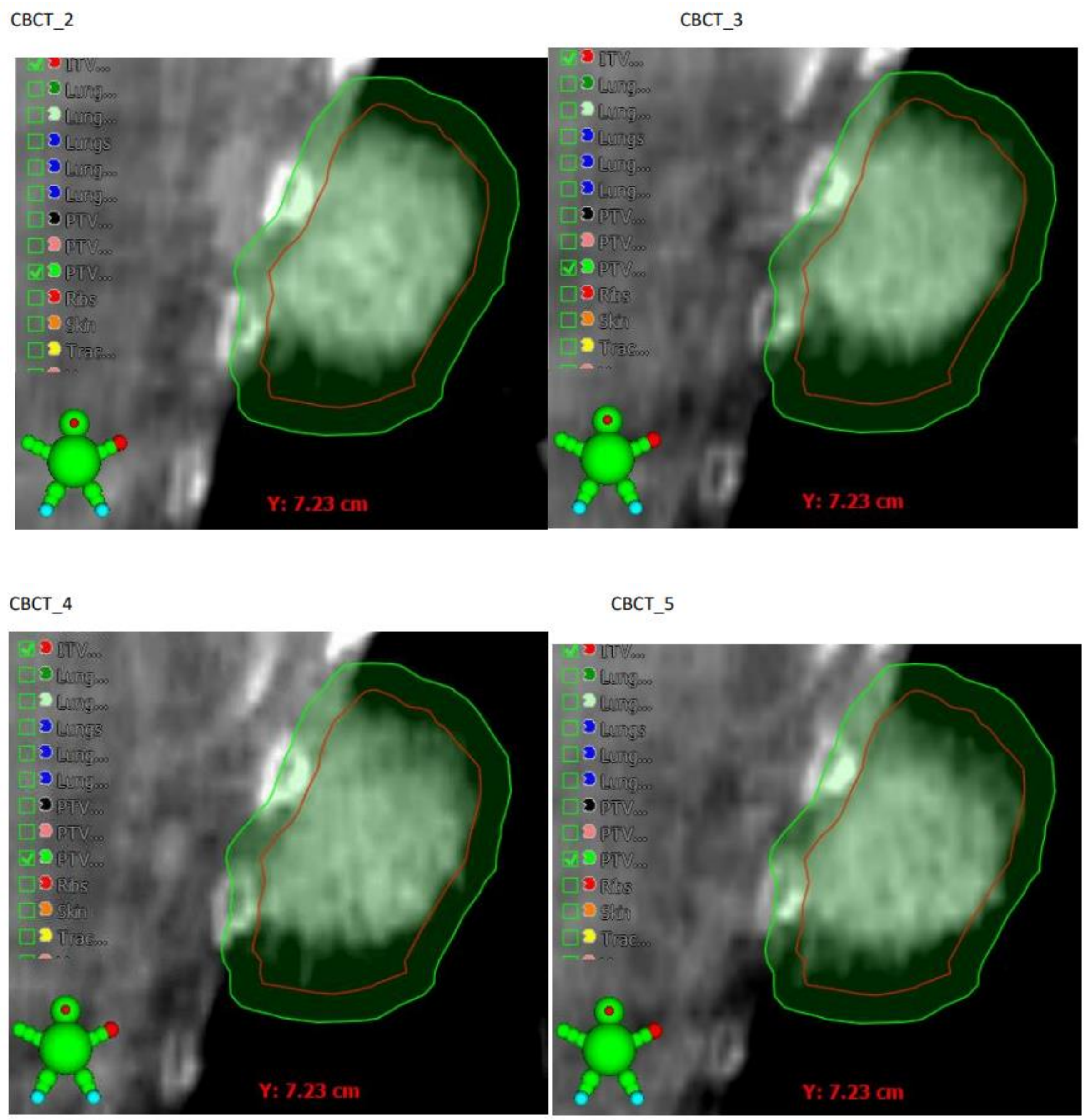
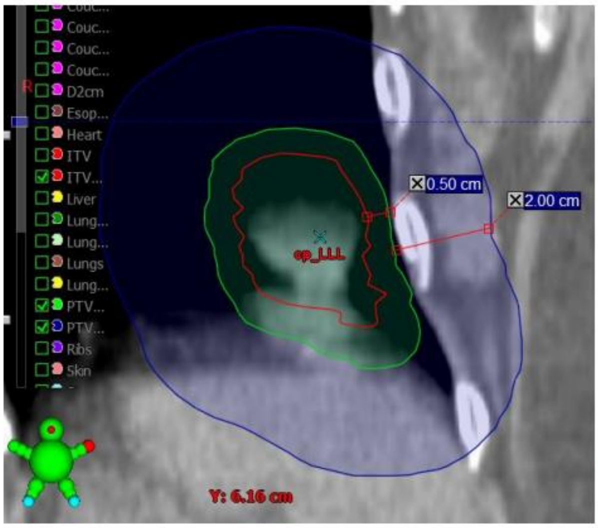


Figure 7: Examples of Tumor Movement Images

Subject 9:

Patient 9

AVE_CT



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