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Article

A Phantom Investigation of the Robustness and Adaptability of the Novel PET LINAC During Lung Cancer Biology-Guided Radiotherapy (BgRT) Characterized by Unplanned Perturbations in the Tumor Trajectory

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Simple Summary

The study is an independent assessment of the robustness and adaptability of the novel PET LINAC to situations that would be otherwise unanticipated or specifically unaccounted for during treatment planning. The focus was on lung cancer biology-guided radiotherapy (BgRT) where perturbations in tumor trajectory are observed that were absent during planning sessions. By designing and delivering phantom experiments that incorporated the known perturbations in the BgRT workflow from simulation to treatment delivery and by measuring and comparing the dose delivered with and without the perturbations, we showed that within the limits of the perturbations studied in this work, the system would safely and accurately deliver radiation dose to the target. More studies are needed to make a general conclusion on the system's robustness and adaptability to more sophisticated perturbations.

Abstract

The novel biology-guided radiotherapy system (BgRT), the RefleXion X1 SCINTIX™ system uses annihilation photons produced from a PET-avid tumor to plan and then subsequently guide the delivery of beamlets of radiation to the tumor, tracking the dose delivered in real time. The current BgRT system is cleared by the U.S. Food and Drug Administration (FDA) to treat tumors in the lung or bone characterized by periodic or non-periodic motion respectively. In this work, we assessed the robustness and adaptability of the dose tracking capability under tumor motion perturbation. We designed a phantom study based on a lung case planned under periodic tracking for four pass (4-Pass) BgRT and then introduced transient translational shifts to the phantom motion continuously under treatment. By comparing the dose delivered under a normal periodic sinusoidal tumor motion to the dose delivered under a perturbed sinusoidal delivery, with a simple perturbation introduced at the end of the second of a 4-Pass delivery and a more complex situation with perturbation introduced at each of the four passes of the 4-Pass delivery, we assessed the robustness and adaptability of the RefleXion X1 SCINTIX™ system to deliver the correct dose under such circumstances.

Keywords: lung cancer radiotherapy; F18-FDG; biology guided radiotherapy; PET LINAC; SCINTIX therapy

1. Introduction

Some cancers exhibit high metabolic activity, meaning that when injected with a positron emission tomography (PET) radiotracer such as F18-Fluorodeoxyglucose (F18-FDG, or simply FDG),

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there will be preferential uptake that will clearly make this region appear bright on the PET scan [1]. Recent advances in the field of radiotherapy have resulted in a treatment modality that takes advantage of the biology of such PET-avid tumors to design a treatment that guides radiation beams in real time to irradiate such tumors [2–5]. This is the novelty of the RefleXion X1 SCINTIX ™ system (RefleXion Medical Inc., Hayward, CA). The system is currently cleared by the U.S. Food and Drug Administration (FDA) to treat PET-avid cancers of the lung and bone using FDG as the radiotracer via the biology-guided radiation therapy (BgRT) concept [6–8]. Other sites and radiotracers are actively being investigated for future inclusion [8–11]. Given that the system itself is a linear accelerator (LINAC), it can also be used to treat any site in the body if the BgRT concept is not used. The technical composition and workflow involved with this system has been described in detail in several publications [2,9–12], but we will present a summary here.

The RefleXion X1 SCINTIX ™ system is essentially three units in one, namely a slice therapy compact LINAC, a kilo-voltage computerized tomography (kVCT) fan-beam imaging unit, and a positron emission tomography (PET) unit. The components are fixated on a fast-rotating slip-ring gantry system with a bore diameter of 85 cm that consists of two planes on the same ultra-fast 60 RPM. The kVCT imaging axial plane is parallel and anterior to the PET-guided therapy central plane with a separation of 38.6 cm axially (IEC-Y axis). In the PET-guided therapy plane, a LINAC head is placed between two 90-degree PET detector arcs.

The LINAC produces a flattening filter free single photon beam (6MV FFF) with a nominal dose-rate of 1000 cGy/min. It is equipped with a tungsten alloy target, fixed primary collimator, and an adjustable binary multi-leaf collimator (MLC) of 64 leaves for beamlet definition at a source-to-axis distance of 85 cm. An unprecedented rapid movement of collimator leaves exists, capable of switching leaves between open and closed states in about 7 ms. The kVCT imaging system is a 16-slice CT mounted at the gantry entrance and acquires 3DCT fan-beam images for localizing and aligning the patient for treatment delivery. It has a source-to-detector distance of 113.3 cm and source-to-isocenter distance of 64.3 cm for 2 cm axial coverage and 50 cm transverse field of view. The system has scan modes for fast and slow helical CT with settings of up to140 kV and 300 mA and table speeds of 4.5 mm/s to 28 mm/s. The PET detector arcs are comprised of 64 scintillation multi-pixel photon counter (MPPC) modules. The PET scintillators have side shieldings, which consist of lead septa, approximately 2 cm thick for reducing the patient scattered radiation that can cause an afterglow effect in the scintillator crystal.

The PET detector arcs are integral to BgRT, which uses PET emissions from the tumor to rapidly deliver tracked beamlets of radiation. The BgRT workflow uses these PET detectors at three different timepoints: (1) An imaging-only session, also referred to as functional modelling (FM) session to collect PET data from the patient for use in treatment planning (acquisition time of approximately 40 s per 2.1 mm of treatment extent), (2) a PET pre-scan session immediately prior to radiation delivery to evaluate whether the PET radiotracer avidity of the tumor(s) in the treatment plan are sufficiently consistent with the prior FM session to proceed with delivery (acquisition time of approximately 10 s per 2.1 mm of treatment extent), and (3) during BgRT delivery to actively guide the therapeutic beam.

The RefleXion X1 SCINTIX ™ system can be used as a regular medical LINAC for image guided radiotherapy (IGRT) via kVCT only. In this case, the PET subsystem is not utilized at all, and this is also referred to as non-BgRT treatment. This work will focus on the BgRT utility, where currently, only lung and bone cancers have been cleared by the FDA. Also, the only radiotracer that has been approved as of now is FDG. In performing treatment planning for a BgRT case, the current system provides two options for the user to categorize target movement, namely periodic and non-periodic motion. In our practice, lung tumors, characterized by respiratory induced tumor motion, are considered periodic while bone tumors that are rigid and characterized by involuntary motion are classed as non-periodic. This work is focused on lung BgRT.

The ideal candidate for lung BgRT will be one with a periodic and reproducible tumor trajectory from simulation and throughout treatment delivery. The system is designed to support minor

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deviations from the baseline associated with both tumor motion trajectory and variability in tumor-to-background PET signal changes via a bounded dose volume histogram (bDVH) analysis. The bDVH shows a range of possible curves per region of interest (ROI) rather than a single curve by calculating the best-case and worst-case scenario DVH curves, accounting for potential tumor motion (±5 mm) and tumor-to-background PET signal changes (±25%). Another category, where the deviation this time may be due to unwanted patient movement can lead to an instant perturbation in the baseline breathing pattern. In this case, the trajectory would be characterized by a combination of periodic and non-periodic motion during treatment delivery which were absent and unaccounted for at the time of simulation, FM and pre-PET imaging evaluation sessions. This latter category is the focus of this work.

The unwanted perturbation investigated here is a baseline shift in the tumor's mean position, induced by a brief, involuntary event like a sneeze, after which the patient's periodic respiratory motion resumes from this newly displaced baseline. Given the potential for severe dosimetric consequences from a geometric miss in high-dose and high dose gradient treatment, understanding system performance when this happens is crucial. To this end, a phantom study was designed to simulate the entire BgRT workflow and evaluate the system's response to these specific motion perturbations. In particular, the phantom with PET activity on a programmable motion platform was used where various periodic and non-periodic trajectories were carefully introduced and the robustness of the BgRT system assessed via measured dose delivered to the phantom.

2. Materials and Methods

2.1. Overview of the BgRT Clinical Workflow

An overview of the BgRT workflow from consultation and assessment of initial eligibility up to the final treatment is essential to understanding this work and we present a summary here.

2.1.1. Initial Eligibility at the Time of Patient Consultation

There are five major items to assess at the time of consultation, namely (a) that the tumor is PET avid, which can be easily assessed using the diagnostic PET image available at this time (b) the target standard uptake value (SUV) of 6 is desirable, the higher the better. (c) Tumor size requires a maximum dimension of the order of 2cm to 5cm, and ideally between 3 and 4cm. (d) Patient weight, not to exceed 392lbs, which is a limitation due to the maximum weight the system couch can handle. (e)Finally, an initial qualitative assessment should be done to ensure that the treated target is the predominant area of uptake with minor or no other surrounding uptake areas.

2.1.2. CT Simulation

BgRT patients with non-mobile targets undergo CT simulation wherein a thin sliced 3DCT image is acquired with a slice thickness of 2mm or less. For mobile targets, a 4DCT is acquired which amongst others is used to determine the extent of motion. In our current implementation only tumors with peak-to-peak motion of 2.5cm or less are eligible. Other images derived from the 4DCT are used in the treatment planning step and include the maximum intensity projection (MIP) image, and the phase-based or amplitude-based binned images, 0%, 10%…,90% image sets.

2.1.3. Preliminary Treatment Planning

A basic treatment plan which does not involve dose calculation is required for the RefleXion unit to be operated to acquire the FM session PET image needed for the actual planning. For this preliminary plan, the biological tracking zone (BTZ) must be defined and for the lung case the BTZ is the internal target volume (ITV) plus a margin that accounts for day-to-day variability of breathing pattern. We have in our practice used a uniform margin of 10mm. During PET image acquisition, the gross tumor volume (GTV) as visible on the PET image is in essence the time-weighted average

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position of the target. In terms of the 4DCT, this will correspond with the GTV as contoured on the image set that is representative of the time weighted average position. For a phantom with regular sinusoidal breathing pattern, this would be the 70% image set. This is not always true for a real patient where the breathing pattern is not necessarily regular and consistent. Therefore, in our practice, we have required three GTVs to be outlined, namely GTV-70%, GTV-80%, and GTV-90% contoured on the 70%, 80%, and 90% image sets respectively. By displaying and evaluating these contours following a PET image acquisition, the best match to the observed PET defined target would represent the actual GTV and thus used further as the gross tumor volume.

2.1.4. Functional Modelling (Imaging Only) Session

The basic treatment plan created earlier is uploaded at the treatment delivery console and used in performing the functional modelling (FM) session, previously referred to as the imaging only session. This is the session that culminates in the acquisition of a PET image that would serve three purposes, (a) the image is the basis for final patient eligibility assessment for BgRT; (b) the PET image is used for treatment planning and, (c) the PET image serves as a baseline for subsequent PET evaluation for delivery of all fractions.

The PET radiopharmaceutical tracer currently approved by the FDA for use with the BgRT treatment is FDG, with a half-life of 109.7 minutes. It is administered intravenously adhering to strict guidelines including a recommended elapsed time from injection to the start of the imaging session. The FDG is typically ordered at least 24 hours prior to injection time. The following is a sequence of steps used to complete the task on the day of the FM session.

(a) Daily Quality Assurance which includes SPC PET (SPC – system performance check) as well as Laser/kVCT/MV/PET isocenter coincidence. The former is a PET specific constancy check for energy and time resolution while the latter is a RefleXion X1 system geometric integrity check that ensures the fidelity of the relationship among system subcomponents.
(b) Patient clearance, which includes amongst others, confirmation that patient was NPO 6 hours prior to injection, and a blood glucose reading within an acceptable range.
(c) The patient is then asked to void and thereafter is administered 15mCi FDG. The exact injection time and injected activity is noted and entered in the treatment console computer.
(d) The patient is requested to wait in the uptake room for at least 30 minutes post injection after which the patient is again asked to void in the hot bathroom. The patient is instructed to flush the toilet at least 3 times after voiding.
(e) Begin patient setup on the treatment couch at around 45 minutes post injection to allow time for CT image set up which may include adjustments and re-imaging. The final CT image alignment is reviewed and approved before proceeding to the next step, namely PET image acquisition.
(f) Begin the PET image acquisition at 1 hour post injection. After the session, radiation survey of the entire treatment room and all other areas of interest including hot bathroom, console area, patient waiting area, trash cans, immobilization devices, hands, and feet of all participating staff are completed and documented.

The FM session results in an acquired PET image which is available for review on the treatment console computer but also available for additional analysis on the TPS. Key eligibility concepts determined by analyzing the PET image from the FM session include the activity concentration (AC), the normalized target signal (NTS), and the maximum activity present within a 2cm annulus of the BTZ (Max_Activity_BTZ+2cm_annulus), compared with the maximum activity within the BTZ (Max_Activity_BTZ). AC represents the amount of radioactive tracer activity per unit volume in the BTZ. It is computed using the mean value of PET voxels above an 80% threshold within the BTZ, ensuring a sufficient signal-to-noise ratio (SNR) against a 3mm background shell. The ratio of the computed AC to the background noise is the NTS. For the patient to be eligible for BgRT treatment,

AC >= 5kBq/ml, (1)

NTS >= 2.0 (*at planning*) and >=2.7(*at treatment*) (2)

Max_Activity_BTZ+2cm_annulus <= 50% * Max_Activity_BTZ (3)

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2.1.5. Treatment Planning and Review

The PET image from the FM session including the average CT from the 4DCT scan are used as input to the treatment plan for BgRT. Additional structures are included from the preliminary planning step that may be needed in the clinical treatment plan. In treatment planning for BgRT, the two options available for the user to designate the expected motion are periodic, used for the planning and treatment of targets characterized by respiratory induced tumor motion such as lung, and non-periodic, to designate other motion such as in bone treatment. Treatments on the RefleXion X1 can be single pass (1-Pass) or 4-Pass serial tomotherapy. In 1-Pass, the target is translated once in its entirety and treated slice by slice until the full target has been treated. For the 4-Pass serial tomotherapy, this process is repeated back-and-forth four times. All BgRT treatments are 4-Pass serial tomotherapy while the 1-Pass is used for the IGRT, non-BgRT treatments. The final treatment plan is optimized and evaluated using dose volume histograms (DVHs) that are specific to the BgRT called bounded DVHs (or bDVH). The plan quality is also assessed at this time and approved if deemed satisfactory. All treatment plans must meet established guidelines including a satisfactory score on all quality indices and the gamma analysis for patient specific QA.

2.1.6. Pre-Treatment Imaging and Treatment Delivery

The PET tracer injection is already detailed in the FM session. The same procedure is followed on the day of treatment. The treatment is delivered following established image guided radiation therapy (IGRT) protocols that utilize RefleXion's kVCT imaging for initial patient setup immediately followed by a PET image pre-treatment scan. This initial PET scan is to confirm that the uptake and distribution acquired on the day of treatment is consistent with that used to develop the treatment plan within acceptable limits. This is known as PET evaluation which compares this information to within the bounds of the bDVH and returns a pass or fail. If it passes, treatment is allowed to proceed after approval. During the delivery of the 4-Pass BgRT, limited time sampled (LTS) PET images are acquired during treatment delivery and used to provide tracked dose delivery which can account for positional offsets or tumor motion during treatment. A PET image is displayed at the end of each pass and represents the cumulative image acquired throughout the given pass. At the end of the last pass, a full image PET image of the full delivery is displayed and represents the cumulative PET image acquired through all four passes. After the therapy is completed, the information about the delivered radiation is captured in the appropriate treatment records and the patient is discharged. The process is repeated for subsequent fractions until all fractions have been delivered.

2.2. Phantom Design Including Trajectory of Tumor Motion with and Without Perturbation

The phantom used for this study was Sun Nuclear Corporation (SNC) ArcCheck with special insert designed to hold an injectable PET radiotracer or a PET point source. We used a PET point source as the center of the PET-avid target. The phantom assembly was placed on the CIRS programmable dynamic motion platform (SN 008PLX). We designed and uploaded 3 types of motion trajectories on the platform namely, (1) periodic motion Cos^4, breathing amplitude of 7.5mm and frequency of 12 breaths per minute, representative of a normal patient breathing pattern with no perturbation throughout the 4-Pass serial tomotherapy treatment, henceforth referred to as N-Case. (2) Periodic motion Cos^4, with a known simple single perturbation introduced midway through the 4-Pass serial tomotherapy treatment, henceforth referred to as SP-Case. This is representative of a patient who was otherwise breathing normally but at one point sneezed and as a result the whole body was shifted but the patient is still breathing normally. (3) Periodic motion Cos^4, with complex multiple perturbations introduced once during each of the four passes of the 4-Pass serial tomotherapy treatment, henceforth referred to as CP-Case. This is representative of a patient who was otherwise breathing normally but, in several instances, sneezed or moved and as a result the whole body was shifted.

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2.3. BgRT Workflow Process with the Phantom Study

We performed CT simulation where the phantom was set up on the dynamic platform uploaded with the Cos^4 trajectory in the superior/inferior direction. The peak-to-peak amplitude was set at 15mm, and the breathing frequency was set at 5 seconds. The MIP as well as 70%, 80%, and 90% phase image sets were sent over to the TPS for preliminary planning.

In the TPS, we contoured the GTV-70%, GTV-80%, GTV-90% from the respective phase images while the ITV was contoured on the MIP image set. The BTZ was generated by adding a 10mm isotropic margin to the ITV. A preliminary treatment plan was completed followed by an FM session which utilized the N-Case trajectory. By comparing the GTV-70%, GTV-80%, GTV-90% with the acquired PET image from the FM session, it was determined that the GTV-70% was the optimal and therefore we proceeded to define a PTV based on a 5mm uniform expansion of GTV-70%. The final treatment plan was completed with a 10Gy per fraction meeting all criteria as one would expect for a stereotactic body radiation treatment (SBRT) plan.

We then proceeded to treatment delivery following the workflow as outlined earlier. The treatment delivery workflow was done for three different programmed phantom trajectories, namely the N-Case trajectory representing the baseline as this was the same trajectory used in the FM session, the SP-Case trajectory where a simple perturbation was introduced in the otherwise normal breathing trajectory and the CP-Case trajectory where a complex trajectory with multiple perturbations was introduced. Each perturbation represented a 7.5 mm displacement in the mean position of baseline motion in the superior-inferior direction (see Figure 2). In each case, the PET evaluation was performed, the AC, NTS, and delivered dose to the phantom measured and compared with the planned dose.

It should be noted that in principle, it is also possible to abort treatment at the end of a given pass when the PET image of that pass is displayed, and one determines a misalignment. The next step following this interruption in treatment delivery will be to do a repeat kVCT imaging and correct the misalignment before proceeding to complete the remainder of the treatment. To test the efficacy of this process, we included a fourth category, SP-Case-Corrected which was the single perturbation case, SP-Case, however with the treatment interrupted immediately following the display of the misaligned PET image in pass 3. Following the interruption, we performed a repeat kVCT image which allowed us to correct for this perturbation and then continued the treatment delivery completing the last pass.

3. Results

3.1. Phantom Design Including Trajectory of Tumor Motion with and Without Perturbation

A picture of the set up is shown in Figure 1 and depicts the ArcCheck on the CIRS platform setup on the RefleXion X1 couch. The trajectories used for the phantom studies, N-Case, SP-Case and CP-Case are as shown in Figure 2.

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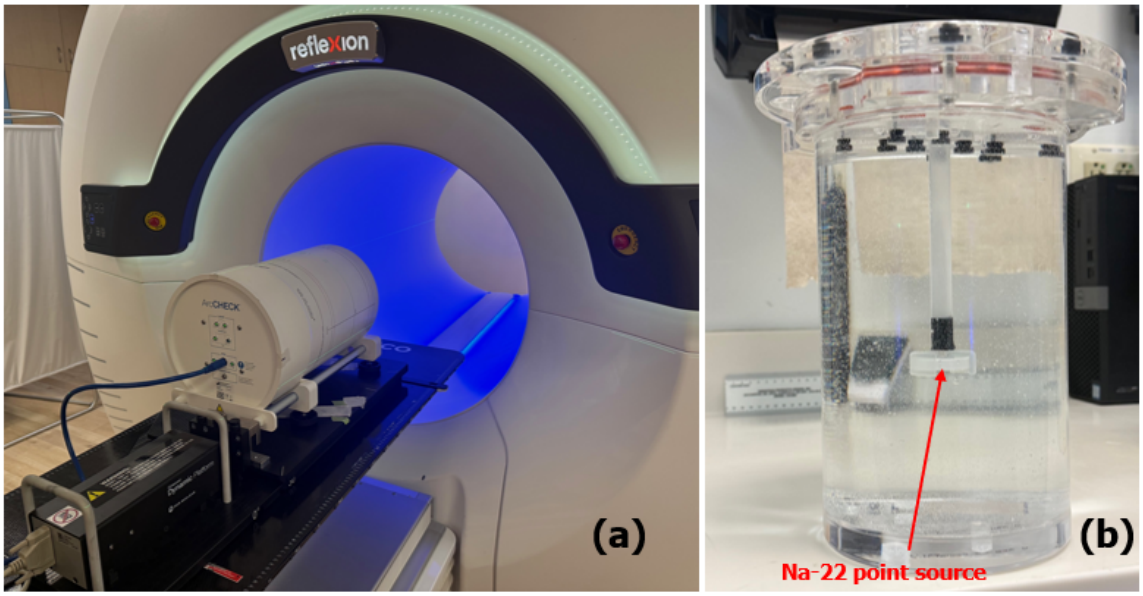

Figure 1. Setup for study: (a) SNC ArcCHECK on the CIRS Enhanced dynamic platform (SN 008PLX) on the RefleXion X1 couch with (b) special insert designed to hold an injectable PET radiotracer. The insert is filled with water.

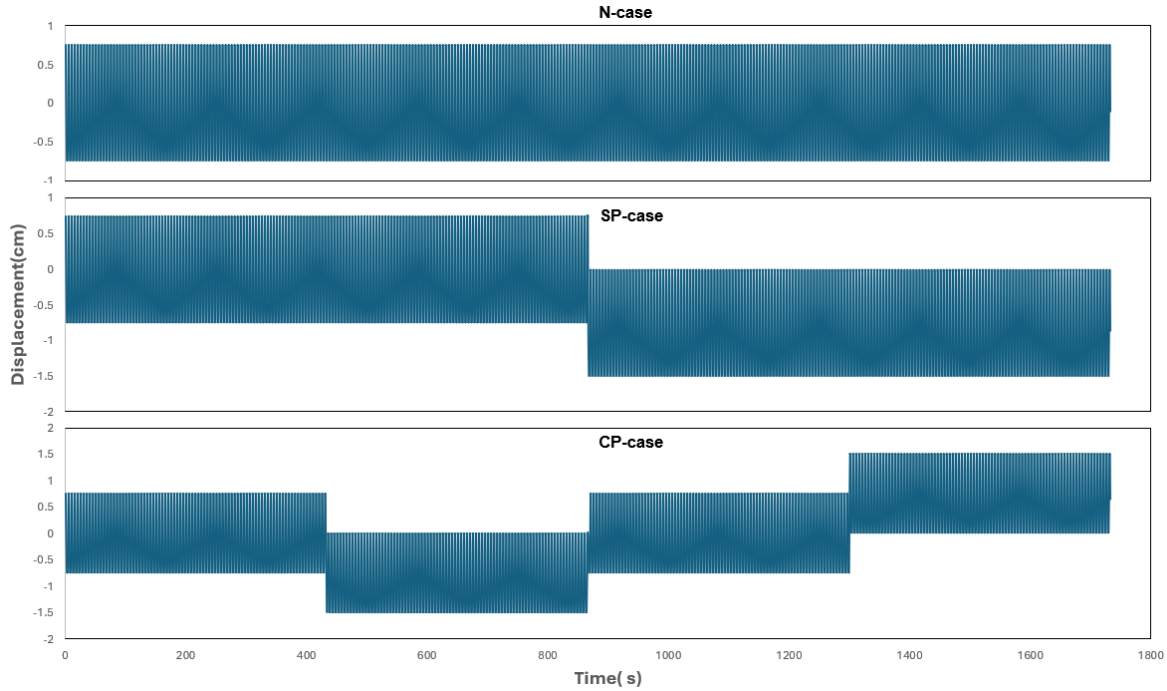

Figure 2. The N-Case (normal breathing pattern) trajectory, the SP-Case, simple (single) perturbation, introduced midway during the 4-Pass serial tomotherapy delivery and the CP-Case, complex (multiple) perturbation where more than one perturbation was introduced, once after each pass of the 4-Pass serial tomotherapy delivery.

3.2. BgRT Workflow Process with the Phantom Study

The eligibility criteria described in equations 1 to 3 were easily met for our phantom study as a point source was used. Note that this is not always the case for real-world patients. The observed values of AC, NTS and bDVH pass % are summarized in Table 1 below for the 3 trajectory types, N-Case, SP-Case, CP-Case as well as the fourth case that involved an interruption and correction, SP-Case-Corrected. The bDVH for the FM session is comparable with that of the pre-PET acquired image

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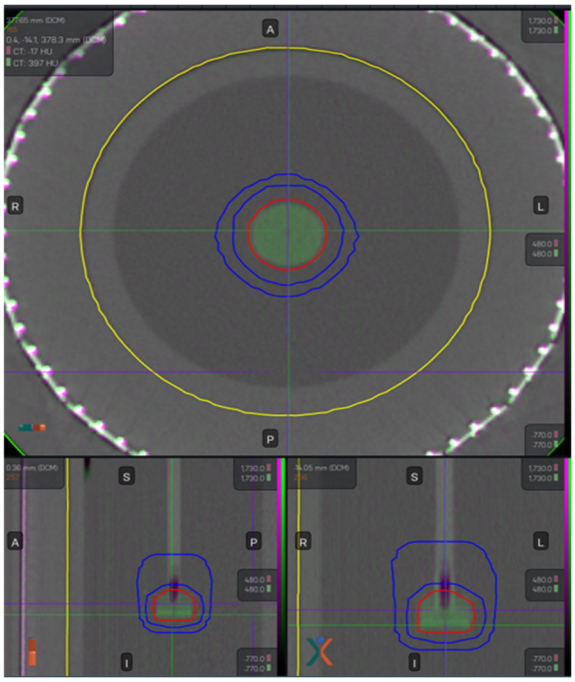
of each of the trajectory cases studied. This is because the perturbations were introduced only during the 4-Pass delivery and this being a phantom study with point source, nothing was expected to change between the FM session and on the day of delivery to affect the bDVH. This is not always the case with a real patient. The bDVH comparison for the FM session versus the N-Case pre-PET imaging is shown in Figure 4 for illustrative purposes.

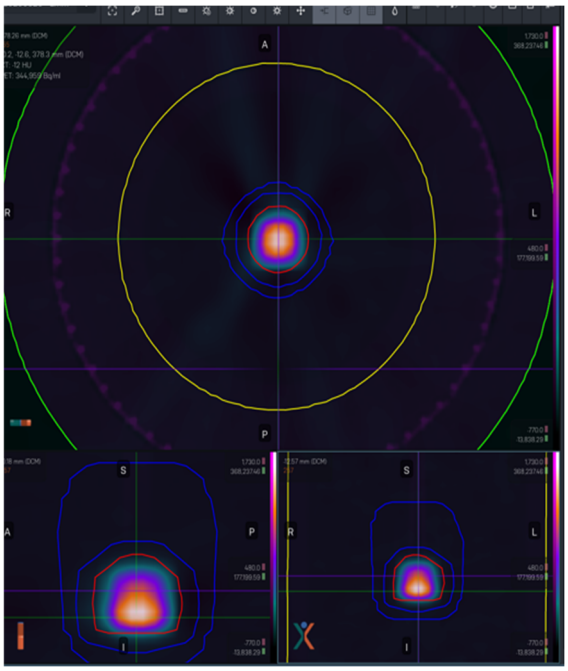
Table 1. Summary of the Activity Concentration (AC), Normalized Target Signal (NTS) and bounded Dose Volume Histogram (bDVH) pass % for the experimented deliveries.

Trajectory Type	AC	NTS	bDVH Pass %
N-Case[1]	335.89 kBq/ml	162.43	100%
SP-Case[2]	318.16 kBq/ml	182.71	100%
CP-Case[3]	320.46 kBq/ml	205.35	100%
SP-Case-Corrected[4]	304.13 kBq/ml	185.83	100%

[1]normal breathing pattern. [2]single perturbation, introduced midway during the 4-Pass serial tomotherapy. [3]multiple complex perturbations; introduced after pass1, 2, and 3. [4]single perturbation, introduced midway during the 4-Pass serial tomotherapy, system aborted when observed, repeat imaging performed and corrected for the remainder of the treatment.



(a) Alignment of acquired kVCT vs reference



(b) Acquired PET image

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(c) PET Evaluation showing bDVH pass rate, AC and NTS

Figure 3. Illustration of set up for the N-Case normal breathing trajectory where (a) in the initial step of the workflow, the acquired kVCT image is aligned with the reference CT image and shifts determined to re-align the patient. In (b), the PET acquisition is the next step where the PET image is acquired and as seen with the displayed GTV-70% image in red, this aligns well with the target. The PET image is then used in the PET evaluation which computes a bounded DVH with a bDVH Pass %, the AC and NTS are also computed.

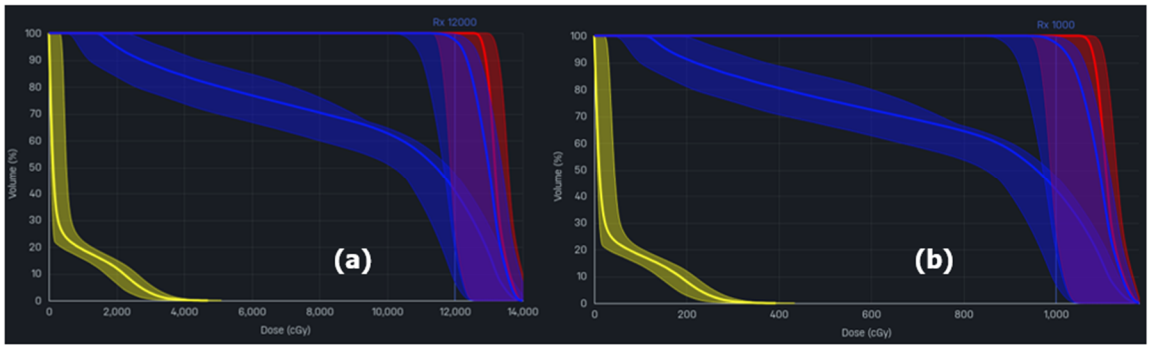

Figure 4. *The computed bounded* dose volume histogram (bDVH) for (a) the plan (10 Gy x 12 fractions) vs. (b) the computed bDVH for the N-case delivery, single fraction.

As expected for the trajectory cases that involved perturbation, we observed a shifted PET acquired image where the PET image was acquired after the perturbation event. In Figure 5, we illustrate this by a coronal view of the PET-avid GTV with the GTV contour superimposed on the image. Observe in Figure 5 that initially in the workflow where there is no perturbation introduced to the breathing motion the acquired PET image aligned with the GTV as expected in the stated areas of the N-Case (all of row (a)), SP-Case (pre-treatment, pass1 and pass2), CP-Case (pre-treatment, pass1 and pass3), and SP-Case-Corrected (pre-treatment, pass1, pass2 and pass4). As perturbation was introduced in the trajectory and another PET image acquired after this event, we can observe the displayed image misalignment with the GTV contour (Figure 5, pass3&4 for row(b), pass2&4 for row(c), and pass3 of row(d)). Note that per the trajectory in Figure 2, the CP-Case self-corrected and returned to baseline in pass 3 which is observed in Figure 5, pass3 of row (c). The GTV is shown in a fixed frame of reference, and this is why the misalignment is visible. Figure 5 is not an illustration of the dose delivered but rather must be interpreted carefully.

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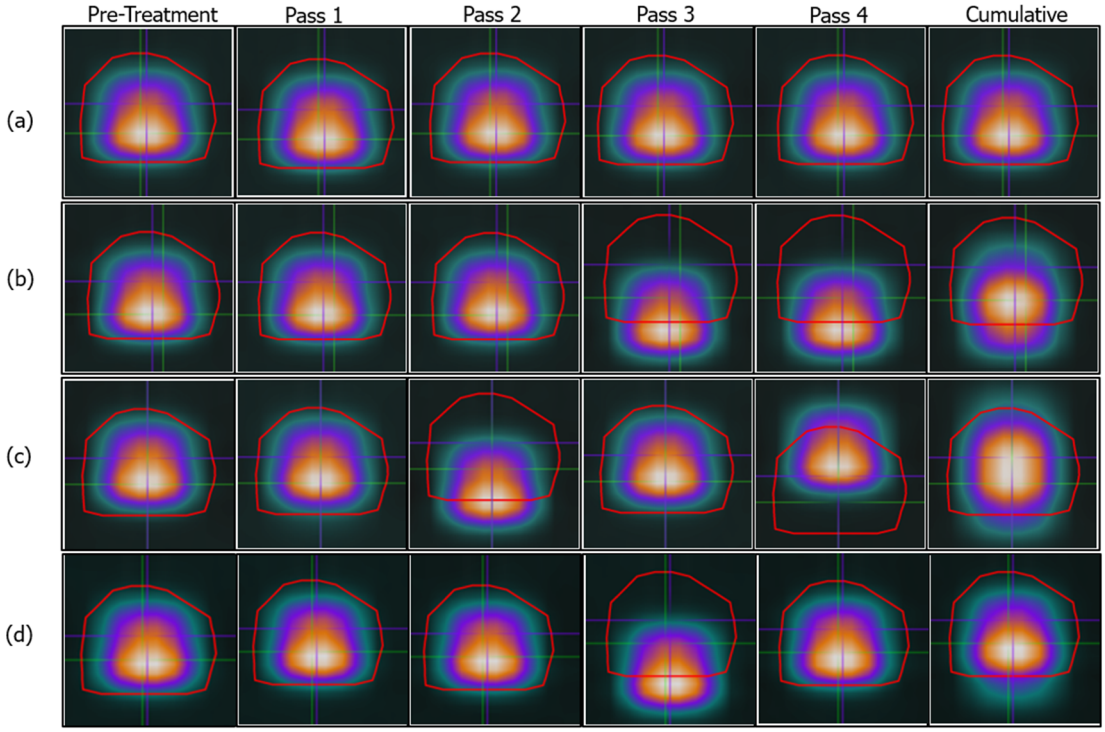
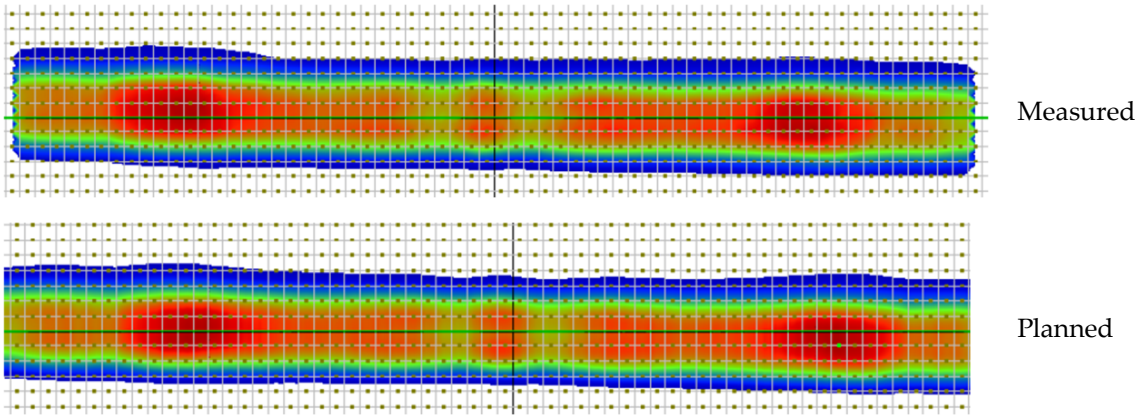


Figure 5. Coronal views of PET image acquired at the start of the treatment (pre-treatment), just before pass 1, the PET per pass, acquired at the end of each pass and post treatment combined PET (cumulative) where the target may have moved based on the introduced known perturbations. The red contour denotes the outline of the GTV for (a) N-trajectory, (b) SP-trajectory, (c) CP-trajectory, and (d) SP-Case-Corrected.

In each of the experiments, N-Case, SP-Case, CP-Case, and SP-Case-Corrected, the delivered dose to the phantom was measured and compared to the planned dose based on no perturbations. Using the gamma index analysis [13], with a dose threshold of 10%, a dose difference and distance to agreement (DTA) criteria of 3%/3mm [14], the percentage of points with a gamma less than or equal to 1 and therefore considered as passing was 97.8%, 95.4%, and 98.2% for the N-Case, SP-Case, and CP-Case, respectively. The analysis was repeated using other criteria like 3%/2mm [15], as well as 5%/1mm [16] and 1%/1mm as summarized in Table 2. These would all be considered passing in clinical practice. We illustrate one of the gamma analysis examples showing the dose comparison and a profile in Figure 6.



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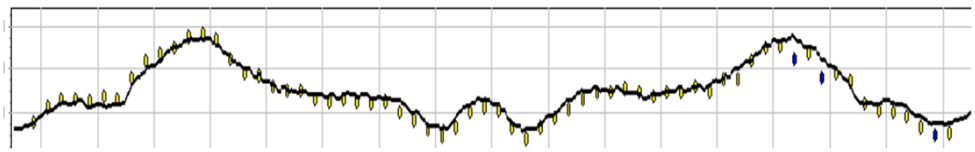

Figure 6. An example pf the measured vs. planned dose used in the gamma analysis on the SNC patient software.

Table 2. Summary of results of gamma analysis using ArcCHECK.

Trajectory Type	Gamma (3%/2mm)	Gamma (3%/3mm)	Gamma (5%/1mm)	Gamma (1%/1mm)
N-Case	96.6%	97.8%	98.4	57.8%
SP-Case	92.2%	95.4%	93.8%	56.3%
CP-Case	97.0%	98.2%	98.4%	71.5%
SP-Case-Corrected	91.1%	93.8%	89.6%	48.9%

We also observed as shown in Table 2 that the special case, SP-Case-Corrected where the treatment was interrupted following an observed misaligned PET image after pass3 delivery and the perturbation corrected via repeat kVCT imaging before completing the remainder of the treatment delivery consistently resulted in lower gamma passing rates compared to the uninterrupted counterpart, SP-Case. The gamma passing for SP-Case-Corrected was 91.1%, 93.8%, 89.6%, and 48.9% compared with 92.2%, 95.4%, 93.8%, and 56.3% for the SP-Case based on 3%/2mm, 3%/3mm, 5%/1mm, and 1%/1mm respectively.

4. Discussion

The RefleXion X1 SCINTIX ™ system is a novel PET LINAC with the capability of BgRT used in the periodic and non-periodic mode. The expected motion associated with the target trajectory informs the user as to what mode is selected for use in the entire workflow starting from the treatment planning step. Lung BgRT characterized by respiratory induced target motion would be planned as periodic whereas the BgRT of rigid body targets such as bone would be non-periodic. For lung cancer BgRT, the target trajectory, even for ideal cases that start off regular and periodic may occasionally experience unwanted perturbations that were unplanned and unaccounted for during the treatment planning step. The goal of our work was to assess if given such perturbations, the system would adapt and still deliver the correct dose to the patient.

To do this, phantom experiments were designed to go through the elaborate BgRT workflow, delivering a 4-Pass serial tomotherapy BgRT treatment and measuring the dose in three different scenarios, (1) N-Case trajectory, characterized by regular sinusoidal target motion with no perturbation introduced in the phantom trajectory, (2) the SP-Case where the same treatment plan was delivered however with a single perturbation introduced midway in the delivery, right after the second pass of the 4-Pass plan, and finally the (3) CP-Case where four complex perturbations were introduced in the course of delivery, one at each pass of the 4-Pass serial tomotherapy delivery.

The eligibility for BgRT treatment was assessed at the beginning of each phantom experiment, including calculation of AC, NTS, and bDVH % pass. Given that a point source was used with no other activity in nearby areas, the eligibility based on these criteria index calculations was always easily met. By measuring the total dose delivered in the course of each phantom experiment and comparing it to the expected dose without perturbation, the robustness of the system to adapt and still deliver accurate dose to the target in such circumstances was readily assessed. Adopting the gamma analysis for dose comparison between planned and measured dose, we observed gamma passing of 97.8%, 95.4% and 98.2% for the N-Case, SP-Case, and CP-Case respectively. These results, although lower for the SP-Case would all be acceptable clinically and therefore with respect to the specific perturbation studied in this work, namely a sudden shift of 7.5mm from the baseline position

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of an otherwise sinusoidal target trajectory, one can state that the system is robust and adaptable to deliver the dose accurately.

The relatively lower gamma passing rate for the SP-Case compared with the N-Case or the CP-Case which is more evident as the gamma criteria are tightened (3%/2mm, 5%/1mm, 1%/1mm) can be explained by taking a closer look at Figures 2, 3, and 4 at how these are introduced. For the single simple perturbation, SP-Case, a one-sided and unrecoverable perturbation was introduced at mid-way of the 4-Pass BgRT, whereas for the CP-case, although it looked complex, the perturbation introduced earlier at the end of the first pass was immediately recoverable at the end of the second pass and the final perturbation was in the opposite direction as the first. One would therefore expect a worst gamma passing rate for the SP-Case which is what was observed and more evident as we tightened the gamma criteria.

The special case, SP-Case-Corrected, namely, interrupting treatment to correct an observed misalignment based on PET image displayed at the end of a pass is of practical clinical interest and it is important to explore this further. There are two main issues with this approach. First, the PET image is only displayed at the end of each pass therefore if the perturbation occurred at time (To) for a pass with duration (T), then by virtue of this process, a portion of the treatment (T-To) would have been delivered without the intended correction. Second, given that the displayed PET image is cumulative, for the perturbation to be visible on the pass image, To must be small compared with T. Nevertheless, although more time consuming and inefficient to the patient delivery process, the expectation was that this approach would be better or at least comparable with the SP-Case where the system corrected for the perturbation via the BgRT method of dose tracking. It turns out that it was not the case. The gamma passing for the SP-Case-Corrected was consistently lower than the gamma passing rate for the SP-Case where the system was uninterrupted. The observed reduction was 1.1%, 1.6%, 4.2%, and 7.4% based on a 10% dose threshold and the gamma criteria 3%/2mm, 3%/3mm, 5%/1mm, and 1%/1mm respectively. Although more studies are needed before any definite conclusions can be made, this single study suggests that it is better to leave the system uninterrupted when the perturbations occur.

We used a gamma criterion of 3%/3mm and a 10% dose threshold to base our clinical acceptability of these scenarios. We underscore that we would still deem all the cases acceptable if we used the tighter criterion 3%/2mm based on the American Association of Physicist in medicine task group number 218 (AAPM TG-218) [15]. The AAPM task group report is based on patient specific QA on a static phantom and considers 95% as a tolerance limit for passing with 90% as the action limit. The phantom deliveries in this work were more involved as it included dose delivery on a moving phantom. Even then, the gamma passing in each case was above the action limit.

5. Conclusions

A phantom investigation of the robustness and adaptability of the novel RefleXion X1 SCINTIX™ system to perturbations introduced by unplanned non-periodic shift to an otherwise periodic target trajectory when delivering a 4-Pass BgRT was presented. By comparing the dose delivered under a normal periodic sinusoidal tumor motion to the dose delivered under a perturbed sinusoidal delivery, with a simple perturbation introduced at the end of the second pass of a 4-Pass BgRT delivery and a more complex situation with perturbation introduced at each of the four passes of a 4-Pass BgRT delivery, we observed acceptable gamma passing rates, greater than 95% gamma passing rate in each scenario based on 10% dose threshold and 3%/3mm criteria thus suggesting that the system is robust and adaptable to deliver the correct dose under such perturbations. This was based on a specific programmed perturbation of 7.5mm shift of the average target position from baseline in the superior/inferior direction of an otherwise periodic trajectory. More work needs to be done to include additional scenarios of perturbation before a general conclusion can be made.

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