

Evaluating Treatment Delivery Performance of SCINTIX Biology-guided Radiotherapy under non-periodic In-treatment Motions

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Abstract The RefleXion SCINTIX system uniquely enables novel biology-guided radiotherapy (BgRT), providing real-time treatment guidance via on-board positron emission tomography (PET). By directly targeting tumor response via PET, SCINTIX has the potential to substantially enhance the accuracy and efficacy of radiotherapy. This technology was only recently released for clinical usage, however, so its performance when dealing with in-treatment patient motion has not been fully explored. In this paper we report a novel study to investigate the performance of SCINTIX under discrete motions using an in-house developed fluorodeoxyglucose phantom. Ion chamber and film were used to measure point dose and 2D dose, respectively, under various scenarios of different discrete motions. The results show good agreement between delivered dose and planned dose, illustrating the efficacy of SCINTIX in resolving discrete motions during treatment delivery.

1 Introduction

SCINTIX radiotherapy (RT), uniquely enabled on the RefleXion X1 RT system (RefleXion Medical Inc, Hayward, CA), is the first commercially available biology-guided radiotherapy (BgRT) treatment platform [1]. It innovatively integrates a ring-gantry LINAC with a positron emission tomography (PET) scanner to provide functional guidance for treatment delivery. With recent FDA clearance for lung and bone cancer treatment, SCINTIX offers great potential to substantially improve the treatment precision and efficacy by adjusting beam fluence based on the PET signal which is updated every 100 milliseconds during beam delivery [2, 3].

To ensure the safe integration of SCINTIX into clinical practice and maximize its potential benefits, it is imperative to thoroughly assess its performance across a diverse range of motion scenarios. This presents a distinctive commissioning challenge. Generally speaking, in-treatment patient motion can be categorized into two main types: discrete non-periodic motion (such as sudden voluntary or involuntary movements) and continuous periodic motion (such as respiratory motion). These motions may occur independently or concurrently during treatment, adding further complexity to the evaluation process. In this paper we focused on investigating the impact of various discrete motions during treatment delivery.

2 Materials and Methods

2.1. Phantom design and fabrication

To assess SCINTIX delivery robustness against in-treatment motions, we developed an in-house fluorodeoxyglucose (FDG) phantom (Fig. 1). Our objective was to fabricate a phantom capable of holding FDG solutions of varying concentrations to simulate realistic FDG distribution within a patient's body. Specifically, the

phantom features a dome-shaped volume for holding FDG, representing the PET-avid treatment target, atop an insert that installs inside a cylindrical water-filled phantom. Additionally, this cylindrical phantom can be filled with FDG at a comparatively lower concentration to simulate surrounding normal tissues in a patient. As highlighted in Fig.1, the insert was designed to also hold a custom-sized Gafchromic EBT3 film for 2D dose measurement. A chamber holder accommodating an Exradin A14SL chamber (Standard Imaging, Inc, Middleton, WI) was also included to facilitate precise point dose measurement.

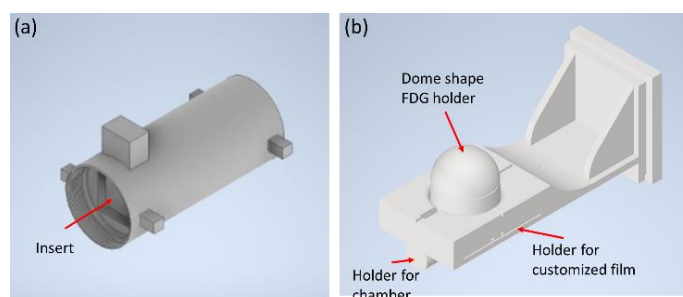


Figure 1. (a) In-house developed FDG phantom. (b) Detailed design for the insert with FDG, film, and chamber holders.

2.2 SCINTIX test plan development

We conducted our motion studies using the aforementioned in-house phantom. To evaluate the dosimetric impact of discrete motions during SCINTIX delivery, two plans were developed for ion chamber (IC) and film measurements, respectively. Specifically, a planning CT scan of the phantom was acquired on our clinical CT simulator with 1 mm in-plane resolution and 2 mm slice thickness. As shown in Fig. 2, the dome-shaped FDG holder was contoured to be the gross tumor volume (GTV) for both plans. Different expansions were then applied to the GTV to create two planning target volumes (PTVs) for the respective IC and film measurements. Note that relatively larger inferior expansions were applied to generate the PTV for the IC plan to ensure the active volume of the chamber remained within the PTV. The biological tracking zone (BTZ), a unique conceptual structure required by SCINTIX planning and treatment, was generated via a uniform expansion of 1 cm from the chamber PTV. The purpose of the BTZ is to filter the real-time PET signal for efficient data processing during treatment delivery. It is required that the PTV always stay within the BTZ during treatment delivery. Note that this BTZ generated from the IC PTV served as the BTZ for both plans since it is sufficiently large for both PTVs. In addition, two cylindrical

pseudo organs at risk (OARs) were contoured anterior and posterior left of the PTVs to make the test plan more realistic.

Prior to initiating SCINTIX planning, an on-board PET image must also be acquired on the RefleXion treatment unit. This PET image is then back-projected to the beam's eye view for each beam angle and convolved with some kernels referred to as “firing filters” to generate fluence maps. The inverse planning process is essentially the optimization process for these firing filters. In our experiment, the in-house phantom was filled with FDG at a target-to-background activity-per-unit-volume ratio of 8:1 for the pre-planning PET scan. This resulted in a target activity of approximately 150 kBq/ml for the preplan PET image, which was subsequently utilized as the planning PET for generating both ion chamber (IC) and film plans. The same experimental setup was maintained across all treatment deliveries.

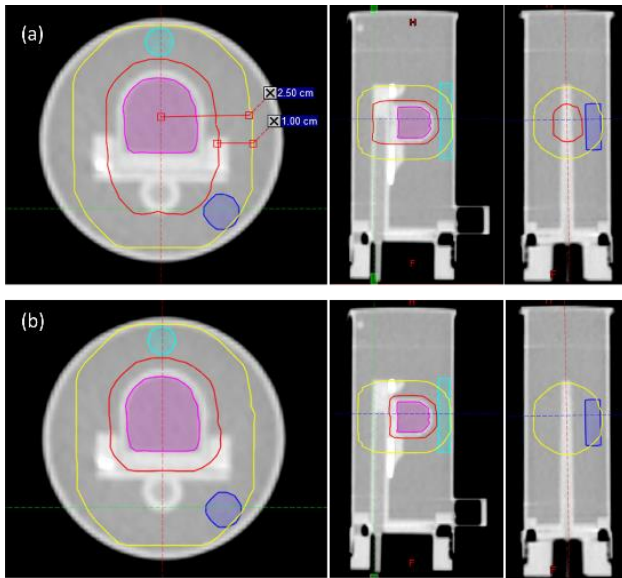


Figure 2. Three views of the planning CT of the in-house phantom for (a) the IC plan and (b) the film plan. Planning structures include the GTV (purple), PTVs (red), BTZ (yellow), and OARs (blue and cyan).

The prescription (Rx) dose to PTV for both plans was set to 100 Gy in 10 fractions with maximal dose objective set as $D_{max} \leq 105\%$ of Rx dose. For film plan we considered both OARs and the planning goals were set as $D_{max} \leq 70$ Gy for the anterior OAR and 80 Gy for the posterior left OAR. In contrast, for the IC plan only the anterior OAR was taken into account in the planning process, with an associated planning objective of $D_{max} \leq 50$ Gy. Snapshots of the dose distributions of the optimized plans are shown in Fig 3. Note that both plans were generated for the purpose of evaluating delivery quality of SCINTIX under different discrete motions, so plan quality was not a major focus.

2.3. Static motion delivery setup

We started the test by verifying point dose accuracy with the IC plan. Specifically, measurements under four

different scenarios in the plan delivery were carried out. In the first scenario, the phantom was held still after being set up to the treatment position via the on-board fan beam CT. This was to mimic BgRT delivery without any in-treatment motion. One or multiple shifts of magnitude of 0.5 cm were then applied to the phantom during treatment delivery as the second scenario. Note that the PTV was still well within the BTZ after applying these shifts. This test aimed to evaluate system performance when abrupt voluntary or involuntary movements of the patient occur during treatment delivery.

The third scenario involved shifting the phantom laterally by 2.5 cm during treatment. This was to mimic relatively larger abrupt in-treatment shifts of the patient. In this case, half of the PTV ended up outside of the BTZ, since the lateral dimension of the BTZ was 5 cm. We wanted to test if the machine could identify this issue and stop delivering dose. If the system did stop treatment, the phantom would be set up again to resume delivery, and the overall dose measured would be compared to the planned dose.

For the fourth scenario, we applied an even larger lateral shift of 4 cm during delivery so that the PTV was moved completely outside of the BTZ. This was to further understand the performance of SCINTIX plan delivery under extreme circumstances of very large shift. Similar to the third scenario, if the treatment system could identify this large motion and stop treatment delivery, we would set the phantom up to the planned treatment position again to resume treatment and compare the overall dose with the planned dose.

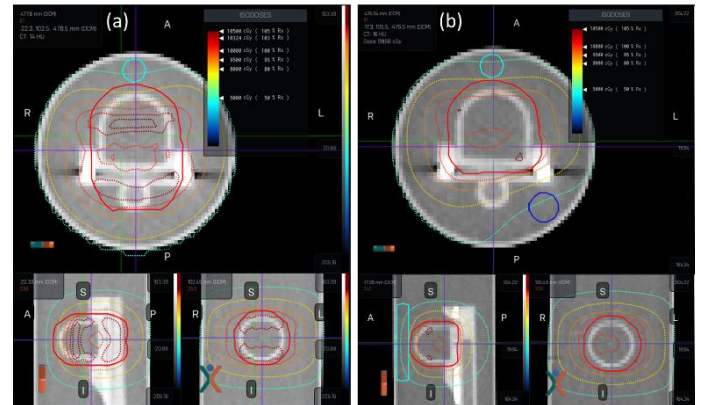


Figure 3. Snapshots of the dose distributions of the optimized (a) IC plan and (b) film plan.

The film plan was then delivered under the aforementioned second and third scenarios to further investigate 2D dose distributions for SCINTIX treatment delivery under discrete motions. We chose these two scenarios as opposed to the fourth one since they are more clinically relevant. Note that the detailed experimental setup, including the directions and magnitudes of the shifts during treatment delivery, was configured to be identical to that used in the IC plan experiments.

3 Results

3.1. Results of IC plan delivery

The point dose measured for the first scenario without in-treatment motion differed by -1.4% compared to the planned dose, illustrating the accuracy of SCINTIX treatment delivery for a static target.

For the second scenario, the phantom was shifted twice at different time points during a single treatment delivery. Specifically, the first shift was lateral, of magnitude 0.5 cm to patient left, when 25% of plan had been delivered. The second shift was superior by 0.5 cm, when 50% of the plan had been delivered. Note that the PTV remained within the BTZ defined in planning stage after these two shifts were executed. The measured point dose was ~0.6% lower than that of the static delivery (i.e. ~2% lower compared to the planned dose). These results indicate the satisfactory tracking capability of SCINTIX in terms of handling abrupt shifts of target within BTZ.

In the third scenario, we shifted the phantom by 2.5cm laterally to patient left when 25% of planned dose had been delivered. The system continued delivering beam until it reached ~35% of plan delivery, at which point an interlock was triggered due to missing target signal in BTZ. After re-setup, we were able to complete the partial delivery and the measured dose was ~4.7% higher than the static delivery (~3.3% higher than planned dose). Based on this test, SCINTIX system was able to detect a large shift and pause the delivery after part of the PTV had moved outside of the BTZ. However, the system response was not instantaneous. Close monitoring for large patient shifts by the treatment team would still be recommended.

We then performed a larger shift of 4cm during delivery to move the PTV completely out of BTZ after 25% of the plan had been delivered. The system suspended treatment after delivering another ~3% of MUs. We then re-set the phantom up and continued the plan delivery till completion. The resulting dose measured was 5% higher than the baseline from the static delivery (~3.5% higher than the planned dose). Compared to the partial-in/partial-out PTV scenario in the previous test, moving the PTV completely out of the BTZ triggered a swifter response of the SCINTIX system. However, the dosimetry results was similar. The experimental setups and the quantitative results of the IC plan are summarized in Table 1.

3.1. Results of film plan delivery

The first film test was carried out using same phantom shifts performed for the second scenario in the IC plan study. The results can be found in Fig. 4 (a). The measured dose generally agreed with the planned dose within 5% of difference according to the line profiles. A relative large decrease in measured dose can be observed in the left side of the horizontal profile. That area is close to the cutting edge of the customized film and hence may introduce a large uncertainty in measurement.

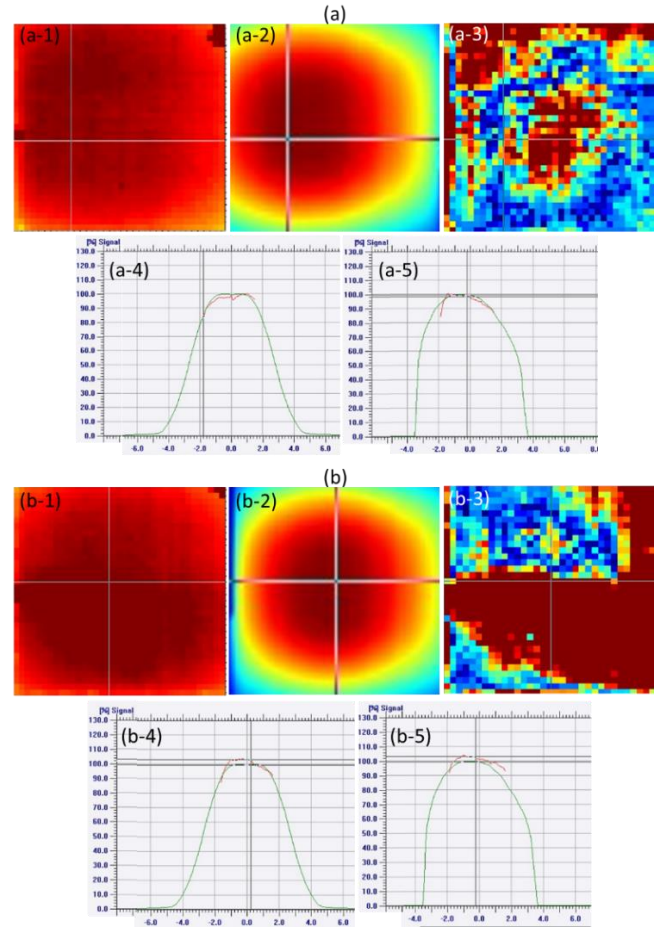


Figure 4. Film analysis results. (a): Two-step shifts with 0.5cm magnitude for each. (b): 2.5cm lateral shift. (a-1) and (b-1): scanned films; (a-2) and (b-2): planned dose; (a-3) and (b-3): gamma analysis (2%/2mm); (a-4) and (b-4): vertical line profile comparisons, (a-5) and (b-5) horizontal line profile comparisons (red: measured, green: planned).

Another film test was conducted with a 2.5 cm lateral shift applied during the treatment, identical to that used in the third scenario of the IC plan tests. The film results have revealed that SCINTIX overdelivered to the target which agrees with the behavior observed in point dose measurement. Similar to the previous film experiment, the measure dose and the planned dose generally match within 5% of difference, although 2D gamma analysis [4, 5] with 2%/2mm shows a relatively large discrepancy. It is also worth mentioning that gamma analysis is not recommended as the evaluation metric for SCINTIX delivery due to the stochastic nature of the PET signals.

4 Discussion

Based on our experimental results, the SCINTIX RT system is capable of recognizing and responding to discrete in-treatment motions. The dose delivery remained accurate for relatively small motions as long as the PTV was still within the BTZ, as evidenced by both point dose (0.6% compared to static delivery and 2% compared to planned dose) and film measurements (well-matched line profiles). When larger motions occurred, moving some or all of the

PTV outside of the BTZ, the SCINTIX system was able to detect the motion and stop the treatment. However, the system did not terminate delivery immediately after the shifts, revealing a continued need for close monitoring of patient movement by the treatment team during SCINTIX treatments. Once delivery had been stopped due to large motions, the system was able to resume treatment after we re-set up the phantom. The point dose measurements differed by 3.2% and 3.5%, respectively, for lateral shifts of 2.5cm (PTV half in/half out of BTZ) and 4cm (PTV completely out of BTZ).

This study only considered relatively simple discrete motions. What could actually happen during treatment could be more complicated than what we have considered here. For instance, in lung cancer treatments continuous periodic motion becomes the major concern. For patients with irregular breathing, abrupt changes in motion magnitude and/or pattern could also occur on top of the periodic respiratory motion. These problems are more challenging and will require further investigations. The study reported here helps us to better understand the behaviors of SCINTIX when discrete movements occur during treatments, and thus lays a solid foundation for future studies on more complex motion patterns.

The gamma analysis results in Fig. 4 depict the difference between measured and planned dose, but this is not recommended for SCINTIX testing. Note that the fluence maps for SCINTIX plan delivery are computed by convolving the back-projected PET signal acquired during treatment with the firing filters optimized on the pre-planning PET. Due to the stochastic nature of the PET signal, the delivered dose will always be different from what was planned. Therefore gamma analysis may not serve the purpose of evaluating plan delivery quality as well as it does for conventional RT. More research is needed to develop a proper metric for 2D dosimetric evaluation of SCINTIX plan delivery quality.

5 Conclusion

We have successfully conducted a discrete motion study to evaluate the performance of SCINTIX RT delivery using an in-house-developed FDG phantom. The results illustrate the efficacy of SCINTIX in recognizing and responding to discrete in-treatment motions to achieve robust delivery.

References

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Motion info		Difference to static	Difference to plan
Scenario 1	NA	NA	-1.46%
Scenario 2	0.5cm to left @ 25% of delivery; 0.5cm superiorly @ 50% of delivery	-0.6%	-2.0%
Scenario 3	2.5 cm to left @ 25% of delivery	4.7%	3.3%
Scenario 4	4cm to left @ 25% of delivery	5.0%	3.6%

Table 1. Summary of point dose measurement results