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3D-Printed Linear Compensator Array-Enabled Automated Treatment Planning System for High-Throughput Small Animal Intensity-Modulated Radiation Therapy

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ABSTRACT

PURPOSE: High throughput small animal IMRT studies are currently impractical because of the time it takes to treat one subject (>2 hours), due to manual organ contouring, computationally expensive dose calculation algorithms, and long treatments which are often overly complex for the radiobiologist to complete without a physicist present. Presented is a user-friendly automated treatment planning system (TPS) with 3D-printed linear compensator arrays (LCA) for accelerated treatment delivery times, providing accurate and efficient preclinical SA-IMRT that matches the clinical IMRT workflow.

METHODS: Improved time-to-treatment efficiency by integrating deep learning-enabled automated organ contouring; GPU-accelerated, 1mm^2 square beamlet kernel-based kV-photon dose calculation algorithm for heterogenous media; and beamlet intensity total variation regularization (TVR) optimization for reduced complexity in Tungsten-doped PLA 3D-printed LCA. The LCA track mechanism provides automated intra-treatment field changeability. Verification of the dose engine was done with both SA irradiator commissioning data and a well-verified Monte Carlo model used to create the square beamlet kernels for all relevant materials.

RESULTS: For a simulated 5-field mouse heart toxicity IMRT plan, workflow was timed and evaluated: CBCT scan (~2 min), auto-contouring (~2 sec), dose and fluence optimization (~1 min), 3D-printing (~10 min), and treatment (~10 min), for a total treatment time of <25 minutes. Planning target volume coverage is reported: $V_{50\%,Rx}$ = 99.5%, $V_{95\%,Rx}$ = 93%, and $V_{100\%,Rx}$ = 72.5%. Organ-at-risk minimum sparing (Left Lung) was $V_{50\%,Rx}$ = 15.5%, $V_{95\%,Rx}$ = 1.1%, and $V_{100\%,Rx}$ = 0.9%. Initial phantom-imbedded Gafchromic film measurement and gamma analysis show consistent passing rates >85% for strict 3%/0.3mm conditions.

CONCLUSION: This LCA-enabled automated TPS designed for high-throughput SA-IMRT enables relatively inexpensive, large-scale, precise preclinical results that can directly translate and improve clinical outcomes and experimental therapies.

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INTRODUCTION

- Modern clinical RT relies on highly conformal intensity-modulated techniques (IMRT/VMAT)
- Preclinical work is limited to simple square or circular treatment fields that do not accurately mimic clinical treatments
- Existing small animal IMRT approaches make great strides to improve dosimetric accuracy, but remain impractical due to complex workflows, manual compensator exchanges, and long treatment times.[1,2]
- We present a fully-automated small animal IMRT TPS that achieves clinically relevant small animal IMRT with treatment times under 25 minutes per mouse.

METHODS & MATERIAL

The automated small animal IMRT TPS uses the SmART+ irradiator for for the following treatment process:

- CBCT of subject
- Imported into organ auto-contouring U-Net-like model for organ segmentation shown in **FIGURE 1**
- Superfast square micro beamlet MC-simulated multi-energy and multi-material kernel-based kV photon dose calculation algorithm
- Dose engine verification by PDD analysis in multi-material slab phantom example shown in **FIGURE 2**
- TVR-optimized fluence and thickness maps and production of DVH curves shown in **FIGURE 3**
- 3D printing aligned thickness maps into LCAs with Tungsten-doped Polylactic Acid (WPLA)
- Pre-treatment alignment QA using flat panel detector in fluoro mode
- During gantry rotation the LCA is driven linearly along the collimator opening to the next field in the IMRT plan
  - A simplified image depicting this process along with a CAD of the full in-house designed collimator aperture is shown in **FIGURE 4**

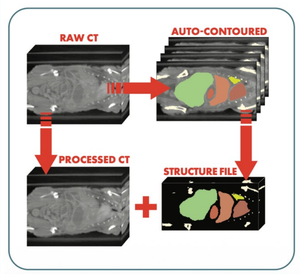

FIGURE 1. *Auto-contouring process from raw 3D CT file (top left) to auto-contoured coronal slices (top right), producing two inputs for the TPS: 3D processed CT file (bottom left) and a 3D structure file (bottom right).*

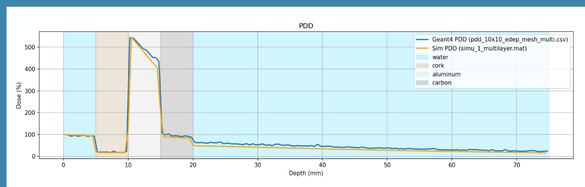

FIGURE 2. *Geant4 versus kernel-based python simulations for percent depth dose (PDD) of phantom containing slabs of water, cork, aluminum, and carbon to mimic the heterogenous material qualities of mice (with correction factors applied).*

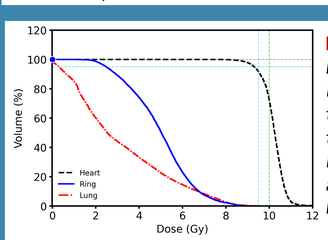

FIGURE 3. *Dose-volume histogram (DVH) curves for Heart Toxicity IMRT treatment plan. Black line is the heart (target), red is the lung (OAR), and artificial ring around the heart shown in blue.*

RESULTS

Presented are initial gamma results from a film embedded in a 2cm thick Virtual Water® Phantom with all fields positioned at gantry position 0 degrees:

- Set-up in the SmART+ is shown in **FIGURE 5**
- Pretreatment alignment QA showed great agreement with planned fluence maps, shown in **FIGURE 6**
- Mean gamma passing rate for all fields: 92.04% at 3%/0.5mm and 82.85% at 3%/0.3mm – example gamma analysis shown in **FIGURE 7**
- Efficiency of the whole process was simulated, shown in **FIGURE 8**

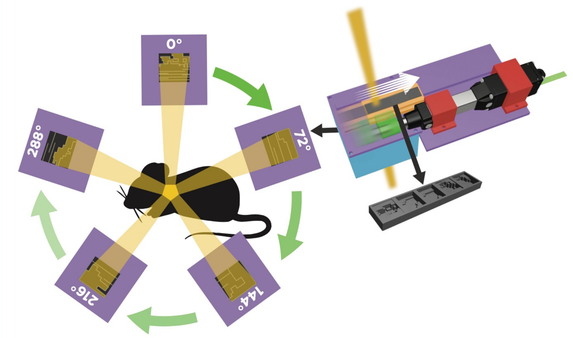

FIGURE 4. *Simplified CAD model of automated collimator exchange system. Blue box structure is secured to a 10mm^2 collimator. Purple platform is secured to the blue box and contains the linear actuator and the track system for the LCA (shown in gray) to be shuttled along the collimator opening during each gantry rotation.*

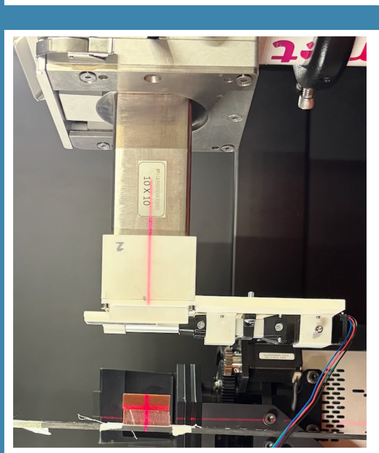

FIGURE 5. *Picture of the automated compensator switching prototype in the SmART+ machine connected to the Arduino control unit.*

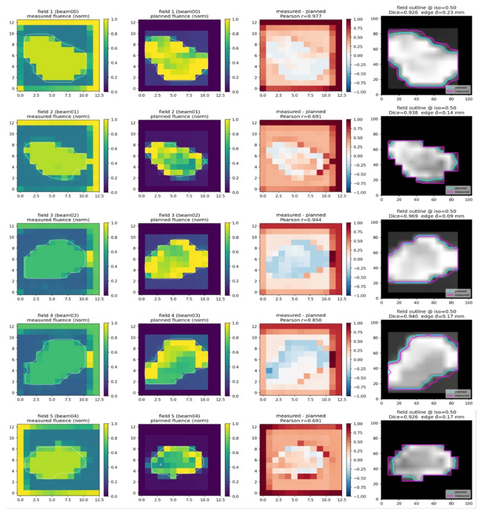

FIGURE 6. *Pretreatment alignment QA results for sample 5-beam angle mouse heart toxicity treatment plan. All 5 compensators were positioned and imaged to ensure alignment with planned fluence maps.*

DISCUSSION

- The automated small animal IMRT TPS provided accurate and efficient highly-conformal clinically relevant treatment fields at 5 gantry angles in under 25 minutes per mouse
- Most error stems from 3D-printing issues, as this work was done with a new filament spool, so the printing settings have yet to be optimized for that spool
- Treatment process was easy-to-follow and easy-to-execute
- To ensure rigor and reproducibility, the SmART+ irradiator undergoes routine QA procedures

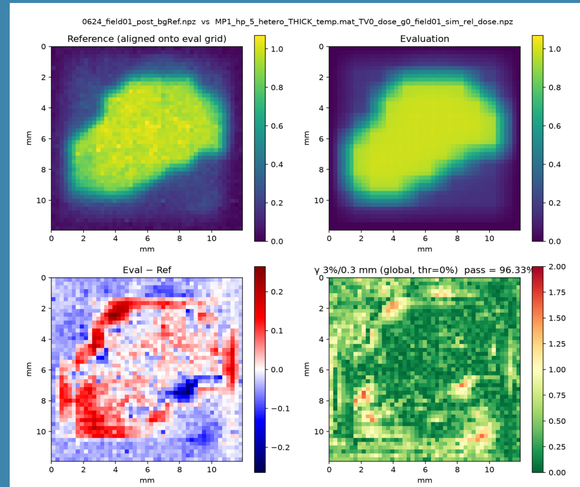

FIGURE 7. *Gamma analysis for field 1 (gantry angle is 0 degrees) for a 10Gy heart toxicity mouse IMRT treatment plan. The reference film measured relative dose distribution is shown on the top left. The top right is the python simulated relative dose-distribution. As shown, under strict dose-to-distance agreement of 3%/0.3mm, a passing rate of 96.33% was accomplished.*

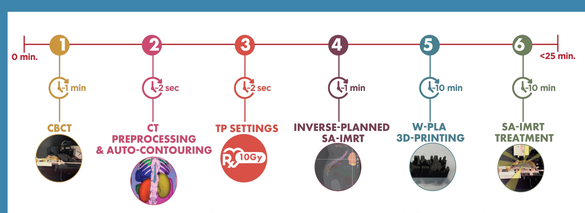

FIGURE 8. *Timeline of the SA-IMRT TPS workflow and estimated completion times.*

CONCLUSION

This LCA-enabled small animal IMRT TPS narrows the gap between clinical and preclinical RT, enabling high-throughput highly statistically significant small animal RT studies. Once the optimal 3D-printer settings are applied to the WPLA filament we can continue with a full end-to-end treatment simulation, performing gamma analysis at each gantry angle as well as a composite analysis. In the future, we hope to implement beam angle optimization, reuse of old WPLA compensators, and VMAT implementation where the treatment beam is active throughout gantry rotation LCA movement.

REFERENCES

1. Brown, K. H. et al. A scoping review of small animal image-guided radiotherapy research: Advances, impact and future opportunities in translational radiobiology. Clin. Transl. Radiat. Oncol. 34, 112–119 (2022).
2. Ghita, M., Brown, K. H., Kelada, O. J., Graves, E. E. & Butterworth, K. T. Integrating Small Animal Irradiators with Functional Imaging for Advanced Preclinical Radiotherapy Research. Cancers 11, 170 (2019).