Out-of-field organ dose reconstruction for pediatric patients undergoing proton therapy

Keith T. Griffin[1,2], Jungwook Shin[1], Matthew M. Mille[1], Yeon Soo Yeom[3], Choonik Lee[4], Jae Won Jung[5], Nolan E. Hertel[2], and Choonsik Lee[1]

[1]Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Rockville, MD, 20850, USA
[2]George W. Woodruff School of Mechanical Engineering, Georgia Institute of Technology, Atlanta, GA, 30318, USA
[3]Department of Radiation Convergence Engineering, Yonsei University, Wonju, South Korea
[4]Department of Radiation Oncology, University of Michigan, Ann Arbor, MI, 48109, USA
[5]Department of Physics, East Carolina University, Greenville, NC, 27858, USA

Purpose: Although there has been exponential growth in proton therapy centers operating around the world, large-scale observational studies on the benefits or risks to these patients have yet to be realized.[1] Current clinical decisions on when proton therapy may be an appropriate treatment modality versus more traditional photon therapy are based on indirect modelling studies. To address this need, the National Cancer Institute (NCI) and Massachusetts General Hospital (MGH) have collaboratively established a record-linkage cohort of pediatric radiotherapy patients. Electronic radiotherapy records of 10,000 proton patients (5,000 passive scattering and 5,000 pencil beam scanning) and 10,000 photon patients treated between 2007 and 2022 are currently being collected. Retrospective dosimetry of normal tissues in these patients will allow for in-depth studies of therapy-related risks in relation to organ-specific doses. The purpose of the current work is to establish groundwork methodology for calculating normal tissue doses using full Monte Carlo (MC) simulation for a subset of passive scattering patients treated at MGH.

While MC methods are considered the gold-standard approach for out-of-field dose estimation, the physics modelling of secondary particle production from high-energy interactions of the beamline is uncertain; various models exist to reenact these interactions. This work will also investigate uncertainties in out-of-field dosimetry in proton therapy simulations due to physics modelling differences.

Methods: The passive scattering dosimetry performed in this work employed the Ion Beam Applications (IBA) beamline model developed at MGH.[2] This beamline was adapted to work in a new environment on the National Institutes of Health's supercomputer, Biowulf (hpc.nih.gov), as shown in Figure 1. An initial round of 13 passive scattering patients were transferred to NCI. Monte Carlo simulation of the patient treatment plan was performed using TOPAS code in two steps: collection of particle history information at the exit of the beamline nozzle (via phase space surface); and simulation of the phase space as a source term onto the patient anatomy. Separation of the problem into two steps allowed reuse of the phase space data to improve code runtime.

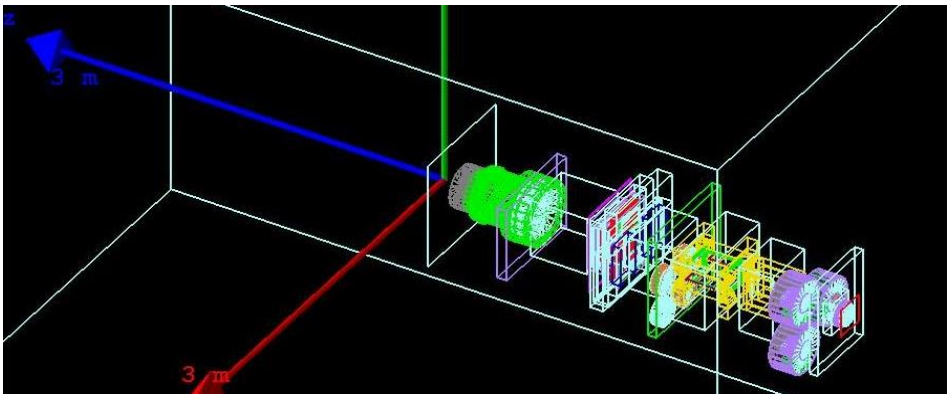

Figure 1. Visualization of the MGH IBA passive scattering beamline model within TOPAS, as configured for one pediatric cohort member

A workflow was built to automatically generate TOPAS input files for both simulation steps for a given patient. Patient anatomy was used when available; in cases where patient CT anatomy was limited, an in-house code was used to extend partial-body into whole-body anatomy using a computational phantom.[3] Neutron, gamma, and total dose maps for the patient were estimated, from which out-of-field organ doses and dose-volume histograms were calculated.

To investigate secondary dose uncertainties in pencil beam scanning proton therapy, the results from three MC simulation codes (MCNP6, PHITS, and TOPAS) were compared with developer-recommended physics settings using a simplified proton pencil beam. Total yield and double-differential (energy and angle) production of neutrons and gammas were determined at six proton energies. Out-of-field tissue doses were estimated for intracranial pencil beam scanning proton treatments of 1-, 5-, and 15-year-old patients using whole-body computational phantoms and a previously published kernel method.[4]

Results: The MC dose estimates and treatment planning system (TPS) reported doses for several out-of-field organs, as shown for one patient in Table 1 and Figure 2, demonstrated that the TPS does not perform well in dosimetry beyond a short distance from the treatment field; dose estimates for near-field organs such as the thyroid and further out-of-field organs such as the lungs benefited from a more detailed MC treatment, as the TPS significantly underestimated these doses. The first round of dose reconstruction for 13 passive scattering patients has been completed along with an automated workflow designed to assist future dosimetry efforts.

Across the studied physics packages, the estimated neutron yield per source proton varied between 15-20%. At all six proton beam energies, TOPAS produced the greatest number of neutrons and the second highest mean neutron energy; as seen in Figure 3, this translated into TOPAS estimating the highest out-of-field organ doses for an intracranial pencil beam scanning treatment. Notably, the range in total secondary dose remained roughly constant (at about 25%) across the codes for all out-of-field organs in the three pencil beam scanning patients.

Table 1. Comparison of D50 values (mean dose to 50% of the tissue volume) between treatment planning system (TPS) and Monte Carlo (MC) estimates for seven normal tissues of one patient treated via passive scattering craniospinal irradiation.

	D50 (cGy)	
Normal tissue	TPS	MC
Thyroid	161	173
Right kidney	8	50
Left kidney	< 1	44
Left lung	< 1	23
Right lung	< 1	22
Heart	< 1	4
Urinary bladder	< 1	2

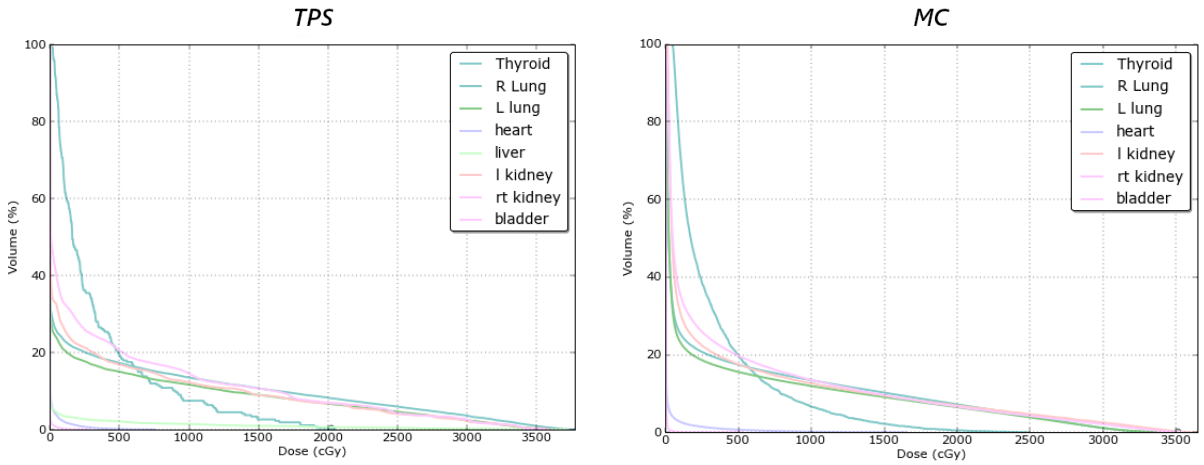

Figure 2: Dose volume histograms of the normal tissues of Table 1, as generated by the treatment planning system (TPS) at MGH (left) and Monte Carlo (MC) simulation of this work (right).

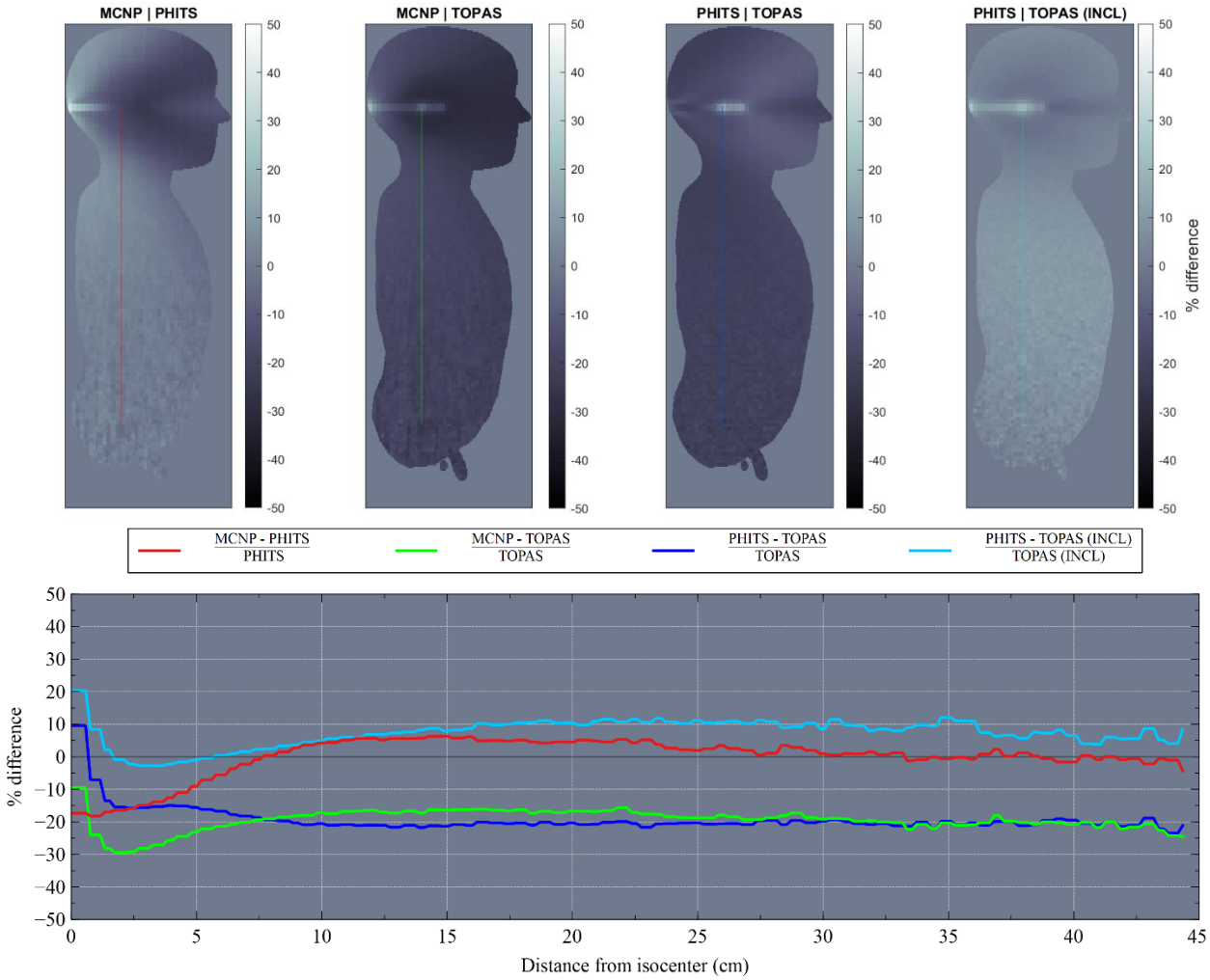

Figure 3. (Top) Percent difference maps comparing the secondary dose distributions as calculated by three MC codes (using developer-recommended physics settings) for the pencil beam scanning intracranial irradiation of a 5-year-old male patient. (Bottom) Plot of the percent differences as a function of inferior distance from the isocenter (down the drawn lines). Results are also shown for TOPAS when using the Liège Intranuclear Cascade (INCL) physics package.

Conclusions: This work has established an automated workflow to generate out-of-field dose estimates for passive scattering patients treated at MGH. Additionally, this study has quantified current uncertainties in out-of-field dose estimates due to high-energy cross-section limitations in proton therapy simulations; these uncertainties may be implemented in future dose response analyses. The automated workflow constructed by this study will be applied to cohort members treated via the passive scattering modality at MGH. Future work will utilize this research to create a more generic model that is applicable to patients at other institutions for whom no beamline model exists.

Relevance to CIRMS: Individualized dose estimates from this work will provide beneficial data to epidemiologists that can improve our current understanding of radiation-related risks to healthy tissues, including key evidence on the relative biological effectiveness of neutrons in humans. Additionally, the data capture on secondary production across multiple MC codes has helped benchmark current uncertainties in this area. The first author plans to continue medical physics and environmental dosimetry research in a government setting following the completion of his doctoral degree.

References:

1. Journy N., et al. 2018 Patterns of proton therapy use in pediatric cancer management in 2016: An international survey. *Radiotherapy and Oncology*.
2. Paganetti H, Jiang H, Lee S Y and Kooy H M 2004 Accurate Monte Carlo simulations for nozzle design, commissioning and quality assurance for a proton radiation therapy facility. *Medical physics*.
3. Kuzmin G. A., Mille M. M., Jung J. W., Lee C., Pelletier C., Akabani G. and Lee C. 2018 A Novel Method to Extend a Partial-Body CT for the Reconstruction of Dose to Organs beyond the Scan Range. *Radiation Research*.
4. Yeom Y. S., Griffin K. T., Mille M., Jung J. W., Lee C. and Lee C. 2020 A dose voxel kernel method for rapid reconstruction of out-of-field neutron dose of patients in pencil beam scanning (PBS) proton therapy. *Phys. Med. Biol.*