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Impact of Nuclear Halo Modeling on Secondary Cancer Risk Estimates in Proton Craniospinal Irradiation

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ABSTRACT

To quantify the impact of proton dose calculation methodology, including nuclear halo contributions, on secondary cancer risk for near-field organs following proton craniospinal irradiation.

Lifetime attributable risk at age 70 (LAR_{70}) for lung and kidney was estimated in nineteen patients treated with proton pencil beam scanning using three dose calculation approaches: an analytical algorithm with simple halo correction (AA), TOPAS Monte Carlo simulation with constant relative biological effectiveness (MC-1.1), and TOPAS Monte Carlo simulation incorporating a variable RBE model based on dose-averaged linear energy transfer (MC-LETd). Lung LAR_{70} was estimated using a BEIR VII–based framework with organ equivalent dose, while kidney LAR_{70} was estimated using the RadRAT kidney model based on mean organ dose. For each patient, LAR_{70} estimates and relative differences for MC-1.1 and MC-LETd were calculated with respect to AA.

Compared with AA, Monte Carlo–based dose calculations resulted in higher estimated lifetime attributable risk at age 70 (LAR_{70}) for both lung and kidney. For lung cancer, LAR_{70} increased from 1.07% (95% CI: 0.84–1.29) with AA to 1.28% (1.02–1.54) using MC-1.1 and 1.35% (1.08–1.61) using MC-LETd, corresponding to relative increases of 21.7% (17.8–25.6) and 28.9% (23.9–33.9), respectively. Kidney cancer LAR_{70} increased from 0.41% (0.21–0.62) with AA to 0.46% (0.24–0.68) with MC-1.1 and 0.50% (0.27–0.74) with MC-LETd, corresponding to relative increases of 24.2% (11.5–36.9) and 40.5% (23.5–57.5). Across both organs, MC-LETd yielded the highest risk estimates, due to the elevated dose-averaged LET (>2 keV/μm) near the field edge.

The findings highlight the importance of accurately characterizing dose in near-field organs when estimating secondary cancer risk. Increases in estimated risk for near-field organs were non-negligible, suggesting that Monte Carlo–based dose calculation may be important for secondary cancer risk assessment in proton craniospinal irradiation.

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INTRODUCTION

- Secondary cancer sites are found more in the near field than out-of-field
  - Approximately 66% of second malignancies following photon radiotherapy arose in beam-bordering regions, with a peak frequency observed in tissues receiving <2.5 Gy. (Diallo *et al.2009*)
- Factors impacting beam-bordering regions (Halo in Fig 1.) in proton therapy
  - Nuclear halo dose likely missing in the TPS dose
  - Dose-averaged LET (LETd) is increasing and potentially RBE > 1.1
  - Neutron contribution but small in the near-field

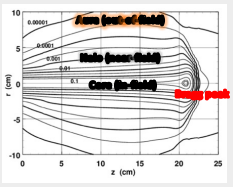

Figure 1. Dose scale as a

- the importance of accurately characterizing dose in near-field organs when estimating secondary cancer risk.

METHODS AND MATERIALS

Patient cohorts

- 18 MGH medulloblastoma patients by PBS treatment
- Male: 13, Female: 5
- Age 5 – 19 yrs
- Dose 21 Gy to 36 Gy
- Dose calculation
  - Monte Carlo: TOPAS/Geant4
  - TPS: Astroid (in-house) with halo approximation
- Target organs: Lung and Kidney

Risk models (Carcinoma)

- $MC_{1.1}$ with fixed RBE
  → $D_{RBE} = D_{phy} * 1.1$
- MC_{LETd} with LETd-based RBE by McMahon et al.
  → $D_{RBE} = D_{phy} * (1 + \kappa LETd)$, k = 0.055 um/keV
  (Meyer et al, 2024)

$$EAR(D,X,s,a) = OED(D)\,\beta_{EAR}\,(1+s)\,e^{\gamma_{e,EAR}H(A_X-X)\cdot(X-A_X)+\gamma_{a,EAR}\log\left(\frac{a}{A_a}\right)}$$

$$LAR_{A_e} = \int_{x}^{A_e} EAR(D,X,s,a=x)\,\frac{S(x)}{S(X)}\,dx$$

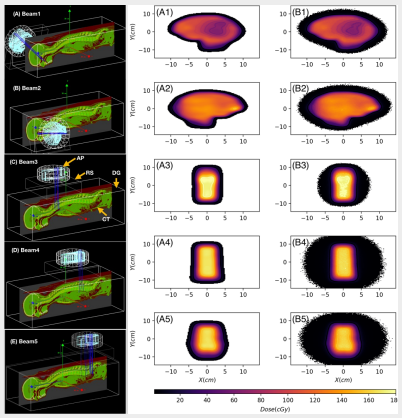

Figure 2. (A-E) Screen capture of TOPAS Monte Carlo simulation of medulloblastoma treatment (Shin et al. 2020). 2D dose distribution from TPS AA analytical dose calculation. (A1-A5) are planar dose distribution from TPS calculated by analytical algorithm (AA) and (B1-B5) are the those from TOPAS simulation.

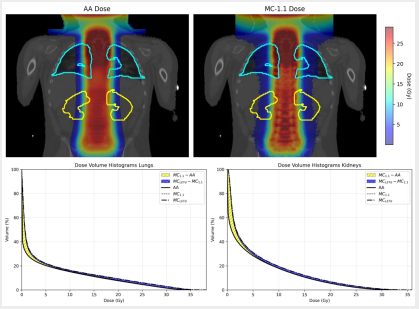

Figure 3. (upper) Plan dose comparisons between AA and MC-1.1 for kidney and lung. (bottom) DVH comparisons among AA, MC-1.1, and MC_{LETd}

Table 1. Summary of LAR for lung and kidney per dose models (all values are statistically significant: $p < 0.001$)

Organ (baseline risk ACS)		Dose model		
		TPS	$MC_{1.1}$	MC_{LETd}
Lung	D_{mean} (Gy)	2.46 [1.92-3.0] (0%)	2.8 [2.22-3.37] (+16.2%)	3.1 [2.47-3.72] (+29.2%)
M:5.8% F:5.6%	LAR_{70} (%)	1.07 [0.8-1.3] (0%)	1.28 [1.02-1.54] (+21.7%)	1.35 [1.08-1.61] (+24.2%)
Kidney	D_{mean} (Gy)	2.23 [1.31-3.15] (0%)	2.51 [1.54-3.48] (+24.2%)	2.76 [1.72-3.79] (+40.5%)
M:2.2% F:1.3%	LAR_{70} (%)	0.41 [0.2-0.6] (0%)	0.46 [0.24-0.68] (+28.9%)	0.5 [0.27-0.74](+40.5%)

RESULTS

- Dose distribution
  - TOPAS simulation results (Fig 2.)
  - Lung and Kidney dose from beam eye's view (Fig 3.)
  - DVH comparisons of Lung and Kidney among AA, MC1.1, and MC_{LETd}
- Relative risks of Lung and Kidney to baseline risks :
  - 18% and 23% from TPS,
  - 22% and 27% from $MC_{1.1}$ due to halo with < 5%* neutron
  - 24% and 30% from MC_{LETd} due to halo + RBE

DISCUSSION

- Increments of D_{mean} and LAR from MC models are substantial
  - up to 24% (Lung) and 40% (Kidney) w.r.t TPS dose
- 2.3 Gy to 3.1 Gy of D_{mean} in this study are closer to mean dose (2.5 Gy) to secondary malignancy neoplasm (SMN) (Diallo et al, 2009)
- Insufficient data to correlate near-field and SMN from proton CSI (Patteson et al, 2021)
  - SNM found a total of 8/178
  - 1 of 8 was found in penumbra region

CONCLUSIONS

2.3 Gy to 3.1 Gy of D_{mean} in this study are closer to mean dose (2.5 Gy) to secondary malignancy neoplasm (SMN) (Diallo et al, 2009)

The findings highlight the importance of accurately characterizing dose in near-field organs when estimating secondary cancer risk.
Increases in estimated risk for near-field organs were non-negligible, suggesting that Monte Carlo–based dose calculation may be important for secondary cancer risk assessment in proton craniospinal

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