

Purpose:

Pediatric patients are uniquely sensitive to radiation; thus there is specific interest in their risk for second cancers (SCs) following radiotherapy. However, because childhood cancer is rare and SC latency is long, current sample sizes are insufficient for clinical trials that compare advanced radiotherapy techniques. We propose a method to improve statistical power in micro-clinical trials, i.e., trials with small samples. Specifically, we use a more biologically relevant quantity, cancer equivalent dose (DCE), to estimate risk instead of mean absorbed dose. Our objective is to demonstrate that when DCE is used fewer subjects are needed for clinical trials.

Methods:

An in-silico, micro-clinical trial was performed to estimate risk of SC in the thyroid following pediatric cranio-spinal irradiations (CSI) with proton vs. photon radiotherapies. Dose reconstruction, risk models, and statistical analysis were used estimate SC risk from primary therapeutic radiation for 18 patients. Absorbed dose was calculated in two ways: with (1) traditional mean absorbed dose (DMA) and (2) DCE. DCE and DMA values were used to determine the estimated relative risk of SC incidence (ERR-DCE and ERR-DMA, respectively) for proton vs. photon CSI. Ratios of ERR values for proton vs. photon CSI (RRR-DCE and RRR-DMA) are then used in comparative power calculations to determine the smallest number of patients needed for 80% statistical power using DCE vs. DMA.

Results:

For all patients, we found that protons substantially reduced the risk of developing a second thyroid cancer when compared to photon therapy. Mean RRR±SD were 0.12±0.16 and 0.19±0.21 for RRR-DMA and RRR-DCE, respectively. Acceptable statistical power (i.e, 80%) was achieved for 18 patients in a preliminary power analysis utilizing DMA values.

Conclusions:

Preliminary results suggest that micro-clinical trials of SC incidence with <20 patients is possible. The DCE concept may further reduce the required patients (analysis in progress).

Funding Support, Disclosures, and Conflict of Interest:

A similar presentation of this work will be made at the ANS, American Nuclear Society meeting in June; the ANS presentation will be more preliminary and delivered to a different audience.