

The Correlation of Clinical Outcome and Radiobiological Modeling of Tumor Control Probability (TCP)

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Abstract

Objectives: Modeling of local TCP and NTCP in lung SBRT has demonstrated not only dependence upon biologically effective dose (BED) and tumor size, but also reliance on dose calculation algorithm utilized. Reported TCP and NTCP modeling has employed calculated dose based on non-Monte Carlo (MC) dose calculation algorithms. MC-based dose calculation algorithms such as X-ray Voxel Monte Carlo (XVMC) are more accurate modeling of dose deposition in heterogeneous media and have been routinely used in clinical practice for lung SBRT. We analyzed the correlation between clinical outcome and the predictive modeling of local TCP and NTCP in patients treated with SBRT using the XVMC dose calculation algorithm.

Methods: Clinical follow-up and treatment planning data from patients with with XVMC based-SBRT (6MV-SRS beams) were retrospectively analyzed. For TCP, we utilized previously defined size-adjusted biological effective dose (s-BED) modeling: $TCP = EXP [sBED - TCD50] / k \div (1.0 + EXP [sBED - TCD50] / k)$, where $k = 31Gy$ corresponding to $TCD50 = 0 Gy$, and s-BED is defined as $BED_{10} - 10 \times \text{tumor diameter (in centimeters)}$ by Ohri et al (IJROBP, 2012). The PTV prescription dose (sBED) and PTV D99 (the dose to 99% volume of PTV) (s-BED D99) were used as predictive parameters to generate 2-year TCP. Due to relatively shorter follow up, Kaplan Meier curves were generated via GraphPad Prism 6.0 software to estimate 2 year clinical tumor control rates to be compared to predicted rates with TCP modeling. Further comparison of clinical tumor control to TCP was stratified into groups according to primary vs. metastatic tumor origin, primary lung cancer histology, and location of tumor. For NTCP evaluation, we employed the Lyman NTCP Model utilizing normal lung and rib DVHs and α/β of 3Gy fitted to predict grade 2 radiation pneumonitis and rib fracture.

Results: 180 patients with 137 either primary lung (n=74) or metastatic lung (n=53) tumors were treated with XVMC based-SBRT (35-70 Gy, 3-10 fractions). Median follow up was 12 months. Overall clinical tumor control rate was 96%. Kaplan Meier generated 2- year clinical tumor control rate was 87.5%. The 2-year TCP (s-BED) and TCP (sBED D99) were $97\% \pm 2\%$ and $87\% \pm 8\%$, respectively, suggesting PTV D99 parameterization might be a more realistic method to predict clinical outcome than PTV prescribed dose. The 2-year clinical tumor control rate vs. predicted TCP (sBED D99) according to tumor site origin, location, and histology were the following: primary vs. metastasis were 94% vs. $88\% \pm 7\%$ and 79% vs. $86\% \pm 9\%$, respectively;

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central and peripheral tumors were 100% vs. $83\% \pm 9\%$ and $91\% \pm 9\%$, respectively; adenocarcinoma and squamous carcinoma were $87\% \pm 8\%$ and $100\% \pm 8\%$, respectively. Grade 2 pneumonitis was observed in 2% of patients with $3\% \pm 5\%$ predicted value of NTCP modeling. In a subset of patients ($n=21$) with peripheral tumors in close proximity to the chest wall, ribs fractures occurred in 9.5% of patients ($n=2$) with 12.6% predicted value of NTCP modeling.

Conclusions: Despite relatively shorter follow up interval, our TCP and NTCP results and associated clinical correlation are encouraging and yield validation to previously described predictive models. Furthermore, we present for consideration D99 as another potential predictive parameter in the TCP model for better correlation with clinical outcome. Longer follow up and confirmatory data are needed to validate our observations.