Implementation of Risk-Based Plan Evaluation and NTCP Estimation From Intermediate Dose Levels

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Introduction

- Three dimensional treatment planning allows for plan quality evaluation based on isodose distribution, differential and cumulative dose-volume histograms (DVHs) for organs-at-risk (OARs) and target structures.
- Guided mostly by partial organ tolerance doses this approach does not leverage normal tissue complication probability (NTCP) models that were created in an effort to correlate dose metrics to the probability for adverse effects. These NTCP models utilize DVH-reduction to parametrize the entire DVH curve in a single metric.
- Correlating the entire, or at least a larger portion of the dose distribution throughout an OAR with NTCP can be superior than cut point evaluation.

Materials and Methods

Utilizing the Varian Eclipse™ Scripting API we created a module implementing dose volume histogram manipulation and calculation of dose metrics.

1. Implemented Models:

Lyman-Kutcher-Burman (LKB) NTCP models were implemented with parameters recommended by QUANTEC for rectum and small bowel (tab. 1).

2. Plan Selection:

We randomly selected 27 patients treated for prostate cancer with radiation therapy to 77.4 Gy in 1.8 Gy per fraction with 45 Gy to the pelvis followed by sequential boosts to the prostate and seminal vesicles. VMAT was used for all patients. All DVHs were converted to 2 Gy fraction sizes assuming $\alpha/\beta = 3$ Gy.

3. Reported Dose Metrics and NTCP:

We calculated mean and maximum doses, organ equivalent doses (OED), and generalized equivalent uniform doses (gEUD) for both organs at risk (OAR); from the latter we calculated the LKB NTCP for each separate plan as well as the total plan sum. We then correlated the $NTCP_{total}$ from the plan sum to dose metrics from the individual (i.e. partial) plans.

	D_{50}	m	n
small bowel	59.0 Gy	0.30	0.09
rectum	76.9 Gy	0.13	0.09

Tab. 1: Lyman-Kutcher-Burman NTCP model parameters for small bowel and rectum as recommended by QUANTEC.

Spearman's rank correlation coefficients (ρ_S) and polynomial fits were calculated for the relationship between NTCP estimated from the total plan dose ($NTCP_{total}$) and dose metrics from the sequential plans.

Results and Discussion

	small bowel		rectum	
corr(X, $NTCP_{total}$)	**ρ_S**	**p**	**ρ_S**	**p**
$gEUD_{45Gy}$	0.91	< 0.01	0.41	0.03
$gEUD_{54Gy}$	0.56	< 0.01	0.76	< 0.01
$gEUD_{77.4Gy}$	0.57	< 0.01	0.73	< 0.01
$D_{mean,45Gy}$	0.82	< 0.01	0.31	0.11
$D_{mean,54Gy}$	0.72	< 0.01	0.64	< 0.01
$D_{mean,77.4Gy}$	0.74	< 0.01	0.66	< 0.01

Tab. 2: Spearman's rank correlation coefficients and associated p-values of dose metrics to plan sum NTCP.

1. **Small bowel:** NTCP correlated most strongly with $gEUD_{45Gy}$ and $D_{mean,45Gy}$. For the sequential boosts (54 Gy / 77.4 Gy) significant albeit weaker correlation was found for both (tab. 2). $NTCP_{45Gy}$ values were within 8.3% ± 2.0% of $NTCP_{total}$ on average. This was expected due to the D_{50} being within 14 Gy of the 45 Gy prescription.
2. **Rectum:** Correlation between $NTCP_{total}$ and $gEUD_{45Gy}$ was significant, while $D_{mean,45Gy}$ was not significantly associated. Stronger correlation was found on sequential boost plans for gEUD and D_{mean} (tab. 2). Higher variance (fig. 2) was anticipated due to the irradiated volume at each dose level being similar and given the higher D_{50}, reducing the impact of the primary plan.
3. **Limiting Risk:** To achieve 5% or 10% $NTCP_{total}$ in small bowel the primary plan should not exceed $gEUD_{45Gy}$ values of 29.5 Gy and 35.6 Gy, respectively. For the rectum these values were found to be 36.7 Gy and 41.2 Gy (both fig. 1).

Conclusions

Our scripting module can be used for NTCP-based plan evaluation. Using the correlation between $gEUD_{45Gy}$ and $NTCP_{total}$ we can derived gEUD targets that can be used in optimizing 45 Gy primary prostate plans to achieve a certain acceptable NTCP after sequential boosts to 77.4 Gy at a point where the sequential plans have not yet been created.

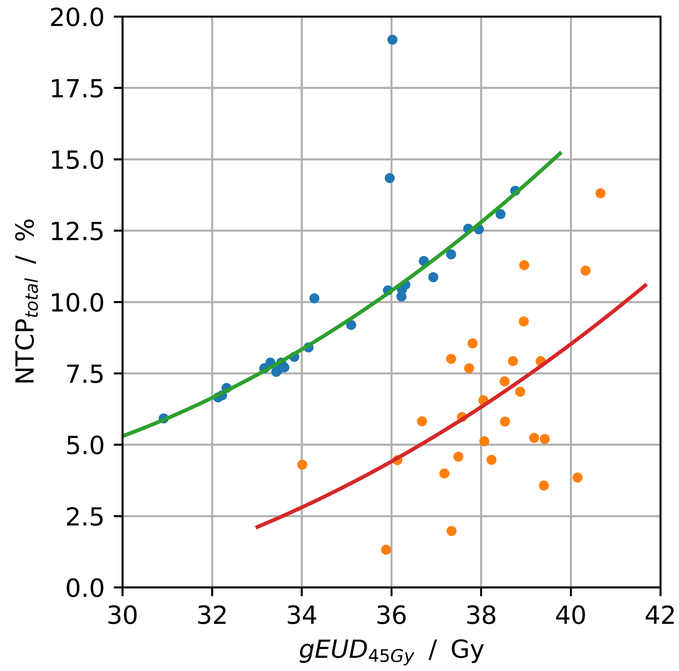

Fig. 1: $NTCP_{total}$ calculated from the plan sum over sequential plan $gEUD_{45Gy}$ (blue/green: small bowel, orange/red: rectum).

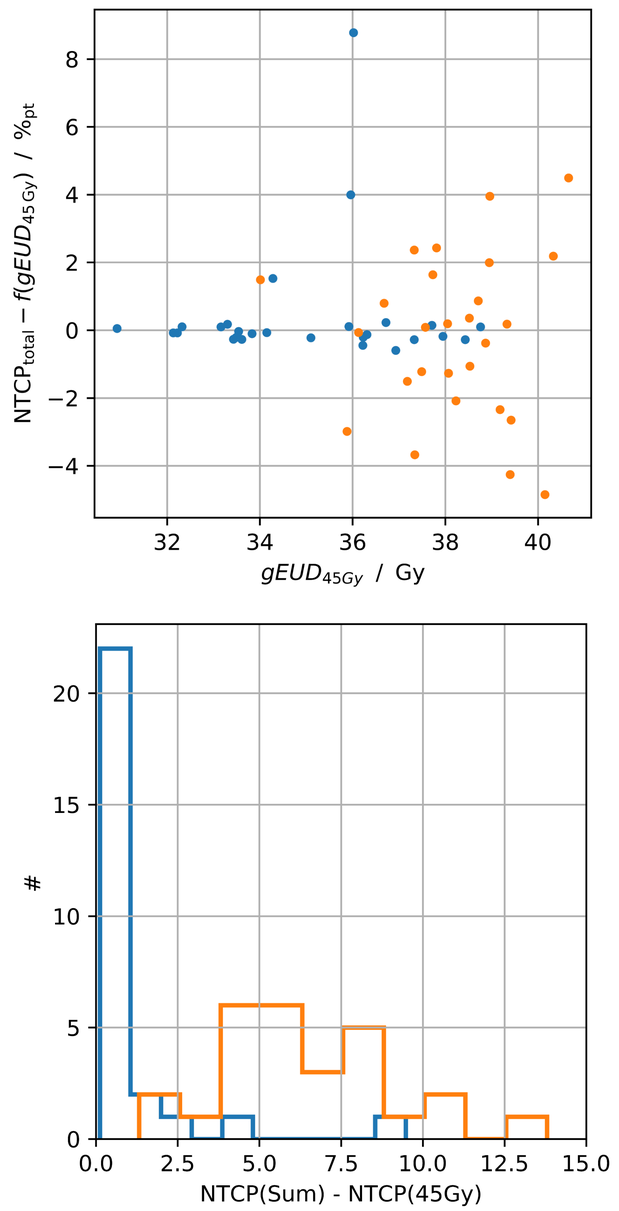

Fig. 2: (top) Residuals of plan sum NTCPtotal and 2nd degree polynomial fit. (bottom) Differences of $NTCP_{total}$ and $NTCP_{45Gy}$ (blue: small bowel, orange: rectum).