Supplemental Methods and materials

Normal tissue complication probability calculation

Normal tissue complication probability (NTCP) for the rectum and bladder were calculated using the Lyman-Kutcher-Burman (LKB) model with Niemierko's equivalent uniform dose [1–3]. Rectum NTCP was calculated using the best estimate QUANTEC parameters for late grade ≥2 rectal toxicity or bleeding [4]. Bladder NTCP was calculated using the parameters derived by Kole et al. for late urinary symptom flare after prostate SBRT in 5 fractions [5].

First, the cumulative dose volume histograms (DVHs) of the rectum and the bladder were extracted from the treatment planning system and converted into relative volume differential DVHs using an in-house Matlab script (MathWorks, Natick, MA).

For the rectum, DVH dose bins were converted to the equivalent dose in 2 Gy fractions according to,

$$EQD_2 = D \frac{\alpha/\beta + d}{\alpha/\beta + 2}$$

with D the total dose and d the dose per fraction. An α/β ratio of 3 Gy was used as recommended by the QUANTEC study and the late rectal toxicity endpoint analysis of the CHHiP trial [4,6].

For the bladder, biological effective dose correction was not necessary as the studied fractionation scheme (5 fractions) was identical to the one used for modelling by Kole et al. [5].

Next, the (corrected) differential DVHs were used to calculate Niemierko's equivalent uniform dose (EUD):

$$EUD = \left(\sum_i D_i^{\frac{1}{n}} V_i \right)^n$$

with V_i the relative differential volume of dose bin i that receives a dose D_i and n the volume effect parameter [3]. The dose D_i is calculated as the average of the lower and upper dose limit of the dose bin.

The NTCP was then calculated according to:

$$NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{t} e^{-\frac{x^2}{2}} dx$$

with

$$t = \frac{EUD - TD_{50}}{m \cdot TD_{50}}$$

where TD_{50} is the dose that will result in 50% of complication in a uniformly irradiated tissue and m is inversely proportional to the slope of the steepest point on the NTCP versus EUD curve.

The NTCP parameters were $n = 0.09, m = 0.13$ and $TD_{50} = 76.9\ Gy$ for the rectum NTCP [4] and $n = 0.03, m = 0.19$ and $TD_{50} = 38.7\ Gy$ for the bladder NTCP [5].

References

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