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# Modelling the biological effect of temporally feathered radiotherapy

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**Purpose:** Temporally feathered radiotherapy (TFRT) replaces a standard treatment plan by 5 iso-curative sub-plans (López Alfonso et al. Med Phys 2018). Each sub-plan is created such that one of five chosen organs-at-risk (OARs) receives a higher dose compared to the standard plan in one fraction, allowing the other four OARs to receive a lower dose. Each OAR then receives one high and four low doses in alternation, weekly. There are two potential benefits. First, TFRT can deliver a lower total physical dose to the feathered OARs by distributing the dose on different days. Second, a time-dependent normal tissue complication probability (NTCP) model suggests that the damage caused by the high dose is offset by increased repair during the low doses. However, the radiosensitivity parameters  $\alpha$ ,  $\beta$ , and recovery rate  $\mu$ , needed for NTCP calculation are not well defined for OARs.

We investigate the potential benefit of TFRT for ranges of  $\alpha$ ,  $\beta$ , and  $\mu$ , independently of the physical dose reduction effect.

**Methods:** We calculate OAR toxicity for a treatment delivering 2 Gy to the tumour in 25 fractions and a dose  $d_s$  to the OAR in a standard fractionation. With TFRT, the high and low doses are  $d_s + 0.4$  Gy and  $d_s - 0.1$  Gy respectively so the total physical dose is the same as in the standard plan. Toxicity is calculated for ranges of  $\alpha$  (0.05-1.00 1/Gy),  $\mu$  (0.05-0.50 1/day) and  $d_s$  (0.1-2.0 Gy), with  $\beta$  such that  $\alpha/\beta = 3$  Gy (constant).

**Result:** The OAR toxicity reduction from TFRT for the investigated values is at the maximum  $\alpha = 1.0$  1/Gy, the minimum  $\mu = 0.05$  1/day and for  $d_s = 0.3$  Gy with a toxicity reduction of 11%-points. Of the investigated combinations, 14% reach a toxicity reduction of at least 1%-point and none have a negative effect for TFRT.

**Conclusion:** TFRT can reduce OAR toxicity compared to standard fractionation with the same total physical dose. However, radiobiological parameters must be determined.

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