Purpose: Study the feasibility and planning robustness of a novel biological dose painting approach prescribing biological effect instead of dose.

Methods: Prescribed 'effect maps' were generated using models relating FMISO-PET tracer uptake to hypoxia reduction factors (HRF). HRFs decrease the LQ-model radio response parameters α and β and therefore the delivered biological effect. The model is driven by four parameters (m, K, p50, I_max), whose values have been determined through a comprehensive literature search. A planning study on ten previously treated patients with oropharyngeal cancer was conducted. Dose-painted plans were generated with the KonRad inverse planning system (DKFZ, Heidelberg). Simulated FMISO-PET images were generated by defining clinically relevant hypoxic sub-volumes within the GTV. Tracer uptake values were derived from various PET imaging studies for head and neck cancer. Each treatment plan was developed in four steps: 1) Simulate hypoxia tracer distribution in GTV. 2) Prescribe biological effect. 3) Optimize dose-painted plan under the same normal tissue constraints of the nominal clinical plan. 4) Conduct robustness analysis by evaluation of the dose-painted plan for 27 parameters combinations of K, m, p50 (mean ± 1SD).

Results: The predicted biological effect of clinical plans under normoxic conditions overestimates the delivered effect due to decreased radio-sensitivity in hypoxic tumours. Biological dose painting compensates for hypoxia by delivering a higher dose to hypoxic sub-volumes while still maintaining all critical structure dose limits. Model parameter uncertainties clearly affect robustness. The high uncertainty on p50 (pO2 for which tracer concentration is half of maximum uptake) was found to cause the largest variations in the delivered biological effect.

Conclusions: Clinically acceptable dose-painted plans can be generated without sacrificing the normal tissue constraints. Planning robustness suffers from the high uncertainty on the p50 value. Improved methods to determine the model parameters would be desirable.

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