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SIGNIFICANT MULTI-DOSE RADIOTHERAPY IMPROVEMENTS BY NUMERICAL SIMULATION AND GA SEARCH

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ABSTRACT

Multi-dose radiotherapy protocols (fraction dose and timing) currently used in the clinic are the product of human selection based on received wisdom, physician experience and intra-day patient timetabling. However, due to combinatorial considerations, the potential treatment protocol space for a given total dose or treatment length is enormous and beyond the capacity of traditional in-vitro methods. In contrast, high fidelity numerical simulation of tumour development is well suited to the challenge. Building on our previous single-dose numerical simulation model of EMT6/Ro spheroids, a multi-dose irradiation response module is added and calibrated to the effective dose arising from 18 independent multi-dose treatment programs examined experimentally. With the developed model a constrained, non-linear, search for better performing candidate protocols is conducted within the vicinity of two benchmarks by genetic algorithm (GA) techniques. The candidate protocols were identified by the GA which conferred an average of 9.4% (max benefit 16.5%) and 7.1% (13.3%) improvement (reduction) on tumour cell count compared to the two benchmarks, respectively. This study provides powerful evidence towards the hypothesis that even simple inter-fraction timing variations for a given fractional dose program may present a facile, and highly cost-effective means of significantly improving clinical efficacy.

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