

**Purpose:** To develop novel methodologies for determination of the relative biological effectiveness (RBE) in treatment plans created with a feasibility search optimization scheme for the spot scanned proton pencil beams at the Proton Therapy Center in Houston.

**Methods:** We explored methods with clinical practicality to calculate related physical and RBE-weighted doses for spot scanned proton beams. We studied a test case in which an organ-at-risk (OAR) was surrounded by the PTV. Results were demonstrated with simulated proton therapy data. We optimized the dose distribution for a planning treatment volume (PTV) within a water phantom with a feasibility search method, used previously to design conventional photon and electron beam radiation therapy plans and applied here for the first time to proton therapy planning. Prospective and retrospective intercomparison scenarios were run with computed RBEs using linear quadratic model parameter values taken from the in vitro measured survival data of Chinese hamster V79 cells.

**Results:** We designed methods to carry out intercomparisons between treatment plans with different modalities. We found a higher RBE-weighted dose in the OAR than that expected with a constant RBE value of 1.1, which is currently used in clinical practice for range modulated proton beams. The TCP (tumor control probability)/NTCP (normal tissue complication probability) dose-response analysis showed that our test planned irradiation would not have been acceptable if the OAR structure connection were highly serial, such as in the spinal cord.

**Conclusion:** This exploratory study has provided a framework which should be helpful in the ongoing search to include detailed RBE effects in intensity modulated proton therapy treatment planning.