Purpose: To evaluate potential gain in therapeutic effect from delivery of daily inhomogeneous fractional dose distributions in proton therapy, using pencil beam scanning.
Methods: For a sample case of prostate cancer, we consider a standard course of 39 fractions of 2 Gy (78 Gy total), and a hypofractionated course of 20 fractions of 3 Gy (assuming alpha/beta=1.5, the equivalent dose in 2 Gy fractions (ED2Gy) is 77.1 Gy). Two sets of dose distributions were planned: (1) the standard approach, with a uniform dose (100% of prescription) delivered in every fraction to the entire target; (2) delivery of inhomogeneous fractional dose (IFD) distributions, which varied within the target volume between 65% and 135% of the nominal prescription. For IFD, the daily distributions were optimized in such a way that the two hemispheres of the prostate (split sagittally through the urethra) received, in alternating fractions, either 65% or 135% of the nominal fractional dose (e.g., 1.3 and 2.7 Gy), while the urethra received approximately 100% (e.g., 2 Gy) daily. The equivalent uniform dose (EUD), and ED2Gy were compared for different plans.
Results: In the IFD course, the whole prostate received a nearly uniform dose over every 2 fractions, however ED2Gy was higher than with standard uniform dose: 81.9 Gy (5% increase) for the conventional, and 82.6 Gy (7% increase) for the hypofractionated course. Rectal and bladder EUD increased by <5%, while urethral EUD was unchanged.
Conclusions: In treatment of prostate and other sites, improved therapeutic outcome can be expected with delivery of inhomogeneous daily dose distributions, while administering the prescribed uniform dose to target over the entire course of treatment. The extent of expected gain is dependent on model parameters (alpha/beta, EUD-a, etc.), and dose distributions may potentially be designed to maximize the gain specifically for a certain assumed range of parameters.

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