Purpose: Hypofractionation is expected to improve therapeutic ratio for prostate radiotherapy, due to the relatively low alpha/beta ratio of the prostate tumor (~1.2 to 2.0 Gy). However, the gain in tumor equivalent dose in 2-Gy fractions (EQD2) is accompanied by the increased uncertainty in delivered dose due to inter-fractional variations. The purpose of this study is to evaluate how this trade-off is affected by the uncertainty of the tumor alpha/beta.

Methods: We used serial CT images acquired from two prostate cancer patients. Target and normal organs were contoured on the simulation and daily images. A 3D conformal proton plan was designed based on standard fractionation (78 Gy in 39 fractions) and renormalized for hypofractionation (between 5 and 28 fractions). The fraction size of the hypofractionated protocols was adjusted so as to maintain the maximum rectal dose at 78 Gy-EQD2 (alpha/beta = 3 Gy). The fractional dose, calculated on each daily CT, was mapped to the simulation geometry via deformable registration. The worst-case-scenario PTV dose for a hypofractionated protocol was estimated by summing the fractions (e.g., 28) with the lowest D97%. The target dose (e.g., D100%) was evaluated for alpha/beta of 1.2 to 2.0 Gy.

Results: The dose delivery uncertainty due to inter-fractional motion increased as the treatment became more hypofractionated. D100% was <78 Gy-EQD2 for protocols with 28, 26, 23 and 20 fractions when alpha/beta was >1.25, 1.46, 1.68 and 1.84 Gy, respectively. At alpha/beta of 2 Gy (1.2 Gy), D99% ranged from ~79 (81) to 85 (98) Gy-EQD2 for treatments in 28 to 5 fractions. Below D97%, the target dose was predominantly determined by alpha/beta, and the motion impact was minimal.

Conclusions: In prostate treatments, the impact of inter-fractional motion on tumor dose escalation is small for alpha/beta <2.0 Gy, and is of minimal concern to hypofractionated proton therapy.

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