

**Purpose:** To quantify the dosimetric impact of inter-fractional anatomical variations during the course of fractionated proton therapy of prostate cancer, and assess the robustness of the standard treatment planning techniques. **Method and Materials:** We used pre-treatment simulation and daily in-room CT from ten prostate carcinoma patients. Treatment plans for proton therapy (39 fractions, 2 Gy/fraction) were created, with 25 fractions targeting PTV<sub>50Gy</sub> (expanded from prostate and seminal vesicles to account for intra-fraction motion) followed by 14 boost fractions targeting PTV<sub>78Gy</sub> (expanded from prostate). The plan was then applied to daily CT, with beams aligned to the prostate center. For three patients having sufficient daily imaging volume, contours were drawn and plans were evaluated for all CT sets. For the other seven patients, the plans were evaluated at the beginning, mid and end point of the treatment course. The daily CT was registered to the simulation CT through deformable registration, and fractional doses were summed to yield the accumulated dose. **Results:** The fractional PTV<sub>78Gy</sub> coverage fluctuated within ~6% around the planned value, mainly due to the deformation of prostate. Loss of coverage was observed in the AP and SI direction, when PTV<sub>78Gy</sub> deformed and approached the field edge. Lateral coverage was stable even in the presence of considerable anatomical variations. The accumulated PTV<sub>78Gy</sub> coverage was slightly lower than planned, but remained acceptable. Although bladder dose per fraction increased in all three patients due to reduced daily volume, the accumulated dose remained within tolerance. No increase in the rectum dose was observed, most likely due to the smearing of the daily high-dose volumes. **Conclusion:** The results confirm that standard proton therapy planning techniques are generally robust to inter-fractional anatomical variations. Deviations in the dose to normal organs can be reduced with efforts aimed to maintain consistent levels of rectal and bladder filling.