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Multifield optimization intensity-modulated proton therapy (MFO-IMPT) for prostate cancer: Robustness analysis through simulation of rotational and translational alignment errors

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ABSTRACT

To evaluate the dosimetric consequences of rotational and translational alignment errors in patients receiving intensity-modulated proton therapy with multifield optimization (MFO-IMPT) for prostate cancer. Ten control patients with localized prostate cancer underwent treatment planning for MFO-IMPT. Rotational and translation errors were simulated along each of 3 axes: anterior-posterior (A-P), superior-inferior (S-I), and left-right. Clinical target-volume (CTV) coverage remained high with all alignment errors simulated. Rotational errors did not result in significant rectum or bladder dose perturbations. Translational errors resulted in larger dose perturbations to the bladder and rectum. Perturbations in rectum and bladder doses were minimal for rotational errors and larger for translational errors. Rectum V45 and V70 increased most with A-P misalignment, whereas bladder V45 and V70 changed most with S-I misalignment. The bladder and rectum V45 and V70 remained acceptable even with extreme alignment errors. Even with S-I and A-P translational errors of up to 5 mm, the dosimetric profile of MFO-IMPT remained favorable. MFO-IMPT for localized prostate cancer results in robust coverage of the CTV without clinically meaningful dose perturbations to normal tissue despite extreme rotational and translational alignment errors.

Introduction

In spot-scanning proton therapy, magnetic beam scanning technology is used to individually place monoenergetic Bragg peaks within a 3-dimensional target; allowing for intensity-modulated proton therapy (IMPT).[1] IMPT offers the promise of conformal target coverage by optimizing the energy fluence of spot-scanning proton beams by differentiating incident proton beam energy in layers at different depths. This approach exploits the beneficial physical properties of proton beams at both the proximal and distal margins of a target, producing a highly conformal dose distribution.[2] For the treatment of prostate cancer, recent comparative dose modeling studies have demonstrated superior dose distribution to nontarget tissue in the low-, medium-, and high-dose ranges with IMPT compared with intensity-modulated radiation therapy (IMRT) and passive scattering proton therapy.[3-5]

When multiple beam angles are used to deliver IMPT, spot optimization can be performed for each proton beam angle independently or for all beam angles simultaneously. In IMPT using single-field optimization (SFO-IMPT), each beam is optimized individually to deliver the prescribed dose to the target while respecting the dose tolerances of normal tissue.[6] In IMPT with multifield optimization (MFO-IMPT), all spots from all fields are optimized simultaneously. MFO-IMPT allows for superior dose distributions compared with either passively scattered proton therapy or SFO-IMPT. MFO-IMPT is also the most complex form of IMPT, where a homogenous dose distribution can be achieved within diverse geometric targets while limiting the radiation dose to normal structures near the target.

Treatment planning for proton beam therapy must consider potential sources of error inherent in all forms of external-beam radiation therapy (*i.e.*, daily patient positioning reproducibility,

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interfractional anatomic changes, and intra-fractional organ motion) as well as proton-specific uncertainties, such as intrinsic proton range uncertainty, Hounsfield unit stopping power conversions, and range degradation along the beam path. Dense tissues (*i.e.*, bone) scatter protons more than less dense tissues.[7] All of these factors in combination create uncertainty about the actual point of dose falloff at the distal edge of a proton beam. When ultraconformal radiation, such as IMPT, is used to treat prostate cancer, the combination of dose distribution uncertainty in the pelvis with a relatively steep dose gradient around the target volume underscores the importance of developing a treatment planning technique that preserves target-volume coverage and normal tissue sparing despite the potential for patient misalignment. We previously described the use of a scanning target volume (STV) for SFO-IMPT treatment planning and reported on the dosimetric consequences of rotational and translational errors using this planning technique.[6] In this study, we apply this planning technique to MFO-IMPT and evaluate the fidelity of this treatment planning technique by simulating rotational and translational alignment errors.

Methods and Materials

Institutional review board approval was waived for this dosimetric analysis.

Treatment planning technique

Ten control patients with localized prostate cancer underwent treatment planning for MFO-IMPT. For all patients, 2 carbon-coated zirconium dioxide fiducial markers were placed within the prostate under ultrasound guidance before computed tomography (CT) simulation. Patients were instructed to have a comfortably full bladder and all patients underwent an enema before the simulation. Bladder filling was quantified and recorded using a portable ultrasound bladder scanner (Verathon, Bothell, WA). A gas-release endorectal balloon (RadiaDyne, Houston, TX) was inflated with 60 to 100 mL of water to standardize rectal filling and immobilize the prostate. The patient was in the supine position, and the thighs and legs were immobilized in a leg and foot cradle. Initial scout films were obtained in the anterior-posterior and lateral directions to confirm symmetric alignment of the pelvic bones. Once the treating physician verified optimal positioning, 2.5-mm-thick CT images with 3-dimensional reconstruction were obtained from L4 through the midfemur. The entire setup and imaging process was repeated to confirm setup reproducibility. The acquired study sets were uploaded to the Eclipse (Varian Medical Systems, Palo Alto, CA) treatment planning system for target-volume delineation, identification of organs at risk, and MFO-IMPT treatment planning.

The clinical target volume (CTV), namely, the bladder, rectum (with balloon), femoral heads, and fiducial markers were contoured by a single physician. The CTV was defined as the prostate and caudal seminal vesicle (proximal 1 cm). The rectum was defined from the ischial tuberosities to the sigmoid flexure. Gas cavities in the rectum were identified and assigned water density. A STV was generated as an expansion around the CTV as follows: 12-mm lateral, 6-mm anterior-superior-inferior, and 5-mm posterior accounting for proton range uncertainty along the proximal and distal margin of the CTV and patient setup error. The concept of STV-based treatment planning has been empirically validated for spot-scanning proton beams and has been described previously,[6] and is consistent with IMPT treatment planning methodology described by Liu *et al.*,[8] Pflugfelder *et al.*,[9] and Fredriksson *et al.*[10] where proton range uncertainty and intrafractionationl motion considerations are factored into the CTV expansion.

IMPT treatment planning

The spot-scanning proton beam plans were optimized using MFO, where all spots from all fields were optimized simultaneously. Each plan consisted of opposed right and left lateral beams (gantry angles of 270° and 90°, respectively) with incident proton beam energies typically from approximately 150 to 200 MeV. Both fields were treated daily, with equal beam weighting. The total prescribed dose was 75.6 Gy (relative biological effectiveness [RBE]), delivered in 42 equivalent fractions. The RBE correction factor for physical to biological dose was 1.1. Treatment was designed to cover 100% of the CTV and > 95% of the STV. For simplicity, the treatment planning algorithm was solely optimized for target coverage without avoidance structure inclusion. Dose distributions were calculated using a pencil beam convolution algorithm for proton beam therapy. The spot spacing was set to 0.65 times the full width at half-maximum of the spot in air at the isocenter for the maximum energy used for each lateral field. Typical spot spacing was 7 mm. Each spot position was visited once if the maximum optimized raw monitor unit for the position was <0.04. The spot was revisited if the maximum raw monitor unit was > 0.04.

Simulation of setup errors

Rotational alignment errors were simulated using ± 3° and ± 5° symmetric rotations of each lateral beam about the original treatment axis. To simulate a + 5° rotational setup error, the right and left lateral beam gantries were set at 275° and 95°, respectively. This process was repeated for − 5° (gantry positions of 265° and 85°) and for ± 3°. Yaw alignment errors were simulated through table rotations of ± 3° and ± 5°. Translational alignment errors were simulated through bidirectional 3-mm and 5-mm isocenter displacements along each of 3 axes: anterior-posterior (A-P), superior-inferior (S-I), and left-right (L-R). Thus, a total of 20 alignment errors were simulated for each patient. After misalignment simulation, the dose distribution of each MFO-IMPT plan was recalculated using the control-case spot delivery pattern without reoptimization. The simulated setup errors were assumed to be present for each individual fraction over the duration of the prescribed therapy.

Absolute and volumetric dose assessments for all contoured structures were recorded for the control plans and for each alignment error simulated. CTV coverage was determined by modeling the minimum CTV dose (CTV min), the maximum CTV dose (CTV max), the mean CTV dose (CTV mean), and the percentage of the CTV receiving at least the prescription dose of 75.6 Gy (RBE) (CTV V75.6). The minimum, maximum, and mean dose to the bladder and rectum were recorded, as were the percentages of each structure receiving at least 45 Gy (RBE) (V45) and 70 Gy (RBE) (V70). Finally, the maximum dose to the femoral heads was recorded.

Statistical analysis

For each measured value, the mean and standard deviation (SD) of the percentage differences between control cases and test cases were calculated. A corrected t-test using the Dunnett correction for multiple comparisons was used to evaluate for statistical significance, which was defined as $p < 0.05$.

Results

Characteristics of control cases

Spot-scanning proton beam parameters for MFO-IMPT delivery for the 10 control cases are listed in Table 1. The resultant dosimetric characteristics of the control cases are shown in Table 2. An example of dose modeling for a control case is shown in Fig. 1.

Effect of rotational errors

CTV

Acceptable CTV coverage was maintained with all rotational misalignments simulated. There were no significant differences in dose delivery for CTV maximum, CTV mean, or CTV V75.6. CTV minimum was modestly affected by rotational setup errors; the mean percentage difference between control and test cases for all rotational errors was − 0.8 (range, − 1.10 to − 0.44, SD, 0.47). All CTV comparisons are shown in Table 3.

Rectum

Rotational errors of up to 5° resulted in no significant dose perturbations to rectum V70 or V45. The maximum rectum dose

Table 1
Baseline beam characteristics for the 10 control cases

Characteristic	Mean value (range)
CTV, cm^3	78 (48 to 113)
STV, cm^3	179 (128 to 238)
Right beam maximum nominal energy, MeV	199 (188 to 209)
Right beam layers	23 (21 to 24)
Right beam spots	2047 (1529 to 2616)
Left beam maximum nominal energy, MeV	201 (196 to 209)
Left beam layers	22 (21 to 24)
Left beam spots	2023 (1520 to 2559)