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Particle beam therapy

Dosimetric effects of residual uncertainties in carbon ion treatment of head chordoma

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ABSTRACT

Purpose: To investigate dose distribution variations due to setup errors and range uncertainties in image-guided carbon ion radiotherapy of head chordoma.
Materials and methods: Ten treatment plans were retrospectively tested with TRiP98 against ±1.0 mm and ±1.0° setup errors, as observed in clinical routine, and 2.6% range uncertainty when 2 mm CTV-to-PTV margins were applied. Single-fraction simulations were compared with the total treatment dose in terms of DVH bands, conformity and inhomogeneity. The contribution of image processing artifacts on reported results was also discussed, as a function of the imaging dataset resolution.
Results: Results showed that safety margins grant the conformal target coverage in presence of setup errors with $D95_{CTV}$ variations below 10% in 7 patients out of 10. Instead, the inclusion of range uncertainty yielded to appreciable dose degradation, reporting larger effects for CTV and dose conformity, whereas reduced impact is found on the organ-at-risk. The fractionation scheme positively affects dose conformity and inhomogeneity; conversely its influence on DVH bands is strongly related to the patient anatomy.
Conclusion: Besides safety margins, setup and range uncertainties lead to non-negligible combined contribution. Systematical treatment plan robustness assessment against expected uncertainties is thus encouraged, selecting beam settings and fractionation schemes where homogeneity is preserved.

Scanned particle therapy is the most conformal technique for high-precision external beam radiotherapy, coupling intensity modulation with a favorable depth-dose profile. Even though safety margins are considered for the definition of the planning target volume (PTV) [1,2], the errors inherently introduced by the treatment process [3] result in target dose coverage degradation. In the treatment of cranial lesions, the major source of geometrical deviation is the relative motion of skin and bone anatomy, significantly affecting the repositioning accuracy, as assessed for commonly used immobilization devices [4–6]. Clinical protocols featuring image guidance and six degrees-of-freedom (DOF) robotic patient alignment [7–9] break down systematic geometrical errors to the millimeter scale. In addition the particle range control in typical head&neck tissues is reported to be around 1 mm for both protons [10,11] and carbon ions [12], representing a further source of systematic error throughout a fractionated treatment [2].

Lomax extensively discussed the role of uncertainties in proton therapy [2,13]. Following the same approach, Albertini et al. [14] assessed treatment plan robustness to range and setup uncertainties with respect to errors measured in clinical practice at the Paul Scherrer Institute, Switzerland. Inter-fractional setup errors, limited to translations, were simulated by recalculating the dose on spatially shifted patient CTs to represent worst-case scenarios. The same group, though limited to rotational errors about a single axis, reports the experimental verification of these findings [15]. A statistical approach has recently been detailed by Park et al. to quantify the dosimetric errors due to setup and range uncertainties in proton treatments [16]. The probability density function of dose distribution errors under uncertainties is estimated on a large number (600) of simulations, characterizing the clinical variability. Rotational errors are not covered in the latter study, thus hindering to account for changes in beam orientation with respect to the patient. The co-existence of rotation and translation errors has been partially addressed by Meyer et al. [17], who studied the effect of rotation, yaw and anterior–posterior shifts in prostate treatments.

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The enhanced biological effectiveness offered by the therapeutic use of heavier particles, like carbon ions, is expected to provide better tumor control, though increasing the sensitivity to treatment uncertainties. In this field, however, the literature is poor and mostly focused on the treatment of extra-cranial lesions. The role of inter-fractional organ motion on prostate cancer treatment was investigated by Nikoghosyan [18], whereas Jelen et al. [19] recently reported a robustness study to evaluate the feasibility of target-based isocenter realignment. From the same group, Ammazzalorso et al. investigated the dose consequences of intra-fractional organ motion in prostate treatment with scanned ion beams, simulating different motion patterns and beam settings [20]. The effect of beam-spot size variation with respect to the delivery system commissioning has also been reported by Chanrion [21], but results are not discussed as a function of other treatment uncertainties. Recently Tessonier et al. [22] described a Monte Carlo tool for the simulation of dose delivery and range uncertainties without including geometrical errors. Translational errors were extensively simulated and discussed as a function of safety margins on PTV by Hopfgartner on five cranial patients [23]. The shifts are based on clinical measurements at the Department of Radiotherapy and Radiation Oncology of UKGM [24] and from literature [5]. The rotational errors study is though limited to the patient longitudinal axis (roll).

In this paper we tested the robustness of carbon ion plans optimized for ten clivus chordoma cases enrolled in the phase II clinical trial at Centro Nazionale di Adroterapia Oncologica (CNAO, Italy). We simulated the treatment delivery in presence of both setup errors and range uncertainties due to inaccurate estimation of tissue stopping power from CT Hounsfield Units. The magnitude of setup errors was defined to replicate the clinically observed rotational and translational residual setup errors following image guided patient positioning at our institution. We limited the particle range uncertainty study to a worst case scenario, considering the biological tissues involved in the head&neck treatments.

Materials and methods

Patient setup errors were simulated by processing the planning CT images to implement 6 degrees-of-freedom (DOF) geometry transformations. The CT voxel intensity mismatch inherently introduced by the image transformation has been preliminarily quantified to provide an insight about the accuracy of reported results. A particular sampling strategy was considered to properly sample the considered setup error space in a reduced number of simulations. Uncertainties in Hounsfield Unit (HU) – Water Equivalent (WE) path conversion were addressed by altering the look-up table available for treatment planning.

The simulation study was designed to assess both the individual and combined contribution of setup and range uncertainties on the overall dose degradation for single-fraction treatment. Then, we further investigated how the application of clinical protocol for fractionated treatment results in mitigated patient dose degradation, simulating fraction-specific setup errors.

Patient data

Ten patients were selected considering similar target location and the presence of the brainstem as organ-at-risk (OAR). Each dataset included a CT scan at $0.98 \times 0.98 \times 2$ mm resolution, manually drawn contours and clinically approved treatment plan. The CTV underwent isotropic expansion obtaining planning target volumes (PTVs) at 2 mm CTV-to-PTV margin, in agreement with the clinical guidelines for the considered treatment site thus not accounting for field-specific uncertainties [25]. The total treatment dose clinically prescribed was 70.4 Gy (RBE) to be delivered in 16 treatment fractions, 4.4 Gy (RBE) each. In this study we considered the first nine fractions resulting in 39.6 Gy (RBE) total dose. In the clinical protocol the remaining six fractions are delivered to a shrinked CTV to boost the treatment in a localized tumor volume. The dose threshold for the brainstem was limited to 30% of prescription per-fraction. Number of beams and field directions imported from the clinical record and verify system feature two opposite beams for all the patients but three, where three fields are applied.

Treatment planning

The treatment planning was based on treatment planning for particles TPS (TRiP98) for carbon ion radiotherapy [26,27] from GSI Helmholtzzentrum für Schwerionenforschung (Darmstad, D) integrating local effect model (LEM) version I ($\alpha/\beta = 2$) tables for RBE-weighted dose optimization [28]. Treatment beam settings were generally defined, without specific reference to a certain particle therapy facility. Namely, 2 mm raster pitch in lateral dimensions and 3 mm in-depth peak distance were considered, alongside with 6 mm nominal beam full width half maximum. At the voxel level, the dose calculation algorithm accumulates contributions of all the neighboring raster beam spots [27] up to 1.4 times the true focus, as explicitly calculated at each iso-energy slice with a Gaussian shape pencil beam model. Treatment plans were optimized with the Fletcher–Reeves algorithm, a fast option for the simultaneous optimization of multiple fields with complementary shapes, to assure uniform biological dose coverage [29].

Setup uncertainties

The setup error range for simulations was defined considering the experience in image-guided patient setup at CNAO. At this institution, inter-fractional setup errors are minimized by relying on robotic treatment couch to implement 6DOF corrections as derived from image-based patient registration. The clinical procedure considered for the patients included in this study relied on the commercial Verisuite® software provided by MedCom GmbH (Darmstadt, Germany), featuring 2D–3D registration capabilities. The treatment procedure beholding this system envisages the acquisition of a further image pair for verification purposes after patient setup correction, before beam delivery. With specific reference to cranial treatments Desplanques et al. [9] report post-alignment maximal errors equal to 0.15 ± 0.47 mm and $-0.06 \pm 0.45^\circ$ mean ± standard deviation (SD) in 633 fractions. By considering such clinical data, we have reasonably defined the range of setup uncertainties for simulation as ±1.0 mm and ±1.0°, corresponding to a 2SD interval to cover 95% of residual errors following image-guided alignment.

In order to explore efficiently the 6DOF of possible single-fraction setup errors, the transformation parameters were obtained through orthogonal sampling over defined domains of rotation and translation [30,31]. We considered six-dimensional sampling with 2 subspaces per dimension and one sample per subspace resulting in 64 trials. Rotational and translational parameters considered for the assessment of total treatment dose were defined following a similar approach, i.e., by adapting orthogonal sampling to match the number of prescribed fractions. Accordingly, the defined error range was sampled with a single subspace and 9 samples per sub-space. For each set of parameters, the first three dimensions were consistently interpreted as translational offsets. (Fig. 1) In this way, positive and negative shifts are evenly sampled. Corresponding rotational parameters defined by remaining dimensions, are ensured to be sparsely distributed within each quadrant by the sampling strategy.

At first, patient CT images were resampled on a nearly isotropic grid, featuring $0.98 \times 0.98 \times 1$ mm resolution, by linear