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Particle physics

Residual motion mitigation in scanned carbon ion beam therapy of liver tumors using enlarged pencil beam overlap

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ABSTRACT

Background and purpose: Interplay effects may limit the applicability of scanned ion beam therapy for moving tumors even if the motion amplitude is reduced by techniques such as gating or abdominal compression (AC). We investigate the potential of enhanced pencil beam overlap to mitigate residual motion interplay effects in scanned ion beam therapy.

Material and methods: Eight patients with hepato cellular carcinoma were selected who were either treated under AC (5 clinical target volumes (CTVs)) or with gating (6 CTVs). We performed 4D dose calculations for treatment plans with variable beam parameters (lateral raster spacing, beam full-width-at-half-maximum (FWHM), iso-energy slice spacing, gating window (GW)) and assessed under- and overdose (V_{95} and V_{107}), dose homogeneity ($HI = D_5 - D_{95}$), and dose volume histograms. The influence of the beam parameters on *HI* was studied by multivariate regression models.

Results: Motion amplitude and FWHM had the largest impact on dose homogeneity, while decreased iso-energy slice spacing and lateral raster spacing had a much smaller or no significant effect, respectively. The multivariate regression models including FWHM, motion amplitude, and IES-spacing explained 86%, 42%, and 71% of the observed variance for AC, 30% and 50% GW, respectively.

Conclusions: Residual motion in scanned carbon ion therapy of liver tumors can lead to considerable dose heterogeneities. Using an increased beam spot size dose degradation can be significantly mitigated. Especially for large tumors, increasing the beam spot size is an efficient motion mitigation option readily available at most scanning facilities.

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Treatment of intra-fractionally moving tumors with a scanned particle beam can result in interference effects (interplay) which lead to under-dosage of the clinical target volume (CTV) [1]. Even for treatment of tumors with small motion or residual motion as in beam gating [2] or under abdominal compression (AC) [3], interplay effects can cause dosimetric inhomogeneities. To reduce these, Furukawa et al. proposed to combine gating with rescanning (called phase-controlled rescanning) [4,5]. The group showed in simulations and experiments that the dose deposition achieved with a scattered beam can then also be achieved with a scanned beam despite intra-fractional target motion. An alternative approach was reported by Bert et al. [6]. They propose an increased overlap of adjacent pencil beams in the lateral plane as well as of iso-energy slices (IES). The increased overlap ensures that an increased number of pencil beams contribute to a single voxel in the CTV such that the dosimetric impact of residual motion is reduced.

The described concept was so far only tested in experiments and simulations using simplified geometries [6]. Thus, 4D treatment planning studies with patient data are essential to explore the dosimetric effects and the clinical applicability of enlarged lateral and longitudinal beam overlap. At the Heidelberg Ion Beam Therapy Center (HIT) scanned carbon ions are used for treatments of hepatocellular carcinoma (HCC) [7]. Since liver tumors can be subject to a significant amount of respiratory-induced motion [8], HIT uses AC and gating for motion mitigation. Both can reduce the effective motion amplitude. For AC, Eccles et al. report an average reduction of the motion amplitude of 2.4 mm in the superior-inferior (SI) direction [9]. Using beam gating, the residual amplitude can be controlled by the gating window (GW) size [10,11].

We report on the results of a treatment planning study using the concept of an enhanced lateral and longitudinal beam overlap

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for AC, and gating with a 50% and 30% GW. The study is based on data of the first patients treated with scanned carbon ions under AC or with beam gating at HIT [7].

Materials and methods

Patient cohort

For the treatment planning study, eight patients with HCC were selected of which six patients were treated at HIT (4 patients under AC, one each with gating and free-breathing) [7]. For the remaining two patients gated treatment was planned but was finally not delivered for medical reasons. All eight patients were re-planned with the GSI in-house 4D treatment planning system (4DTPS) *TRiP4D*, [12–14]. Supplementary Table S1 lists CTV volumes and average motion amplitudes. Amplitudes were estimated from deformable image registration (DIR) of end-inhale to end-exhale phases using Plastimatch [15]. The quality of the deformation fields was assessed analyzing the Jacobian determinant [16] and the inverse consistency error (ICE) [17]. Average minimum and maximum Jacobian values in the CTV were 0.8 (0.4-1.0) and 1.2 (1.0-1.8), respectively. Average ICE values (vector magnitude) in the CTV ranged between 0.1 and 4.2 mm (mean 1.2 mm).

Treatment planning

Re-planning with the 4DTPS was based on the treatment protocol used for HCC treatments at HIT [7]. All patients received a 4DCT (8 phases) with contrast agent (CA) and a free-breathing or end-exhale breath-hold (G2–G4) planning CT scan; for patients G2 and G3 additional 4DCT phases were reconstructed to cover the respiratory cycle around the end-exhale position in 10% steps of the relative motion amplitude. The physician-approved CTV contours from the clinical planning CT scan were propagated to the reference 4DCT phase in end-exhale using DIR. Registration of all 4DCT phases to the end-exhale phase was performed analogously.

Treatment plan optimization was performed on the 4DCT reference phase. A single, right-lateral field with a dose of 40 Gy (RBE) in four fractions of 10 Gy (RBE) was selected [7]. Internal target volume (ITV) margins for the CTV were optimized according to Graeff et al. [18] to include motion induced range changes. For AC, ITVs were generated using the full respiratory cycle. For gating, only the exhale 4DCT phases of the breathing cycle were taken into account, approximately corresponding to a 50% GW. For reasons of comparability, the same ITV was used for the 50% and the 30% GW. Since no setup uncertainties were considered in the simulations, no additional planning target volume (PTV) margins were applied. For each patient, 12 different treatment plans were optimized without organ-at-risk constraints and using various combinations of lateral raster spacing (Δs = 2 and 3 mm), IES spacing (Δz = 2 and 3 mm water-equivalent) and beam spot full width at half maximum (FWHM, 6, 8, 10 and 15 mm). At HIT, a 6 mm FWHM and lateral raster spacing of Δs = 2 mm is typically used for static targets. For liver treatments, an enlarged FWHM of 10 mm is applied with Δs = 2. A ripple filter (RiFi) optimized for 3 mm IES spacing was considered for all plans.

The choice of Δs is limited by technical constraints: (1) to ensure static dose homogeneity the ratio FWHM/Δs must be $\geqslant 3$ [19] and (2) a smaller Δs implies a lower number of particles per point leading to a lower maximum intensity that can be used by the delivery system without compromising beam monitoring.

4D treatment simulations

The major purpose of this study was to assess the effect of optimized beam parameters on the 4D dose distribution. We used regular patient motion trajectories according to Lujan et al. [20] with breathing periods of 3.6 and 5.4 s which approximately correspond to the normal range of respiratory rate of 12–20 breaths per minute [21]. The specific numbers were chosen to obtain initial motion phases with integer spacing in milliseconds. For AC, six equally distributed initial phase shifts in 60 degree steps were used. For gated treatment, two GWs covering 30% and 50% of the relative amplitude range around the end-exhale position were defined. Due to temporal synchronization of the beam delivery, the initial phase is expected to have less impact on the 4D dose distribution for gating. To confirm this, six initial phase shifts were simulated for one arbitrarily selected patient only (G2). For the remaining three patients we used two initial phases (center and start of the GW).

Beam delivery sequence (BDS) data, i.e. the temporal pattern of the treatment plan application progress [12], were generated assuming a rectangular beam extraction profile. BDS simulation was based on the treatment plan, the motion trajectory (to determine beam gating), average accelerator timing (maximum extraction time of 5 s and spill pause of 5 s) and realistic choice of beam intensities for the HIT accelerator, i.e., between 5×10^6 and 8×10^7 particles s^{-1}, which were determined in accordance with machine and safety constraints.

4D treatment simulations were performed for all patients [12]. Based on the BDS, the treatment plan and the breathing motion surrogate, the 4DTPS distributes beam positions to the 4DCT motion states. By means of the DIR maps and the 4DCT, the 4D biologically effective dose distribution is then accumulated on the reference state CT. In total, more than 1000 4D treatment simulations with varying overlap parameters were performed. Simulations were based on the standard 4DCT with eight phases for all patients. Additional simulations with the same treatment plans were performed on the 4DCT with 14 phases available for patients G2 and G3 only.

Data analysis

The dose delivered to the CTV was assessed for each dose distribution by calculating dose volume histograms (DVH) and the volumes receiving 95% (V_{95}) and 107% (V_{107}) of the prescribed dose. Additionally, the homogeneity index (*HI*) was used to evaluate the dose homogeneity:

$$HI = D_5 - D_{95}.$$

D_5 and D_{95} quantify the dose covering 5% and 95% of the CTV, respectively. Mean and standard deviation (SD) of V_{95}, V_{107} and *HI* over all initial motion phases and motion periods were analyzed as a function of the FWHM and the various raster spacing combinations. A linear regression of V_{95}, V_{107} and *HI* as a function of the FWHM was performed for each CTV and plan parameter combination (Δs, Δz). The slopes of the resulting fits were normalized to the difference of the static values at the smallest FWHM of 6 mm to yield the relative dosimetric improvement per additional millimeter FWHM, respectively.

The influence of a set of measured motion and CTV parameters (see Table S1 in the supplementary materials) as well as varied parameters of the simulations (longitudinal and lateral raster spacing Δz and Δs, FWHM) on *HI* was assessed by linear regression

Table 1
Assessed combinations of treatment plan parameters.

Parameter	Combinations											
	1	2	3	4	5	6	7	8	9	10	11	12
FWHM [mm]	6	6	8	8	10	10	10	10	15	15	15	15
Δs [mm]	2	2	2	2	2	2	3	3	2	2	3	3
Δz [mm]	2	3	2	3	2	3	2	3	2	3	2	3

Overview of the investigated combinations of FWHM, Δs and Δz. Only combinations obeying the rule FWHM/Δs $\geqslant 3$ were included (see text).