Target Motion Compensation by Means of Adjustable Heavy-Ion Beam Slow Extraction: Simulations

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Abstract

Purpose: The treatment of moving tumors with scanned ion beam therapy requires motion mitigation. The purpose of this work was to investigate a technique using adjustable beam slow extraction time of the synchrotron in carbon ion radiation therapy with pencil beam scanning to effectively reduce the sensitivity against target motion.

Materials and Methods: Assuming a realistic beam delivery system, the authors performed computer simulations to evaluate the new method comprehensively. When a scan point is exposed to different durations of the adjustable beam slow extraction for a constant particle number within a beam spill, the irradiation time at the point differs. An averaging effect may result in nearly homogeneous dose coverage over the target volume when the nominal scan point can be scanned several times with the elongated beam extraction time. In fact, a combination consisting of adjustable beam slow extraction with beam rescanning and increase in the overlap of the adjacent spot beams may reduce the sensitivity against target motion further and produce a dual effect on the target motion compensation.

Results: The dose homogeneity within the target volume was gradually better with the increase of beam extraction time. Volumetric rescanning based on tunable beam slow extraction might be very useful in improving dose homogeneity for a moving target if the beam slow extraction time is carefully selected. However, the adjustable beam extraction duration in conjunction with slice-by-slice rescanning would not significantly mitigate the effect of target motion. For the proposed method combined with lateral beam overlap increment, an increase of the beam spot width seems to be more efficient than reduction of the lateral grid spacing in improving dose homogeneity.

Conclusion: Our study reveals that the technique of variable-time beam slow extraction can be a practical and useful method for target motion mitigation.

Keywords: particle therapy; pencil beam scanning; adjustable beam slow extraction; target motion

Introduction

Charged particle beam radiation therapy is becoming an available option for patients with cancer [1–3]. However, organs in the abdominal and thoracic regions are subject to respiratory motion. The interplay between target motion and sequential beam delivery
can cause an intolerable dose inhomogeneity within the target volume [4, 5]. There are several approaches to mitigate the interference introduced by respiratory motion, such as beam rescanning [6, 7], gating [8, 9], and motion tracking [10–14].

We proposed an alternative way to compensate for target motion by means of adjustable beam slow extraction of the synchrotron in carbon ion therapy with pencil beam scanning. The method, which combines ion beam extraction and motion management issues, is different from that described in previous publications [15–17], where the beam extraction time of the synchrotron is fixed. In our study, the beam extraction time was adjustable and the total number of particles within all the beam spills was kept constant. The idea was derived from beam extraction of heavy ions, flexibly elongated up to 10,000 seconds, which has been realized recently at the Heavy Ion Research Facility in Lanzhou (HIRFL), China, where a synchrotron with electron cooler is the main accelerator. An radio frequency (RF)-knockout method was applied to resonantly extract the beam from the synchrotron at the HIRFL complex. During beam extraction, a feedback system was introduced not only to modify the time structure of the beam but also to suppress the ripple and instability. In this way, a tunable duration technique for beam slow extraction has been established at HIRFL. The slow extraction technique generates an isochronous ion beam rather than producing an ion beam with a broad energy spectrum.

This work aims at identifying the efficacy of the proposed new method and selecting the most appropriate extraction time to deliver a nearly homogeneous dose distribution within the moving target volume.

**Materials and Methods**

When a scan point is exposed to different scenarios of the adjustable beam slow extraction, the irradiation time at the point differs. Prolonged beam extraction time mitigates the influence of respiratory motion on dose distribution. In fact, when using the adjustable beam slow extraction technique to compensate for target motion, beam rescanning and an increase in the overlap of adjacent spot beams can be combined. The combinations may further reduce the sensitivity against target motion and produce a dual effect on target motion compensation.

**Synchrotron and Beam Scanning Irradiation System**

The techniques developed at HIRFL have helped to design China’s first hospital-based carbon ion therapy facility (Heavy Ion Medical Machine [HIMM]), which is currently under construction. A tunable duration of beam slow extraction will be realized at the future HIMM facility. For this simulation work, a model of the HIMM synchrotron and spot-scanning irradiation system (with parameters summarized in Table 1) was used, where the beam is scanned in planes perpendicular to the beam axis instead of parallel to the beam axis. The scan steps in the x- and y-axes of the lateral planes were set typically to be 2 mm each. The spot beam was in waiting mode until the prescribed particle number was deposited at a scan point. Because the designed scanning speed is 10 m/s for the HIMM facility, the typical time for changing the lateral spot position is of the order of hundred microseconds.

To simulate the flexibly adjustable duration of the beam slow extraction, beam spills lasting from 1 second to 31 seconds were used in this work. However, the total number of particles within all the beam spills was kept as a constant of $3 \times 10^7$ regardless of the concrete duration of the beam spills. The time interval between 2 successive beam...
spills was fixed at 3.2 seconds, which contains the acceleration time of 1.6 seconds and the deceleration time of 1.6 seconds. If an isoenergy slice was irradiated completely, the rest of the beam flux data was abandoned and the remaining time of the current spill was added to the pause between the 2 successive spills. To facilitate the dynamic beam delivery process, a series of beam-spill profiles, which represented the beam intensity distributions within beam spills varying from 1 second to 31 seconds, were prepared for the simulations. The time resolution was set to 0.001 second for all the beam intensity distributions. For beam slow extraction time of \( t \) seconds, 1000 random numbers were generated and multiplied by a factor so as to normalize the total particle number within the beam spill to \( 3 \times 10^7 \). In this way, the beam intensity distribution was obtained under the condition of the extraction time of \( t \) seconds.

### Table 1. Parameters of the HIMM facility and its scanning irradiation system used for this study.

<table>
<thead>
<tr>
<th>HIMM</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ion species</strong></td>
<td>(^{12}\text{C}^6^+)</td>
</tr>
<tr>
<td><strong>Minimum extraction energy</strong></td>
<td>80 AMeV</td>
</tr>
<tr>
<td><strong>Maximum extraction energy</strong></td>
<td>430 AMeV</td>
</tr>
<tr>
<td><strong>Cycle period</strong></td>
<td>3.2 (\sim) 10003.2 s</td>
</tr>
<tr>
<td><strong>Extraction time</strong></td>
<td>0 (\sim) 10000 s</td>
</tr>
<tr>
<td><strong>Intensity of extraction beam</strong></td>
<td>( 2 \times 10^3 \sim 4 \times 10^8 ) particles/spill</td>
</tr>
<tr>
<td><strong>Emittance</strong></td>
<td>5 (\sim) 13 mm-mrad</td>
</tr>
<tr>
<td><strong>Scanning magnets</strong></td>
<td></td>
</tr>
<tr>
<td>Magnetic center location (x/y)</td>
<td>7050/6250 mm from isocenter</td>
</tr>
<tr>
<td><strong>Mini ridge filter</strong></td>
<td></td>
</tr>
<tr>
<td>Location</td>
<td>2940 mm from isocenter</td>
</tr>
<tr>
<td>Material</td>
<td>Aluminum</td>
</tr>
</tbody>
</table>

Abbreviations: HIMM, heavy ion medical machine.

Because the HIMM facility will provide Gaussian-shaped beam profiles for therapy, the transverse intensity profile in a beam spot can be expressed as follows:

\[
N(x, y) = \frac{N_0}{2\pi \sigma_{xy}^2} e^{-(x^2 + y^2)/(2\sigma_{xy}^2)},
\]

(1)

where \( N(x, y) \) is the number of particles at position \((x, y)\) in the lateral plane of a beam spot centered at \((0, 0)\); \( N_0 \) is the total particle number of the scanned beam; and \( \sigma_{xy} \) is the standard deviation of the Gaussian profile.

According to Kramer et al [18], the partial dose, which is deposited by a single particle beam with energy \( E_{\text{beam}} \) centered at \((x_0, y_0)\) at position \((x, y, z)\), can be described as follows:

\[
D(E_{\text{beam}}, x, y, z) = \frac{N_0}{2\pi \sigma^2} e^{-\frac{r^2}{4\sigma^2}},
\]

(2)

where \( r \) is the distance from the beam center and can be determined by \( r^2 = (x-x_0)^2 + (y-y_0)^2 \) and \( \sigma \) is the actual width of the Gaussian beam profile and is a function of depth. Finally, the resulting dose at each position is a superposition of many
elementary beams as follows:

$$D(x, y, z) = \sum_{E_{\text{beam}}} D(E_{\text{beam}}, x, y, z).$$

(3)

**Simplification of Target Motion**

Some simplifications to the possible target motion have been made in the simulations. The target volume under consideration was assumed to be a sphere of 50-mm diameter centered at 197.7 mm from the surface of a water phantom. The respiration-related motion was assumed to be a periodically 3-dimensional sinusoidal movement. The model was selected to verify the validity of the adjustable beam slow extraction method owing to its sensitivity to the dynamic beam delivery and target motion interference effects. Moreover, the results derived from the model, in combination with realistic dynamic beam delivery parameters, can provide practical significance.

For target volume displacements above 5 mm, gating, breath-hold technique, tracking, or phase-controlled rescanning method can be used as a possible solution [19–24]. Therefore, the maximum displacement in the lateral and longitudinal direction (peak-to-peak distance, ie, 2A) was assumed to be 5 mm for the translation of the moving target in the simulations herein. For the period of respiration-related target motion, periods of 2, 4, and 6 seconds were considered in the simulations, clinically representing rapid, normal, and slow breathing, respectively.

**Phantom Treatment Planning**

*Simulation procedure for moving target volumes in the case of adjustable beam slow extraction*

A heavy-ion specific code system for patient treatment has been developed at HIRFL. The software was designed to manage the parameters of passive and active beam delivery systems, including the beam modeling and dose optimization. According to the optimized parameters, the expected dose distribution can be calculated on the basis of the computed tomography data sets of patients. The validity of the dose calculation has been proved for immobilized target volumes according to the successful use for irradiation of anthropomorphic phantoms and physical detectors for research purpose [25].

To calculate the dose distribution over a moving target, the original dose algorithm for static target volumes in the case of spot-scanning beam delivery was adapted and additional codes were developed. Compared with the calculation for static target volumes, a time-dependent dose calculation for moving target volumes is required owing to varying positions of the targets over the course of the dynamic irradiation. On the one hand, time dependence is related to the dynamic beam delivery derived from simulated beam intensity profiles, which are stored as substantial data sets in our treatment planning system. These beam intensity profiles represent various durations of the tunable beam slow extraction. In the simulations herein, adjustable beam extractions from 1 second to 31 seconds were applied.

On the other hand, the time-dependent dose calculation is related to target motion. For the simulations, the target motion was divided into discrete motion states. When a scan point was exposed to the beam, the position of the target volume was updated every 10 ms to a new actual value. These positions, and also the number of the particles deposited in
them, were recorded for partial dose calculations. When all the nominal scan points were irradiated completely, the final dose to a voxel was computed from the sum of all the partial dose distributions.

**Adjustable Beam Slow Extraction in Combination with Beam Rescanning**

To optimize the beam slow extraction time and examine if beam rescanning based on tunable beam slow extraction can have extra effect, such as fewer rescans compared to rescanning only or a shorter beam slow extraction time to achieve the same expected homogenous dose distribution, a systematic study of rescan mode and number dependence was conducted in the simulations.

We considered 2 different time orders of delivery of the rescanned isoenergy layers. One is slice-by-slice rescanning [26–28] in which an isoenergy layer is rescanned in sequence before the energy is changed. Another is volumetric rescanning [26, 27], indicating repetitive scanning through the whole target volume.

In the simulations, the effective scan speed was changed by adjusting the beam slow extraction time (1 second~31 seconds). For slice-by-slice rescanning, the number of rescans was set at 6, 8, and 10, respectively, and 4 and 6 for volumetric rescanning instead.

**Combination of adjustable beam slow extraction with increased overlap of adjacent pencil beams**

The sensitivity of scanned particle beam application to target motion can be reduced by increasing the overlap of pencil beams laterally between adjacent scan positions as well as longitudinally between isoenergy slices [20]. Increased overlap between pencil beams can be achieved laterally by reducing the distance between scan positions or increasing the pencil beam width. In this study we combined the adjustable beam slow extraction with an increase in the overlap of adjacent particle beams in order to optimize the ratio between beam spot size and the spacing between scan points as well.

In the simulations, the actual width of a Gaussian-like beam spot profile was set to $\sigma$ (a series of beam width values along the beam penetration) and $2\sigma$, respectively, and the effect of the spacing between adjacent scan points was examined for 2 mm and 1 mm. In practice the lateral spot spacing of 1 mm might be too dense. This would result in a large number of spots with low intensity, and the beam delivery uncertainties would be an important issue for those spots with low intensity. However, a threshold (ie, a minimum particle number, for example 1000 particles in this study) could be set in the process of dose optimization. Spots with intensity below this threshold would be set to zero and the beam delivery uncertainties could be eliminated to a maximum extent. Grassberger et al [29] investigated the impact of spot size on the interplay effect, coming from the relative motion of the tumor and proton beam. Their results showed that smaller spot sizes ($\sigma \approx 3$ mm) are inherently more sensitive to target motion. The beam spot width at one standard deviation ($\sigma$) in the beam spot profile used in our simulation work was 3.18 mm at the surface of the water phantom and 3.84 mm at Bragg peak, corresponding to those of the pencil carbon ion beam with energy of 350 AMeV measured in our previous experiment.
Evaluation of Dose Distribution

For dose distribution evaluation, dose homogeneity $H_d$ for the volume of interest (VOI) in each isoenergy slice was used, which is defined as the difference from a fully homogeneous dose distribution as follows:

$$H_d = 1 - \frac{\sigma_d}{\bar{D}},$$  \hspace{1cm} (4)

$$\sigma_d = \sqrt{\frac{1}{N-1} \sum_{i=1}^{N} (D_i - \bar{D})^2},$$  \hspace{1cm} (5)

where $D_i$ and $\bar{D}$ are the single voxel dose and the mean dose over the VOI in the slice, and $N$ is the number of voxels in the VOI of the current slice. Dose-volume histograms for the complete irradiation, dose penumbra (the distance along the major axes between the 80% and 20% points of the maximum dose value) at the middle isoenergy slice of the target volume, and maximum dose variation were computed to estimate the dose conformity as well. To evaluate the influence of the proposed methods on neighboring normal tissue, a margin of 5 mm was added to the VOI, forming an extended VOI (exVOI). The exVOI dose distributions were estimated through $D_{95\%}$ and $D_{5\%}$, defined as the minimum dose (percentage of the prescription) covering respectively 95% and 5% of the volume. Target coverage and tissue sparing were assessed by using $\Delta D_{\%}$, the change with respect to the planned value expressed in percentage points (pp).

We also reduced the dose errors of each dose distribution into a single error number (root-mean-square, RMS). Within the VOIs of the target volume, the RMS was calculated for the dose distribution in a state of motion against the stationary state representing uniform dose coverage, that is:

$$RMS = \sqrt{\frac{1}{n} \sum_{i=1}^{n} (D_i^s - D_i^u)^2},$$  \hspace{1cm} (6)

where $i$ is an index of all voxels within the VOIs of the target volume; $n$ is the total number of the voxels; and $D_i^s$ and $D_i^u$ are the voxel dose in the specific case under simulation and in the case of the uniform dose distribution, respectively.

Results

Changes in Dose Distribution under Diverse Beam Slow Extraction Durations

The RMS and total irradiation times for irradiation of the prescribed dose of 1Gy under the various beam slow extraction durations varying from 1 second to 31 seconds were calculated and are shown in Figure 1. The top 3 curves in the upper panel of Figure 1 clearly reveal that dose homogeneity within the target volume was gradually better with increased extraction time, and high-frequency motion led to a more uniform dose distribution across the target volume under the same extraction time. The curve, shown in the bottom panel of Figure 1 and corresponding to all the cases of the 3 motion frequencies, illustrates that the total irradiation time went up linearly with the increase of extraction time. However, a compromise between dose homogeneity and total irradiation time was achieved when the beam slow extraction time varied from 7 to 9 seconds, when
the RMS was less than 5% of the prescribed dose regardless of motion frequency; meanwhile, the total irradiation time was tolerable and not more than 10 minutes.

The International Commission on Radiation Units and Measurements (ICRU) recommendations for cold and hot spots are 95% and 107%, respectively, of the prescribed dose (see ICRU [30] and ICRU [31]). When the beam slow extraction time varied from 7 to 9 seconds in the simulations, a maximum dose variation between 95% and 106% of the prescribed dose was obtained. Additionally, the simulations in this subsection show that the dose penumbra at the middle isoenergy slice of the target volume almost kept a constant of 5.5 mm under the different extraction times and motion frequencies, while it was 5.0 mm for the static target volume. The adjustable extraction time method slightly expanded the dose penumbra 0.5 mm at the edge of the target volume, and the smallest coverage deterioration was observed with all exVOIs $D_{95%}/D_{5%}$.

Therefore, these results reveal that the technique of adjustable beam slow extraction proposed in this article can be applied to compensate for target motion within acceptable irradiation times if the extraction time is elaborately selected.

**Slow Extraction Time and Rescan Number Dependence on the Dose Homogeneity**

**Volumetric rescanning in combination with beam extraction time variation**

Using the same phantom-target configuration as above, volumetric rescanning was introduced into the target motion compensation in conjunction with the proposed tunable beam slow extraction. Shown in Figure 2 are the results of the extraction time and rescan number dependence on dose homogeneity and the total irradiation time for the moving target. The total irradiation time, by means of the adjustable extraction beam in combination with beam rescanning, increased significantly with the increment in rescan number for any breathing cycle. Although the total irradiation time almost doubled from no rescan to 4 times rescan, and from 4 to 6 times for any beam extraction time, there was only little difference in dose homogeneity improvement for the rescan from 4 to 6 times, especially with a rapid target motion.

Interestingly, a resonance phenomenon by which the dose homogeneity deteriorated every 2, 4, and 6 seconds for respiration cycles of 2, 4, and 6 seconds, respectively, was clearly shown in Figure 2, when the volumetric rescanning was applied. The
Volumetric rescanning in conjunction with the tunable beam slow extraction. Root-mean-square and total irradiation time spectra for various extraction times and rescan numbers: (a) $T = 2$ seconds; (b) $T = 4$ seconds; (c) $T = 6$ seconds.
precise regularity of the motion pattern could have been accidentally in phase with the time to scan the target volume once, and then caused a destructive interference with the volumetric rescanning, even making the volumetric rescanning ineffective. The constructive and destructive interferences are displayed along a wide range of beam extraction times as shown in Figure 2. For the constructive cases, the dose homogeneity was significantly improved by means of the tunable beam extraction combined with beam rescanning as compared with the adjustable beam slow extraction alone. The results for volumetric rescanning may be due to the choice of a regular breathing motion. To rule out this hypothesis, a noise was added to the regular breathing motion in our simulation, and the position of the target volume was updated to a new one with a Gaussian-distributed uncertainty of 0.5 mm. No obvious differences between simple regular breathing motion and regular motion in the presence of noise were found in our simulation. Since any target volume can be divided into multiple spheres, the choice of a spherical target volume for the simulations is reasonable. The results derived from the model, in combination with realistic dynamic beam delivery parameters, can provide practical significance.

According to the results shown in Figure 2, for the combined method, the beam extraction time of 1 second and 3 seconds with 4 times rescan may be chosen for the motion cycle of 2 seconds, with extraction time from 1 second to 3 seconds with 4 times rescan for the breathing cycles of 4 seconds and 6 seconds, in order to keep the treatment time within a reasonable and acceptable period (for instance 10 minutes), where a maximum dose variation between 97% and 105% of the prescribed dose was obtained. Among the constructive cases, the dose penumbra at the middle isoenergy slice of the target volume nearly remained a constant of 5.5 mm in all circumstances, compared with 5.0 mm for the stationary target. The smallest coverage deterioration was observed with all exVOIs $\Delta D_{95\%} \leq 1.2$ pp, $\Delta D_{9\%} \leq 1.1$ pp. Therefore, the volumetric rescanning based on the tunable beam slow extraction might be very useful for dose homogeneity improvement for a moving target if the beam slow extraction time is carefully selected, depending on the motion parameters.

Figure 3 shows the dose-volume histograms and the dose homogeneity distributions in the different isoenergy slices for the 16 beam extraction times (1 second to 16 seconds) with rescan of 4 times and motion period of 4 seconds. The target motion caused a redistribution of the delivered dose to the target volume. The percentage volume with a dose less than that prescribed inside the target volume was larger in the destructive interferences than the constructive interferences, as shown in Figure 3a. Strong interference significantly reduced the dose homogeneity inside the target volume as shown in Figure 3b.

**Slice-by-slice rescanning combined with beam extraction time variation**

Being different from the volumetric rescanning, the total irradiation time with the adjustable beam extraction in conjunction with slice-by-slice rescanning remained the same as that with the adjustable beam extraction only for the breathing cycle and extraction time, as shown in Figure 4. Slice-by-slice rescanning involves repetitive scan of the same isoenergy layers, with no time interval for energy change between 2 successive scans. Upon finishing rescan of a layer, the beam energy is changed to irradiate the next adjacent proximal isoenergy layer. This process is repeated until all the isoenergy layers are irradiated. Therefore, the total irradiation time may remain the same as that of one scan.
Figure 3. Dose-volume histograms (a) and dose homogeneity distributions (b) in the different isoenergy slices of the target volume with 16 different beam slow extraction times with volumetric rescan of 4 times and motion period of 4 seconds.
Figure 4. Slice-by-slice rescanning combined with beam extraction time variation. Root-mean-square and total irradiation time spectra for different extraction times and number of rescans: (a) $T = 2$ seconds; (b) $T = 4$ seconds; (c) $T = 6$ seconds.
Although the slice-by-slice beam rescanning was applied, dose homogeneity across the moving target volume was not improved even for 10 times rescan in cases of shorter beam extraction time especially when the target moved rapidly. For longer extraction times from 8 to 31 seconds, the dose homogeneity slightly improved for the motion cycles of 4 and 6 seconds by using the combined method compared with the adjustable beam slow extraction alone. However, the total irradiation time was beyond tolerable limits for treatment in almost all the cases for the longer beam extractions. The extraction time from 8 to 10 seconds with rescan of 6, 8, and 10 times seemed applicable to the adjustable beam extraction in combination with slice-by-slice rescanning for the breathing cycles of 4 and 6 seconds in order to keep the treatment time within 10 minutes, where a maximum dose variation between 95.6% and 106% of the prescribed dose was obtained. The dose penumbra at the middle isoenergy slice of the target volume was enlarged slightly at 5.5 mm for all the moving cases by the combined method versus 5.0 mm for the static target, and the smallest coverage deterioration was observed with all exVOIs $\Delta D_{95\%} \leq 1.3$ pp, $\Delta D_{5\%} \leq 1.8$ pp.

Lateral Overlap Increment of Adjacent Pencil Beams Combined with Adjustable Beam Extraction for Mitigation of Motion Effect

The parameter combinations used in the simulations of the tunable beam slow extraction in conjunction with lateral overlap increment were $\sigma & 2.0$ mm, $2\sigma & 2.0$ mm, and $\sigma & 1.0$ mm, respectively. Shown in the upper panel of Figure 5 are the RMS spectra for the various combinations of beam spot width and lateral grid spacing. When the parameter combination of $2\sigma & 2.0$ mm was used, the dose homogeneity became better than the parameter combination of $\sigma & 2.0$ mm with RMS reduction of 71% at beam slow extraction time of 1 second. On the contrary, the dose homogeneity did not change significantly when reducing the grid spacing from 2 to 1 mm at the same beam spot width $\sigma$. As shown in the bottom panel of Figure 5, the total irradiation time increased almost 5 minutes only for longer extraction time up to 30 seconds with the parameter combination of $2\sigma & 2.0$ mm. Therefore, the extraction time from 1 to 8 seconds with the parameter combination of $2\sigma & 2.0$ mm seemed applicable to mitigation of motion effect, where the RMS was less than 5% of the prescribed dose, while the total irradiation time was not more than 10 minutes and the maximum dose...
The variation was exactly between 95% and 107% of the prescribed dose. However, when the dose penumbra was taken into account, we found that the dose penumbra at the middle isoenergy slices of the target volume for the parameter combinations of $2r \& 2.0$ mm and $2r \& 2.0$ mm were 10.0 mm and 5.5 mm, respectively, for different beam slow extraction times and motion frequencies. Moreover, an increased exVOI $\Delta D_{95\%} \leq 15.3$ pp, $\Delta D_{5\%} \leq 7.3$ pp was observed for almost all cases. Therefore, the proposed adjustable beam extraction combined with lateral overlap increment improved the dose homogeneity across the moving target volume at the expense of dose penumbra at the edge of the target volume. According to the results presented here, for lateral beam overlap an increase of the beam spot width seems to be more efficient than reduction of the lateral grid spacing in improving the dose homogeneity across a moving target, which coincides with the results obtained by Steidl [32] but differs from the observations by Bert et al [20].

**Discussion**

A dynamic simulation study of the interplay between organ motion and pencil beam scanning has been performed. Under the framework of compensating for target motion, target motion mitigation was simulated dynamically with adjustable beam slow extraction, tunable beam extraction in conjunction with beam rescanning and overlap increment of adjacent pencil beams. The dose homogeneity within the target volume was gradually better with an increase in beam extraction time; the technique for adjustable beam slow extraction proposed in this article can be applied to compensate for target motion if the extraction time is elaborately selected. Through careful selection of beam slow extraction time, volumetric rescanning made it possible to use the combined method to realize a nearly uniform dose distribution inside the target volume while avoiding destructive interferences. For slice-by-slice rescanning, the dose homogeneity across the moving target volume was not improved even for 10 times rescan with shorter beam extraction especially for a rapidly moving target. Therefore, the tunable beam slow extraction in combination with this pattern of rescanning may not mitigate the influence of target motion significantly. For the tunable extraction duration combined with lateral overlap increment of adjacent pencil beams for mitigation of motion effects, an increase of the beam spot width seems to be more efficient than reduction of the lateral grid spacing in improving the dose homogeneity across a moving target at the expense of dose penumbra at the edge of the target volume. The simulations presented in this article provide a substantial basis for subsequent feasibility experiments with the method of adjustable beam slow extraction.

**ADDITIONAL INFORMATION AND DECLARATIONS**

**Conflicts of Interest:** The authors have no conflicts to disclose.

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