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Calculation and experimental verification of the RBE-weighted dose for scanned ion beams in the presence of target motion

A Gemmel\textsuperscript{1}, E Rietzel\textsuperscript{1}, G Kraft\textsuperscript{2}, M Durante\textsuperscript{2,3} and C Bert\textsuperscript{2}

\textsuperscript{1} Siemens AG, Healthcare Sector, Imaging & Therapy, Particle Therapy, Hofmannstr. 26, 91052 Erlangen, Germany
\textsuperscript{2} GSI Helmholtzzentrum für Schwerionenforschung, Planckstr. 1, 64291 Darmstadt, Germany
\textsuperscript{3} TU Darmstadt, Hochschulstr. 6, 64289 Darmstadt, Germany

E-mail: alexander.ag.gemmel@siemens.com and c.bert@gsi.de

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Abstract
We present an algorithm suitable for the calculation of the RBE-weighted dose for moving targets with a scanned particle beam. For verification of the algorithm, we conducted a series of cell survival measurements that were compared to the calculations. Calculation of the relative biological effectiveness (RBE) with respect to tumor motion was included in the treatment planning procedure, in order to fully assess its impact on treatment delivery with a scanned ion beam. We implemented an algorithm into our treatment planning software TRiP4D which allows determination of the RBE including its dependence on target tissue, absorbed dose, energy and particle spectra in the presence of organ motion. The calculations are based on time resolved computed tomography (4D-CT) and the corresponding deformation maps. The principal of the algorithm is illustrated in \textit{in silico} simulations that provide a detailed view of the different compositions of the energy and particle spectra at different target positions and their consequence on the resulting RBE. The calculations were experimentally verified with several cell survival measurements using a dynamic phantom and a scanned carbon ion beam. The basic functionality of the new dose calculation algorithm has been successfully tested in \textit{in silico} simulations. The algorithm has been verified by comparing its predictions to cell survival measurements. Four experiments showed in total a mean difference (standard deviation) of $-1.7\% \ (6.3\%)$ relative to the target dose of 9 Gy (RBE). The treatment planning software TRiP is now capable...
to calculate the patient relevant RBE-weighted dose in the presence of target
motion and was verified against cell survival measurements.

(Some figures in this article are in colour only in the electronic version)

1. Introduction

The treatment of moving organs is a challenge in radiotherapy. Several studies have examined
the magnitude and extent of intrafractional motion (Erridge et al. 2003, Seppenwoolde et al.
2002, Shirato et al. 2004). In photon therapy a common approach to mitigate these motions
is achieved with the ITV concept (ICRU 1999), where additional margins are used to deliver
the planned dose to the tumor volume in all motion states. For ion beams, several motion
mitigation techniques have been proposed (Keall et al. 2001) and some of them are already in
use (Minohara et al. 2000) or under development (Bert et al. 2010). For scanned ion beams,
interplay of beam and organ motion introduces an additional source of difficulties to take care
about.

At the GSI Helmholtzzentrum für Schwerionenforschung (GSI) intensity-modulated
beams of carbon ions are delivered using the raster scanning technique (Haberer et al.
1993). More than 440 patients were treated at stationary tumor sites in the head, neck,
spinal chord and pelvis with promising clinical results (Schulz-Ertner et al. 2007a, 2007b).
In 2009, the Heidelberg Ion-Beam Therapy Center started patient treatments (Combs et al.
2010). During treatment with heavy charged ion beams the radiobiological effects of densely
ionizing irradiation such as carbon ions has to be taken into account (Kraft 2000), since heavy
charged particles show an increased relative biological effectiveness (RBE) which converts
the absorbed dose into the RBE-weighted dose (RBED). Formally, the RBED at a location \( \vec{x} \),
\( D_{bio}(\vec{x}) \), can be written as the product of the RBE and the absorbed dose, \( D_{phys}(\vec{x}) \)
\[
D_{bio}(\vec{x}) = D_{phys}(\vec{x}) \cdot RBE(\vec{x}).
\] (1)

In the following the essential dependences of the RBE are briefly summarized. Beyond others,
the RBE depends on the linear energy transfer (LET) of the ion beam, i.e. on the residual
energy \( E \) of the particles. This is a consequence of the track structure of the ion beams.
A higher energy has a low LET and a large track diameter leading to a low ionization density.
Toward lower energies the LET increases and the track diameter decreases leading to a high
ionization density and therefore to complex and clustered DNA damage that can hardly be
repaired. Furthermore, the RBE for the same LET is different for different atomic numbers
\( T \). The RBE also depends on the dose level, i.e. on the particle numbers \( N \) that are delivered,
and decreases with increasing dose. Moreover, the RBE depends on the repair capacity of the
cells under consideration and thus on the type of tissue.

Under therapy conditions different compositions of the mixed particle field will be
generated at different locations (\( \vec{x} \)) within the treatment field that consists of a superposition
of many individual pencil beams with different energies, beam positions and particle numbers.
Additionally, nuclear reactions lead to fragmentation of the primary carbon ion beam into
lighter particles whose abundance increases with increasing depth. In order to evaluate the
RBE for a given location the total particle and energy spectrum \( dN/dE(E, T) \) has to be
evaluated. Using a biological model the RBE can be obtained as a function of the total particle
and energy spectrum:
\[
RBE = RBE(dn/dE).
\] (2)
The conversion of the spectrum to the RBE is based on the local effect model (LEM) (Scholz et al 1997). The LEM is used to generate tissue specific input tables containing initial RBE values as a function of particle species and LET. Together with a pre-calculated database of LET values the resulting biological effect of the mixed radiation field is determined according to the approach described by Kanai et al (1997). In our treatment planning software Treatment Planning for Particles (TRiP), these calculations are realized both by a general implementation described in detail by Krämer and Scholz (2000) and a purely analytical approach (Krämer and Scholz 2006). It should be emphasized that in both methods the knowledge of the total particle and energy spectrum is sufficient to determine the biological effect of the radiation for a given tissue type.

TRiP was extended by 4D treatment planning capabilities (Bert and Rietzel 2007). The extended code includes calculation of the absorbed dose in the presence of motion and integrated motion mitigation techniques such as rescanning, gating and tracking. It is based on time resolved computed tomography (4D-CT) with corresponding non-rigid transformation maps as described in Rietzel and Chen (2006), motion trajectories and the accelerator’s particle extraction. These algorithms were carried out for the absorbed dose only. The calculation strategy is based on summation of the sub-doses delivered in each motion phase and requires a linear dependence on the particle numbers. However, the RBED is nonlinear in the particle numbers. Therefore, as a prerequisite to treatment with ions showing RBE modulation over the beam’s track a different strategy has to be considered. Consequently, this work describes a method to calculate the patient relevant RBED and cell survival in the presence of target motion. Additionally, the algorithm is tested in simulations and compared to experimental results from cell survival measurements.

2. Materials and methods

2.1. Calculation of the RBE-weighted dose

The calculation scheme can be described as a four-step process, in which

(1) the motion is virtually divided into discrete phases,
(2) the beam parameters that contribute to a location \(\vec{x}\) are determined with respect to the patients’ geometry,
(3) the total energy and particle spectra are computed and
(4) the RBE is calculated from these spectra.

In the following the steps are described in detail with respect to figure 1.

2.1.1. Discretization. The basis of the calculation scheme is 4D-CT where the patient’s motion is divided into discrete phases (Rietzel et al 2005). Each phase contains a complete volumetric data set that serves as the input of the range calculations that are a substantial part of the dose algorithm for particles. One of the phases, usually the exhale phase, is defined as the reference phase. Deformable image registration is used to acquire transformation maps \(^0\mathbf{M}\) that establish a relationship between anatomically identical locations of the reference phase and all other phases of the 4D-CT. In our current realization, optimization and application of these transformation maps are performed with \(\text{vtkCISG}\) (Hartkens 2003), but incorporation of other deformation algorithms (Khamene et al 2009, Shackleford et al 2010) is in preparation. During beam delivery of the treatment plan target motion is measured and divided into phases accordingly. Beam position and target motion are measured temporally correlated. From these measurements sub-treatment plans are generated as described by Bert and Rietzel (2007).
In brief, raster spots that were delivered during the reference phase are collected in one sub-treatment plan and the spots that were delivered in other phases form other sub-treatment plans. The sub-treatment plan that corresponds to the reference phase 0 may contain raster spot \( l \) and another phase \( i \) may contain raster spot \( n \) as indicated in figure 1. In the case of beam tracking the position of raster spot \( n \) is possibly shifted by \((\Delta_1x_n, \Delta_1y_n, \Delta_1z_n)\).

2.1.2. Geometry and beam parameters. The range of the raster spots of the sub-treatment plans is calculated based on a look-up table that converts HU numbers of the CT phases into water equivalent path lengths (Jäkel et al. 2001). Together with the lateral position of the beam spots during delivery this defines the position of the beam within the CT phase. The dosimetric impact of the raster spot \( l \) on the location \( \overline{X}_{0k} \) is determined by the geometric relationship between the spot and the beam (Krämer et al. 2000). This can be described by the radial distance \( r_{l0} \) and depth \( z_{0k} \) of the voxel \( k \) relative to the raster spot \( l \). Furthermore, the beam parameters \( E_{in}^l \), initial beam energy, focus \( F_l \) and particle number \( N_l \) are stored in a list that contains all raster spots that contribute to the location \( \overline{X}_{0k} \). In order to determine the physical relationship of the raster spots from the other sub-treatment plans, the location \( \overline{X}_{0k} \) is transformed to the other CT-phase, which can be written as

\[
\overline{X}_{ik} = 0^M \overline{X}_{0k}.
\]

After that the geometry \( r_{nk} \) and \( z_k \) as well as the beam parameters \((E_{in}^n, F_n, N_n)\) are determined and stored. The radiological depth \( z_k \) is determined based on the 4D-CT state of motion phase \( i \).
2.1.3. Energy and particle spectra. From the list of contributions the total energy and particle spectra \( \frac{dn}{dE} \) are calculated, i.e. histograms, that contain the energy resolved abundance of the primary carbon ion beam and the fragments produced due to nuclear reactions. For this task, a pre-calculated database is used which is part of the TPS base data set. The database contains normalized, multi-dimensional histograms, \( \frac{dn}{dE}(z, E^\text{in}, T, E) \), that list the amount of fragments per particle type \( T \) and their energy distribution \( E \) as a function of depth \( z \) and initial beam energy \( E^\text{in} \). Together with the geometry and beam parameter list, the total energy and particle spectra are calculated as a sum over all phases \( i \) by

\[
\frac{dn}{dE_k} = \sum_i \sum_j \frac{dn}{dE}(z_{ki}, E_{ij}^\text{in}, T, E) \cdot N_j \cdot g(r_{jki}),
\]

(3)

where the factor \( g \) represents the decrease of the particle number due to the Gaussian-shaped beam profile at the radial distance \( r_{jki} \) between the beam trajectory of raster spot \( j \) and the location \( \vec{X}_k \) (Krämer et al 2000). The factor \( g \) can also be modified by adding a second Gaussian to account for lateral scattering effects (Gemmel et al 2008).

2.1.4. RBE calculation. The energy distribution and the abundance of the primary carbon ions and its fragments at location \( \vec{X}_k \) clearly define the resulting RBE of the mixed radiation field (equation (3)).

2.2. In silico simulations of a phantom irradiation

The effect of motion on the change of the particle and energy spectra of a mixed field was studied in a computer simulation of a phantom irradiation. For the simulation we introduced a spherical volume with a diameter of 13 mm as the target volume. The sphere was placed in a virtual water tank and moved behind a fixed ramp-shaped absorber of increasing thickness introducing different radiological depths. The irradiation of the stationary reference plan comprises a grid of beam spots with a spacing of 2 mm in the lateral dimensions and 3 mm in depth. To ensure homogeneous target coverage an isotropic margin of 2 mm was applied. The beam spot width was 5.4 mm (FWHM) and the energies range from 181 to 221 MeV u\(^{-1}\). The target was moved sinusoidally perpendicular to the beam direction with a period of 4 s. The target motion with a peak-to-peak amplitude of 10 mm was divided into five motion phases. A measured beam extraction profile from GSI’s accelerator was taken to generate the sub-treatment plans for each motion phase according to Bert and Rietzel (2007).

Three irradiation schemes were simulated:

(a) stationary reference irradiation;
(b) beam tracking, i.e. adaptation of the beam position to the target’s motion;
(c) non-adaptive irradiation, i.e. beam delivery on a moving target without adaptation of the beam position.

As part of the calculation of the RBED the energy and particle spectra resulting from all phases were collected and displayed for three positions within the target volume. Beam tracking and non-adaptive irradiation were compared to the stationary reference irradiation to illustrate the principles of the algorithm.

2.3. Cell survival experiments

Four cell survival experiments were performed to verify the algorithm to calculate the RBED in the presence of motion. For verification of the calculation procedure non-adaptive irradiation
Figure 2. The cell culture container is put on a table whose motion is recorded. The beam is applied without adaptation of the beam position to the motion and the extraction sequence is recorded in temporal correlation to the table’s motion.

schemes were utilized, where an irradiation plan optimized to a stationary geometry is applied to a moving geometry. As a result, the interplay of target movement and beam motion leads to inhomogeneous dose distributions, which are highly dependent on the combination of the motion trajectory and the particle extraction pattern of the accelerator (Bert et al 2008). Therefore, a non-adaptive irradiation scheme was utilized in all experiments to challenge the algorithm with the correct prediction of the distinct dose maxima and minima, whose position and level are characteristic for a particular combination of beam extraction and target motion.

2.3.1. Experimental setup. We used our dynamic phantom for biological dosimetry (Gemmel et al 2010). The phantom uses Nunc F96 MicroWell™ plates that are positioned in a medium filled container to allow for cell survival measurements with a spatial resolution of 9 mm. The target was put on a sliding table following a sinusoidal motion. The setup is schematically shown in figure 2. Four irradiations were carried out each with a motion period of 3.9 s. The peak-to-peak motion amplitude was 40 mm for the first two irradiations and 20 mm for the last two irradiations. The initial motion phase was altered between 0° and 90° within either choice of amplitude. A stationary ramp-shaped absorber introduced changes in the radiological depth as the table moved. Beam extraction was recorded by monitoring the accelerator signals, which indicate the events ‘Beam on’, ‘Beam off’, ‘Next beam spot’ and ‘End of energy slice’. Temporally correlated, the table motion trajectory was recorded with a calibrated camera which was focused on an infrared LED attached to the table.

2.3.2. Treatment planning and dose calculation. A pseudo-CT of the setup was constructed with TRip rather than taking a real CT. The particle numbers were optimized to cover a stationary cubic volume (width: 28 mm, depth: 23 mm, height: 45 mm) homogeneously with a RBED of 9 Gy (RBE). As in previously reported experiments (Gemmel et al 2010), the same input parameters and LEM version (Elsässer et al 2008) are used. The treatment plan consists of carbon beam energies ranging from 265 to 299 MeV u⁻¹ with a spacing of
Calculation and experimental verification of the RBE-weighted dose

approximately 2 mm from one iso-energy slice (IES) to the next. Within each IES a rectangular
grid was irradiated with a spacing of the raster spot positions of 2.5 mm and a beam width of
7.5 mm.

After beam delivery the beam extraction record and the motion trajectory were used for
dose calculation. The motion was divided into 21 discrete phases and sub-treatment plans that
contained all beam spots which were delivered in the corresponding phase according to the
method of Bert and Rietzel (2007). Finally, the new dose algorithm was used to calculate the
resulting RBED and the cell survival distribution for the four irradiations.

2.3.3. Cell processing procedure. Chinese hamster ovary cells (CHO-K1) were used to
perform the experiments. Cell survival was determined according to the assay by Puck and
Marcus (1955). The cells were cultured under standard conditions (Weyrather et al. 1999).
24 h prior to the irradiation up to 10 000 cells in 350 μl medium per well were grown in the
well plates under sterile conditions. At the same time the phantom’s containers were treated
with a disinfectant (MBT Brand) to ensure sterile conditions.

Shortly before the irradiation the containers were filled with the medium and the well
plates were inserted in upright position. The containers were cooled during transport to
the irradiation facility. Careful positioning of a single container on the sliding table and its
irradiation took approximately 10 min and 5 min, respectively. After irradiation the containers
were delivered back to the laboratory and stored for about 1 h to allow for decay of induced
radioactivity. Due to the tedious cell processing procedure which requires mainly manual
interventions and due to limited incubator space 40 cell samples in total and 10 cell samples
per irradiation were selected for cell analysis. The selection criterion was a small standard
deviation of the dose distribution within the area of the cell sample. For the selected samples
only, the medium was removed from the wells and the cells were covered with a trypsin for
6 min outside the incubator. Then, the cells were singularized, counted and re-seeded with
respect to the expected survival level to achieve an appropriate number of colonies after 7 days
of incubation. Re-seeding was performed three times per well to estimate the systematic error
of the re-seeding procedure. Finally, the cell colonies were stained and manually scored using
a microscope.

As part of the cell survival assay, a fifth, mock irradiated container served as a control. Its
cells underwent the same procedures as the irradiated cells. These cells allow determination
of the plating efficiency (PE), i.e. the fraction of cells which attach to the tissue culture treated
bottom and start proliferation. The PE is needed to determine the absolute survival (Puck and
Marcus 1955).

2.3.4. Data analysis. As a result of the cell processing procedure the cell survival $S_{ij}$ for
each experiment $i = 1, \ldots, 4$ and cell sample $j = 1, \ldots, 10$ was determined from the number
of colonies taking the PE into account. Also, the measurement error $\sigma_{ij}$ was calculated taking
the variations of the number of colonies and the standard deviation of the control cell samples
into account. Details of these steps were described before (Gemmel et al. 2010). Cell survival
$S_{ij}$ and its error $\sigma_{ij}$ were compared to the calculated survival level. For further analysis these
values were converted to the RBED $D_{ij}^{meas}$ and its error $\sigma_{Dij}^{P}$. Then, the mean measurement error
$\bar{\sigma}_{ij}^{P}$ was determined for each experiment. Furthermore, the differences $\Delta D_{ij} = D_{ij}^{meas} - D_{ij}^{calc}$
for each measurement point $j$ were calculated and the resulting mean difference $\bar{\Delta D_{i}}$ and its
standard deviation. These values were compared to mean measurement error $\bar{\sigma}_{ij}^{P}$. 
3. Results

3.1. In silico simulations of a phantom irradiation

Figure 3 shows the resulting distributions of the RBED. The reference plan leads to a homogeneous dose distribution within the target. For beam tracking the dose distribution is identical in comparison to the stationary irradiation scheme, since adaptation of the Bragg peak positions was simulated under ideal conditions, e.g. delays that are inevitable in a real beam tracking system were not considered. In the non-adaptive irradiation scheme, where the beam positions are not adapted to the target’s motion, the dose distribution is inhomogeneous due to interplay.

Figure 4 illustrates the energy and particle spectra for selected target positions in the three irradiation schemes that are indicated in figure 3. They provide a detailed look at the composition of the mixed field at a proximal, medium and distal target position.

For the reference plan, spectrum 1, corresponding to the proximal position of the target volume, comprises carbon ions with a reduced energy due to penetration of material in front of the target. With a remaining maximum energy of 114 MeV u$^{-1}$ the carbon ions’ range is 30 mm, which corresponds to the diameter of the target volume. With increasing target depth (spectra 2 and 3) the amount of low energy particles increases while the amount of high energy particles decreases. The same holds for the spectra of the fragments at a level lowered by one to two orders of magnitude. The impact of the fragment spectra on the RBED is low within the target area in comparison to the primary particles but becomes increasingly important.

For beam tracking particle spectra (4–6) are equal in comparison to the stationary irradiation scheme.

In the case of a non-adaptive irradiation the spectra clearly change. Spectrum 7 shows an almost complete absence of low energy carbon ions (<15 MeV u$^{-1}$), i.e. Bragg peak particles, compared to the reference. These particles are delivered to a different position, because the beam spots of the lowest energy slice are delivered during a motion phase, where the target has moved. Therefore, the radiological depth of the proximal target position at the time of irradiation is smaller as compared to the reference phase, i.e. the particle energy is higher. Due to this effect, the RBED at position 7 in figure 3 is reduced by 5% relative to the reference. Additionally, the RBED is further diminished by 5% for the moving target, since
Figure 4. Energy and particle spectra at the voxels of interest for the stationary reference (upper row) and the irradiations for a moving target with adaptation (middle row) and without adaptation of the beam position (lower row). The voxel positions are indicated in figure 3 and enumerated accordingly. To ease the comparison, the stationary reference data are included in the last row as dashed lines. The frequencies of the primary carbon ions were multiplied by a factor 0.1 as compared to the secondary ions.

the beam spots from the highest energy slice and thus the highest particle numbers are laterally mispositioned and do not contribute to the dose on the central axis of the target.

Spectrum 8 also shows a lack of low energy carbon ions at the medium target position. Carbon ions with Bragg peak locations in close vicinity of the medium target position according to the reference plan are delivered during motion phases with more material within the beam path. Thus, the contribution of these particles to the RBED clearly decreases. Additionally, carbon ions with Bragg peak locations distal to the medium target position in the reference plan are delivered in motion phases with less material in the beam path. Therefore, the energy deposition of these particles decreases as their dose contribution is determined from the plateau region of the Bragg curve rather than from the rise of the Bragg curve. In total, this results in
Table 1. Statistical analysis results of the differences between measured and calculated RBED.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Mean dose error ( \bar{\sigma}_i^D ) of the measurements (mGy (RBE)) (%)</th>
<th>Mean dose difference ( \Delta \bar{D}_i \pm \bar{\sigma}_i^{\Delta D} ) (mGy (RBE))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>579 (6.4)</td>
<td>−298 ± 500</td>
</tr>
<tr>
<td>2</td>
<td>480 (5.3)</td>
<td>−238 ± 414</td>
</tr>
<tr>
<td>3</td>
<td>460 (5.1)</td>
<td>−12 ± 202</td>
</tr>
<tr>
<td>4</td>
<td>532 (5.9)</td>
<td>−209 ± 767</td>
</tr>
<tr>
<td>Total</td>
<td>513 (5.7)</td>
<td>−149 ± 565</td>
</tr>
</tbody>
</table>

a reduction of 18% of the RBED relative to the stationary reference irradiation (position 8 in figure 3).

Finally, spectrum 9 shows an increased amount of low energy carbon ions. This is the consequence of two competing effects. On the one hand, the Bragg peak positions proximal to the voxel are shifted forwards and the Bragg peak positions distal to the voxel are shifted backwards due to the target motion. This leads to accumulation of low energy ions from longitudinally shifted beams. On the other hand, lateral misposition of beams from the highest energy slice decreases the number of low energy ions. Overall, the number of low energy ions is increased and the RBED at position 9 is increased by 9% compared to the stationary reference.

3.2. Cell survival experiments

Figure 5 shows the experimental results together with the calculated cell survival distributions. The position and size of the wells in comparison to the resulting dose distribution are indicated in the 2D cell survival distributions. The profiles reveal a detailed view on the measured and calculated cell survival levels as well as the experimental errors.

The results of the statistical analysis are listed in table 1. The calculated distributions of the RBED match to the measured values within the precision of the measurements. For each experiment the mean dose difference is smaller than the mean dose error. The standard deviation of the dose differences is about the same size as the mean dose error. Considering the entire set of measurement points the mean dose difference is \(-149 \text{ (SD: 565) mGy (RBE)}\). Normalized to the target dose of 9 Gy (RBE) this corresponds to a relative deviation of \(-1.7\% \text{ (SD: 6.3\%)}\).

4. Discussion

A dedicated algorithm for the calculation of the RBED for moving target geometries was implemented to the GSI treatment planning system TRiP. It is a prerequisite for investigations concerning the impact of inter- and intra-fractional target motion. The algorithm enables detailed analysis of motion mitigation techniques such as gating or beam tracking. This will complement the work of other groups that investigated motion effects in ion therapy looking at range uncertainties (Engelsman and Kooy 2005, Mori et al 2008). For scanned beams, the dosimetric impact of motion was investigated (Furukawa et al 2010, Knopf et al 2010) based on the absorbed dose or the RBED based on the microdosimetric kinetic model (Inaniwa et al 2010).
4.1. In silico simulations of a phantom irradiation

In silico simulations were performed to illustrate the principal functionality of the RBED calculation algorithm for moving targets, that is based on determining the energy and particle spectra. Ideal beam tracking was compared to a stationary reference irradiation and equal dose distributions were observed. This proves the consistency of the calculation algorithm.
Also, a non-adaptive irradiation scheme was compared to a stationary reference irradiation. Over- and under-dosage were reconstructed in detail at a proximal, medium and distal target position. Differences in the composition of the energy and particle spectra could be attributed to a change of the beam spots’ contribution due to target motion. The finding, that the dose variations due to interplay are less pronounced in the proximal part of the target volume for a non-adaptive irradiation scheme, is in accordance to previously published results (Bert et al 2008).

4.2. Cell survival experiments

Cell survival calculations are in good accordance with the experimental data. Residual differences are within the experimental precision of the cell survival measurements. The observed measurement errors in the range of 500 mGy (RBE) were comparable to previously published data (Gemmel et al 2008, 2010). They are introduced due to the inherent variability of in vitro cell systems and the necessary cell processing procedure.

The four experiments showed inhomogeneous cell survival distributions due to interplay which depends on the initial motion settings and the beam extraction pattern (Bert et al 2008). In all experiments the calculations match the experimental findings.
4.3. General considerations

As the dose calculation algorithm works on a various number of input data, such as the 4D-CT, the transformation maps or the depth dose distributions of the ion beam, and various models such as the beam transport model or the LEM, the precision of our algorithm highly depends on the precision of these inputs and models. A key role for the validity of our algorithm to describe the ‘real world’ is the precision and validity of the underlying 4D-CT data set. It is obvious that an invalid or ill-reconstructed 4D-CT including artifacts will lead to improper dose distributions, which describe all but the dose actually delivered. In particular range uncertainties, which are already an issue in the treatment of stationary tumor sites (Jäkel et al 2001), become increasingly important when setting up a treatment plan for ion beams in the presence of motion. Also, the transformation maps introduce an additional error, which directly translates into the error of the dose distribution computed with our algorithm. In addition, the calculated RBED depends strongly on the precision of both the biological model, i.e. the LEM in our case, and the physical beam model. The accuracy of the biological model and approximations used in the physical beam model have been previously investigated (Elsässer et al 2008, Krämer et al 2000). However, the striking feature of our algorithm is that, in general, it introduces no additional error to the dose calculations, since no additional approximations or interpolations have to be performed as compared to the standard version of our treatment planning software. If the size of the phase CTs, the number of motion phases and the number of raster spots do not exceed any reasonable limits the memory space needed for the calculations will be in the range of several hundred MBs but below 1 GB.

5. Conclusion

We presented an algorithm which allows for the calculation of the RBED in the presence of motion. It is based on 4D-CT data sets and corresponding transformation maps and part of our treatment planning software TRiP4D which incorporates 4D planning capabilities. The algorithm was investigated in detail in in silico simulations for different beam delivery schemes. At selected positions in the irradiation field we analyzed the impact of motion on the composition of the energy and particle spectra and consequently on the RBED. Finally, cell survival measurements were carried out with a dynamic phantom aiming at verification of the new dose algorithm. Good agreement of calculations and measurements was obtained.

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