Abstract

Ionization chamber-based dosimetry for carbon-ion beams still shows a significantly higher standard uncertainty than high-energy photon dosimetry. This is mainly caused by the high standard uncertainty of the correction factor for beam quality \( k_{Q_0} \). Due to a lack of experimental data, the given values for \( k_{Q_0} \) are based on theoretical calculations. To reduce this standard uncertainty, \( k_{Q_0} \) factors for different irradiation conditions and ionization chambers (ICs) can be determined experimentally by means of water calorimetry. To perform such measurements in a spread-out Bragg peak (SOBP) for a scanned carbon-ion beam, we describe the process of creating an almost cubic dose distribution of about \( 6 \times 6 \times 6 \text{ cm}^3 \) using a 2D range modulator. The aim is to achieve a field homogeneity with a standard deviation of measured dose values in the middle of the SOBP (over a lateral range and a depth of about 4 cm) below 2% within a scanning time of under 100 s, applying a dose larger than 1 Gy. This paper describes the optimization and characterization of the dose distribution in detail.

1. Introduction

Over the last several years, radiation therapy with carbon-ion beams has become an attractive tool for cancer treatment (Karger et al 2010, Lodge et al 2007, Amaldi and Kraft 2005). However, dosimetry for carbon-ion beams is not yet as accurate as for conventional high-energy photon beams. The standard uncertainty for dosimetry in terms of the absorbed dose to water in clinical photon beams by means of calibrated ionization chambers (ICs) is at about 1% (Andreo et al 2006, Mitch et al 2006, Van Dyk et al 2013), whereas the standard uncertainty for carbon-ion beams is about three times higher (Andreo et al 2006). This is mainly due to the high standard uncertainty of the correction factor \( k_{Q_0} \) (Karger et al 2010).

The absorbed dose to water for a given beam quality \( Q \) is determined via

\[
D_{w,Q} = M_Q \ast N_{D,w,Q_0} \ast k_{Q,Q_0},
\] (1)

with the corrected IC reading \( M_Q \) in the beam quality \( Q \), the chamber-specific calibration factor \( N_{D,w,Q_0} \) for the beam quality \( Q_0 \) in which the chamber was calibrated (usually \(^{60}\text{Co}\)) (Andreo et al 2006, Palmans et al 2002). The correction factor \( k_{Q,Q_0} \) corrects for the different response of the IC to the beam qualities \( Q \) (here: \(^{12}\text{C}\)) and \( Q_0 \) (\(^{60}\text{Co}\)). \( k_{Q,Q_0} \) is defined as the ratio of the chamber calibration factors for beam quality \( Q \) and \( Q_0 \) (Andreo 1992). It can be experimentally determined by measuring the absorbed dose to water and the
corresponding reading $M_Q$ of the IC under the same irradiation conditions:

\[ k_{Q,0} = \frac{N_{D,w,Q}}{N_{D,w,0}} = \frac{D_{w,Q}}{D_{w,0}}. \]  

Due to a lack of experimental data, $k_{Q,0}$ values are based primarily on theoretical calculations using equation (3), which is given, for example, in the International Code of Practice for the Dosimetry of External Radiotherapy Beams TRS-398 (Andreo et al. 2006):

\[ k_{Q,0} = \frac{(s_{w,air})_Q}{(s_{w,air})_0} \frac{(W_{air})_Q}{(W_{air})_0} \frac{P_Q}{P_0}. \]  

In the TRS-398, constant values are assumed for the stopping power ratio $(s_{w,air})_0$, the mean excitation energy per ion pair $(W_{air})_0$ and the perturbation factor $P_0$ for the beam quality $Q$. The resulting relative standard uncertainty of $2.8\%$ for $k_{Q,0}$ factors leads to a high overall standard uncertainty in carbon-ion dosimetry. The German dosimetry protocol DIN 6801-1 (DIN-Normenausschuss Radiologie NAR 2019) calculates $(s_{w,air})_Q$ as a function of the particle’s residual range and assumes constant values for $(W_{air})_Q$ and $P_Q$, leading to a relative standard uncertainty for $k_{Q,0}$ of $2.2\%$.

Within the scope of an ongoing project, $k_{Q,0}$ factors for different irradiation conditions and ICs are being determined experimentally using the water calorimeter designed at Physikalisch-Technische Bundesanstalt (PTB) (Krauss 2006, Krauss et al. 2012) to reduce their standard uncertainty. This was done previously for the entrance channel of a monoenergetic carbon-ion beam for two Farmer-type ICs, achieving a standard uncertainty of $0.8\%$ (Osinga-Blättermann et al. 2017). This region is characterized by a shallow depth, a monoenergetic field and relatively low LET. Based on this, $k_{Q,0}$ factors for a further eight different cylindrical ICs and three different plane-parallel ICs were determined by means of cross-calibration, showing a standard uncertainty of $1.1\%$ (Osinga-Blättermann and Krauss 2018). As a continuation of this work, $k_{Q,0}$ factors are determined in the spread-out Bragg peak (SOBP) of a carbon-ion beam. Here, the goal is to achieve a relative standard uncertainty for $k_{Q,0}$ in the same order as it is given for $k_{Q,0}$ factors in photon beams, as it was also achieved for the entrance channel of a carbon-ion beam.

To this end, a homogeneous irradiation field of reasonably size and dose irradiated in a short time is needed. The irradiation field parameters that shall be presented are detailed in the following.

**Total dose and field size:** As the radiation induced temperature rise to be measured within the calorimetric experiment only amounts to about $0.24 \text{ mK Gy}^{-1}$ (Krauss 2006), doses larger than $1 \text{ Gy}$ are typically applied in water calorimetry (Krauss 2006, Sassoysky and Pedroni 2005) for a reliable signal to noise ratio. The field size chosen had to be a compromise between irradiation time (as described below), the dose that can be applied within this time and the field size’s influence on the heat conduction. As a dose $>1 \text{ Gy}$ should be applied, a large field size (as e.g. the reference field size of $10 \times 10 \text{ cm}^2$ according to TRS-398 (Andreo et al. 2006)) would require a long irradiation time. A very small irradiation field would directly influence heat conduction effects making greater corrections necessary and thereby also increasing their uncertainty (Krauss 2006, Krauss and Kapsch 2014). Also taking the characteristic of the beam delivery system at HIT (e.g. irradiation time) into account, a field size between $5 \times 5 \text{ cm}^2$ and $7 \times 7 \text{ cm}^2$ seems to be appropriate for the $k_{Q,0}$ determination in this investigation. Therefore, we chose a size of $6 \times 6 \text{ cm}^2$, as it was also done in Oisinga-Blättermann et al. (2017), fully covering the sensitive parts of the calorimetric detector as well as the ICs used. The SOBP should have a depth of $6 \text{ cm}$ resulting in a dose cube of $6 \times 6 \times 6 \text{ cm}^3$.

**Irradiation time:** To determine the $k_{Q,0}$ factors by means of water calorimetry, a number of correction factors are required, e.g. heat conduction corrections. The heat conduction corrections are particularly dependent on the duration of irradiation, as heat conduction effects lead to the initially induced heat dissolving with time (Krauss 2006), making water calorimetric measurements rather time-critical. Medin et al. (2006) obtained $k_{Q,0}$ factors in monoenergetic proton beams with a reasonably low standard uncertainty of $0.7\%$ for an irradiation time of $2 \text{ min}$; Oisinga-Blättermann et al. (2017) achieved a standard uncertainty in the same order of magnitude for the entrance channel of a carbon ion beam for an irradiation time of about $95 \text{ s}$. Based on that, an irradiation time of less than $100 \text{ s}$ should be achieved within this study.

A full three-dimensional active scanning of the irradiation field, as is usually done in carbon-ion therapy (Haberer et al. 2004, Kamada et al. 2015) would take several minutes (about $8 \text{ min}$ for a $6 \times 6 \times 6 \text{ cm}^3$ volume of $1 \text{ Gy}$), leading to a high uncertainty for the heat conduction and thus to a high overall uncertainty for $k_{Q,0}$ factors determined. Therefore, a passive modulation of the SOBP in terms of depth is needed that allows the irradiation to take place within less than $100 \text{ s}$. Using pencil beam scanning, a passive modulation with a moving range modulator (e.g. a modulator wheel) is possible only to a very limited extent. Here, we used a static 2D range modulator (Simeonov et al. 2017), which is comparable to a ridge filter (Kostjuchenko et al. 2001).
Reproducibility and homogeneity: To determine the correction factors needed for the water calorimetric and ionometric measurements correcting for example for a positioning uncertainty of the whole setup, the off-axis position of the thermistor probes inside the calorimetric detector (Krauss 2006) or an IC's volume effect (Osinga-Blätersmann et al 2017), a detailed knowledge of the irradiation field is needed. To achieve a low uncertainty in these factors, and thus a low overall uncertainty in the resulting $k_{\text{Q,0}}$ factors, the irradiation field must be reproducible and homogeneous (Sassowsky and Pedroni 2005). As criteria for the reproducibility, Osinga-Blätersmann et al (2017) determined the relative standard deviation of dose distributions from each other, which were repeatedly measured over a period of seven months; this amounted to 0.3%. A maximum deviation of measured dose values within the $40 \times 40 \text{mm}^2$ lateral dose distribution at the measurement depth of 3% was found. Because we evaluated a 3D dose distribution in contrast to the 2D distribution considered by Osinga-Blätersmann et al, we a priori had to anticipate larger margins for field homogeneity and reproducibility. So, we choose a reproducibility of with a standard deviation of the repeated measurements below 0.5% and a field homogeneity with a standard deviation of dose values with a maximum distance of 20 mm from the center below 2%, for which the influence on several correction factors like for heat conduction correction or correction for IC's volume effect should still be small enough to be used for a $k_{\text{Q,0}}$ determination with a standard uncertainty in the order of about 1%. The range of 20 mm is motivated by the off-axis measurement position of the thermistor probes inside the calorimetric detector (Krauss 2006) and the ICs' volume to be generously covered.

This paper describes the application of a 2D range modulator to create a suitable irradiation technique for water calorimetry in a $^{12}$C-SOBP to fulfill the criteria mentioned above. A detailed field characterization is presented that includes repeated three-dimensional measurements of the irradiation field as well as Monte Carlo simulations to investigate the particle spectra.

2. Material and methods

2.1. 2D range modulator

The spread-out Bragg peak (SOBP) is generated by a so-called 2D range modulator (2DRM) consisting of pyramid-shaped pins (Simeonov et al 2017, Tommasino et al 2019). The pyramid shape is not linear; the pins have a well-defined profile with different gradients at different heights. The pins' shape was optimized for a 60 mm wide SOBP generated by carbon ions with an energy of 278 MeV/u. The designing methods for the range modulator are described in detail in Simeonov et al (2017). There, Simeonov et al describe a 3D range modulator for which each pin creates an individual depth dose distribution to achieve a certain 3D dose distribution, like for example a sphere as given in the reference. In contrast here, we use a 2D range modulator for which the pin's shape and thereby also the created depth dose distribution is constant over the modulator’s lateral area.

To fully cover the desired irradiation field, the 2DRM has a total area of $10 \times 10 \text{cm}^2$; each pin has a height of 57 mm (figure 1). We worked with different pin base areas (period of the pin distance) of $2 \times 2 \text{mm}^2$, $3 \times 3 \text{mm}^2$ and $4 \times 4 \text{mm}^2$, testing their impact on the resulting irradiation field. The 2DRMs were produced using rapid prototyping with a Stratasys Objet30 Pro PolyJet 3D printer, the printing material was RIGUR RGD450.

Two identical 2DRMs were printed using the same 3D printer (as was also done by Simeonov et al (2017)) to investigate the reproducibility of the manufacturing process. Systematic deviations of the 3D printer can be taken into account by a corrected design of the 2DRM. But in this case we did not correct for such deviations, as a satisfying shape of the dose distribution for the purpose of water calorimetry was already achieved with the original design.

For all measurements, the back of the 2DRM was positioned at the isocenter, as was later done for the calorimetric measurements. The pins were pointing towards the beam nozzle. The 2DRMs were placed on a positioning table that allows a relative accuracy of $5 \mu \text{m}$ in x- and y-direction and $1 \mu \text{m}$ in z-direction, as well as a defined tilting around each spatial axis (0.1$^\circ$ around x- and y-axis, less than 0.006$^\circ$ around z-axis). Also taking the positioning accuracy using the wall-mounted laser system of 0.5 mm (Jäkel et al 2000) into account, this gives an alignment accuracy of the 2DRM of 0.5 mm in each direction and less than 0.3$^\circ$ around each spatial axis.

2.2. Irradiation

All measurements were performed at the Heidelberg Ion Beam Therapy Center (HIT) (Haberer et al 2004) using pencil beam scanning (Haberer et al 1993).

As the SOBP is generated by passive scattering, only one iso-energy slice, e.g. a monoenergetic field, is needed. Its energy is defined by the structure of the calorimeter, as shown in Osinga-Blätersmann et al (2017), and by the desired measurement depth in water. Choosing a measurement depth of 10 cm in water...
inside the calorimeter (11.41 cm water equivalent path length), an energy of 278.29 MeV/u is needed. The irradiation field was optimized for homogeneity in terms of the physical dose. The best results concerning field homogeneity were achieved for four monoenergetic layers irradiated in sequence. These layers had a spot distance of 2 mm and were shifted against each other by 1 mm in the x-, y- or xy-direction. Each layer consists of 36 × 36 spots with a focus size of 8.2 mm full width of half maximum (FWHM). Using the 2DRM, this leads to a dose cube of 6 × 6 × 6 cm³. The pattern of the irradiation field is shown in figure 2.

For a short irradiation, the highest clinically used particle flux of 8 × 10⁷ ions per second was chosen, allowing a scan of the whole irradiation field within 90 s for a dose of 1.5 Gy.

2.3. Peakfinder
The PTW Peakfinder Water Column (Freiburg 2019) was used to measure depth dose distributions. It consists of one reference detector fixed at the entrance window and one measuring detector between two water-containing bellows that are adjustable in length. In this way, the depth of the measuring detector can be adjusted. A plane-parallel Bragg peak type 34 080 chamber is used as a measuring detector, while a type 34 082 chamber is used as a reference detector. The measuring detector has a circular sensitive area with a radius of 41 mm. The Peakfinder allows depth dose distributions to be measured with a spatial resolution of 10 µm and positioning accuracy of 100 µm. Its movement is synchronized with the synchrotron’s spill signal. Both chambers were operated at 400 V using a PTW-TANDEM XDR dual channel electrometer.

For all Peakfinder measurements, the Peakfinder’s front window was positioned at the isocenter due to spatial constrains, while the 2DRM was positioned 65.5 cm in front of it. The Peakfinder’s offset of 19.5 mm was taken into account for all measurements.

2.4. IC array and water phantom
To measure the lateral dose distribution, a prototype IC array (PTW Octavius 1000P) was used. The Octavius 1000P consists of 977 ICs arranged in an 11 × 11 cm² rectangle. Compared to the Octavius
Figure 3. Setup of the water phantom for Octavius measurements: Schematic drawing (left), side view (middle), front view (right).

1000SRS (Freiburg 2019), the 1000P is adapted for particle-beam applications whose ICs are filled with air instead of liquid to avoid recombination effects. The ICs have a distance of 2.5 mm in the inner $5 \times 5$ cm$^2$ and 5 mm in the outer part of the detecting area. Each IC has an active area of $2.3 \times 2.3$ mm$^2$ (Bauer 2018).

As the IC array is only used for relative dose measurements, its signal was not corrected for air density. Therefore, for the comparison of measurements, the dose values were normalized to the mean value of the dose values within a 20 mm radius around the center. The array was calibrated for the relative response of its chambers to each other at a well characterized 6 MV photon field at PTB Braunschweig. A correction factor for each chamber was determined and a standard uncertainty of this correction factor of 0.34% was estimated.

For the field characterization measurements, the array was positioned in a water phantom inside a waterproof case made of PMMA (based on the procedure developed by Schuy et al (2019)). At its upper edge, this case is attached to a linear drive at one side and to a smooth-running rail at the other side. This allows the depth of the array to be adjusted via remote control inside the water phantom with a depth positioning accuracy of 0.1 mm. This setup is shown in figure 3.

The water phantom was positioned 65.6 cm behind the 2DRM, i.e. the later position of the water calorimeter. A polyester block was positioned in front of the phantom to mime the calorimeter's insulation layer.

The data measured with the IC array inside the water phantom was compared with the Peakfinder measurements by taking the measurement position relative to the isocenter, the phantom's and array case's PMMA wall thicknesses, the linear drive's offset and the Octavius' measurement depth, in total 51 mm, into account. All depth indications in the measurement data are given as water equivalent path lengths from the isocenter. To compare the depth dose distribution measured with the Octavius water phantom setup with the Peakfinder results, the Octavius signals of the inner chambers within a radius of 41 mm were averaged, roughly corresponding to the active area of the Peakfinder’s measurement chamber.

2.5. Film measurements

A prerequisite for using the IC array for field characterization measurements is a sufficient spatial resolution; it is necessary to ensure that the decomposed spectrum of the irradiation field does not contain high spatial frequencies that are missed by the array. To this end, simultaneous film and IC array measurements were performed to verify the array’s spatial resolution. To take the dimensions of a single IC of the array into account, the plotted one-dimensional film signal was averaged over seven rows of pixels, which correspond to a width of 2.5 mm.

In addition, film measurements were performed to investigate the blurring out of the pattern in the irradiation field introduced by the 2DRM. For this purpose, EBT3 film segments were positioned at different depths inside a phantom that mimics the calorimeter:

- in front of the calorimeter, 65.5 cm in air behind the 2DRM (0.7 mm WET),
- at a 5 cm depth in water inside the calorimeter (60.7 mm WET),
- at a 10 cm depth in water (including the calorimetric detector’s glass wall) inside the calorimeter (111.3 mm WET); this position corresponds to the calorimetric measurement depth.

The values given in parentheses are the sums of water equivalent thicknesses (WETs) of the material in the beam path between the back of the 2DRM and the measurement position. The phantom to mime the calorimeter was a modified version of the one used by Osinga-Blättermann et al (2017); in particular, we
added additional solid water (RW-3, PTW, Germany) slabs of corresponding water equivalent thickness to reach a measurement depth of maximum 10 cm in water whereas Osinga-Blättermann et al used the phantom for a maximum depth of 5 cm. The 2DRM was positioned with its back in the isocenter; the distance between the 2DRM and the phantom was 65.5 cm, as is also the case for the calorimeter setup.

For all film measurements, GafChromatic EB T3 film (lot number 10 031 801) was used. All film segments were scanned on a flatted Epson Expression 10000XL scanner in transmission mode and evaluated using the triple channel analysis defined by Micke et al (2011). We only evaluated relative film signals taken from single, fixed depths perpendicular to the beam and limited to the central region of the field for which the particle spectrum is uniform and therefore the LET-dependent film response is the constant (Martisikova and Jäkel 2010, Castriconi et al 2017).

2.6. Monte carlo FLUKA transport code
We performed Monte Carlo simulations using the FLUKA code version 2011.2.5 (Ferrari et al 2014) to investigate the particle and LET spectra. The simulations were performed both for a passively modulated SOBP using the 2DRM as well as for a SOBP created by several layers of different energies, e.g. active scanning. The actively scanned irradiation field consists of 22 layers with energies ranging from 196.23 MeV/u to 272.77 MeV/u to create a 6 cm SOBP with a distal edge at 14.41 cm WET, comparable to the 2DRM-modulated SOBP.

The particle spectra at the calorimetric measurement position in the middle of both SOBP were compared. This was done to provide a rationale for transferring the results concerning new $k_{Q,0}$ factors for a passively modulated SOBP to active scanning irradiation conditions, as is prevalent in ion beam radiotherapy (Kamada et al 2015). As $k_{Q,0}$ corrects for the different response of an IC to given beam qualities defined by its particle and LET spectrum, $k_{Q,0}$ will be identical for irradiation fields with comparable spectra.

For all simulations, the settings for precise simulations (PRECISIO) were used. A 278.29 MeV/u carbon-ion beam was simulated. We used a rectangular beam shape with an area of $11 \times 11$ mm$^2$ to fully cover the area of the 2DRM implemented.

The 3 mm ripple filter was implemented by means of several rectangular parallelepiped and infinite half-spaces crossing the parallelepiped. The ripple filter material was set to water. The calorimeter was simulated by means of rectangular material slabs mimicking the different calorimeter materials in the beam path. The whole setup can be seen in figure 4. The beam application and monitoring system (BAMS) of the accelerator was not implemented in the simulation. As its WET is already considered in the Peakfinder’s offset, it was not taken into account for the simulation to be able to compare both depth dose distributions as a proof of concept for the simulation setup.

2.6.1. Implementation of the 2DRM
The 2DRM was implemented as voxel geometry. We tested different resolutions ranging from $59 \times 59 \times 56$ voxel per pin (vx/pin) to $160 \times 160 \times 152$ vx/pin to simulate a pin with a $3 \times 3$ mm$^2$ base area and a 57 mm height. We used an online voxelizer program (Westerdieck 2019) to convert the pin STL-file (data file containing the geometric information for 3D printing) into a text file containing the voxel coordinates. After reshaping, the voxel text file was converted into a FLUKA voxel geometry file using the FORTRAN routine writegolem (Ferrari et al 2014). The voxel geometry file was implemented in FLUKA using the VOXELS card. The voxel’s size was scaled with the water equivalent thickness (WET) of the 2DRM’s material and the voxel’s material was set to water, as the exact composition of the 3D printing material is not given by the manufacturer. The WET was experimentally determined beforehand using the Peakfinder. Due to a limitation of the voxel geometry within the FLUKA code, we only simulated a section of the 2DRM of 5 $\times$ 5 pins. For this reason, the full irradiation plan could not be simulated. Instead, we used one single spot beam with an initial energy of 278 MeV/u and a rectangular shape with an area of $11 \times 11$ mm$^2$ to fully cover the 2DRM implemented.

2.6.2. Scoring
The absorbed dose was estimated using the USRBIN DOSE card. The fluence, fluence-weighted LET and dose-weighted LET were determined using the USRBIN ALL-PART card and an independently written FORTRAN routine implemented in the FLUKA simulation. The particle spectra for particles with atomic number $Z = 1$ to $Z = 6$ were determined for each quantity using the AUXSCORE card. Each USRBIN detector implemented had a total size of $5 \times 5 \times 20$ cm$^3$ $(x, y, z)$, with one detecting bin in the x- and y-directions and 400 bins in the z-direction to estimate distributions in depth.
3. Results and discussion

3.1. Characterization of the dose distribution from the 2DRM

The 2DRM’s properties such as resulting dose distributions and their sensitivity to tilting were investigated. The 2DRM was optimized in terms of field homogeneity.

3.1.1. Depth dose distribution

Figure 5 shows depth dose distributions for a 278.29 MeV/u $^{12}$C beam in water after passing a 2DRM with a $2 \times 2\,\text{mm}^2$ (blue), $3 \times 3 \,\text{mm}^2$ (orange) and $4 \times 4 \,\text{mm}^2$ (green) pin base area.

A clear formation of a SOBP can be observed for all 2DRMs. For the $2 \times 2 \,\text{mm}^2$ pin 2DRM, the SOBP shows a peak at the beginning and at the end of the plateau region (region of flat dose distribution, $z = 85...141 \,\text{mm}$), which become smaller for $3 \times 3 \,\text{mm}^2$ pins and disappear for $4 \times 4 \,\text{mm}^2$ pins. These artifacts can be explained by an inaccuracy during the 3D printing process, namely a bending of the pins’ tips and a filling of the grooves between the pins, which slightly changes the weights for contribution of the highest and lowest energy of the SOBP superposition, respectively. With a bigger pin base area, the printed structures become less fine and the relative printing inaccuracies, and thus also the artifacts, become smaller.

Table 1 gives the relative standard deviations and the relative maximum deviations of the dose values measured within the plateau region of the SOBP (without peaks) for the three 2DRMs with different pin base areas. The standard deviation becomes smaller, which means the plateau becomes more homogeneous the larger the pin base area is.

3.1.2. Sensitivity to tilting

The sensitivity of the dose distribution to the alignment accuracy of the 2DRM was investigated. Three 2DRMs with different pin base areas were tested. Measurements of the depth dose distribution for a single spot as well as measurements of the lateral dose distribution in the middle of the SOBP of the whole
irradiation plan, as described in 2.2, were performed. Each 2DRM was first accurately aligned to the beam and then tilted by 0.5°, 1° and 2° around the y-axis (with the beam in the z-direction). For each setup, a Peakfinder and a Octavius measurement (with the Octavius inside the water phantom) were performed. Figure 6 shows the depth dose distributions for each 2DRM for the different tilting angles.

For every 2DRM, the measured distribution differs more from the aligned 2DRM’s distribution the larger the tilting angle is; an influence of a misalignment of the 2DRM can be clearly observed. This effect is greater the smaller the pin base area is. For the 4 × 4 mm² pin 2DRM, nearly no difference in the distributions can be observed up to a tilting angle of 1°, the maximum deviation of the distributions in the plateau region for aligned 2DRM and tilted around 1° is at 0.5%. In contrast, even a tilting angle of 0.5° clearly changes the distribution when using the 2DRM with 2 × 2 mm² pins.

The lateral dose distribution also changes when tilting the 2DRM. Across the x-axis, an increase in the dose towards negative values can be observed. Across the y-axis, the dose distribution stays constant, but the absolute dose rises the larger the tilting angle is. Here, too, the effects observed are greater the smaller the pin base area is. Later simulations of this effect showed that only tilting the 2DRM does not lead to a oblique lateral profile. The effect observed can be explained by a slight misalignment of the IC array with which the shown data was measured. This misalignment leads to a visible effect in the profile measured only in regions with high gradients as given for the depth dose distributions of the tilted 2DRMs (see figure 6). Therefore, the dose profile for a perfectly aligned 2DRM in the flat plateau region of the SOBP is not influenced by this misalignment.

### 3.1.3. Film measurements of the lateral dose distribution

The pattern of the 2DRM’s pins introduces a pattern in the resulting dose distribution, which becomes increasingly blurred the greater the distance from the 2DRM is. To investigate this effect, EBT3 film segments were positioned at different depths inside a phantom, as described in section 2.5. The results are shown in figure 7.

A clear pin pattern can be seen in the lateral dose distributions in front of the calorimeter (65.5 cm air between 2DRM and film) for both 2DRMs. For the 3 × 3 mm² pin 2DRM, this pattern is completely blurred and becomes invisible at a 5 cm depth in water. In contrast, the pattern is clearly visible for the 4 × 4 mm² pin 2DRM at this position. Even at a 10 cm depth in water for the 4 × 4 mm² pin 2DRM, the pattern can still be recognized. This means that the distance between the 2DRM and the measurement is not large enough for a homogeneous dose distribution for this 2DRM.

The relative standard deviations for the dose values within the inner 100 × 100 px ( = 35 × 35 mm²) of the film segment at a 10 cm depth in water for both 2DRMs were calculated. For the 3 × 3 mm² pin 2DRM, this was 1.32% and 1.51% for the 4 × 4 mm² pin 2DRM. This indicates a better homogeneity of the lateral dose distribution for a 2DRM if the pin base area is small.

### Table 1. Relative standard deviation and maximum relative deviation of doses measured within the plateau region of the SOBP for each 2DRM.

| 2DRM          | Rel. std. dev. / % | Max. dev. / % |
|---------------|--------------------|---------------|
| 2 × 2 mm² pins | 0.53               | 2.08          |
| 3 × 3 mm² pins | 0.44               | 1.54          |
| 4 × 4 mm² pins | 0.31               | 1.34          |
Figure 7. EBT3 film measurements of the lateral dose distributions in front of the calorimeter (top), at a 5 cm depth in water inside the calorimeter (middle) and at a 10 cm depth in water (bottom), which corresponds to the middle of the SOBP and the calorimetric measurement position. Measurements were performed with the $3 \times 3$ mm$^2$ (right) and the $4 \times 4$ mm$^2$ (left) pin base area 2DRM in the beam path. Standard deviations were calculated for the inner $100 \times 100$ px as exemplary indicated by the red square in the lower right picture.

Table 2. Relative standard deviation in percentage of measured doses within the plateau region of the SOBP in terms of depth (taken from Peakfinder measurement) and within a certain radius around the center of the lateral 2D dose distribution in the middle of the SOBP (taken from Octavius measurement) for the two versions of the 2DRM with a $3 \times 3$ mm$^2$ pin base area.

|                | Modulator version 1 | Modulator version 2 |
|----------------|---------------------|---------------------|
| in terms of depth | 0.44                | 0.42                |
| laterally (15 mm radius) | 1.13                | 1.00                |
| laterally (20 mm radius) | 1.35                | 1.34                |

3.1.4. Selection of the 2DRM type for further measurements

Finally, we selected the 2DRM with a $3 \times 3$ mm$^2$ pin base area for further investigation. This is a good compromise between axial and lateral field homogeneity; in addition, for this 2DRM, the pin pattern induced in the irradiation field is completely blurred in the SOBP region.

As a backup for this 2DRM, via which all subsequent measurements were performed, a second, identical 2DRM was produced. By comparing these two versions of the $3 \times 3$ mm$^2$ pin 2DRM, the reproducibility of the manufacturing process was investigated. To clarify the difference between both 2DRM versions, table 2 gives the standard deviations calculated for both 2DRMs in terms of depth within the plateau region (figure 5 ($3 \times 3$ mm$^2$ pins) between $z = 85$ mm and 141 mm) and laterally within a radius around the center of the dose distribution. Here, we used both a 15 mm and a 20 mm radius. The 20 mm radius from the central beam axis was chosen because the corresponding area is comparable to the area that was investigated in terms of field homogeneity by Osinga-Blattermann et al (2017), based on which we defined the field homogeneity that shall be achieved. For all following evaluations of the irradiation field characterization in the SOBP, a spherical volume with a 20 mm radius was used.

The two versions of the final 2DRM create very similar dose distributions in terms of depth as well as laterally, even though there are small differences. For comparison, the differences between the single normalized measurement points of the distributions created with the versions of the 2DRM were calculated, these are below 0.4% for the lateral dose distribution and below 1.1% for the depth dose distribution (within...
the plateau region). The standard deviations for the measured values in the plateau region in terms of depth and laterally are also of the same order, although they differ slightly. From these results, it can be concluded that both 2DRMs can be used for calorimetric measurements as well, although they must be characterized individually.

### 3.2. Field characterization

Repeated measurements of the three-dimensional dose distribution around the later calorimetric measurement position were performed. To this end, the Octavius was moved in terms of depth inside a water phantom.

#### 3.2.1. Comparison of film data with IC array data

To verify the spatial resolution of the Octavius before using it for all subsequent field characterization measurements, simultaneous EBT3 film measurements were performed. The film signal measured was corrected using the triple channel analysis, normalized to its maximum and compared to the relative Octavius signal. For each data set, the measurement was performed four times.

Both distributions agree very well. The film data has a standard deviation of the measured data points in the inner $100 \times 100$ px ($35 \times 35$ mm$^2$) of 1.3%; for the Octavius data, the standard deviation in the inner $35 \times 35$ mm$^2$ is 0.8% and thus in the same magnitude as the film data's standard deviation. This shows that the Octavius resolution is sufficient and that no higher spatial frequencies have been missed. Therefore, all subsequent measurements are performed using only the Octavius.

#### 3.2.2. Homogeneity and reproducibility of the irradiation field

For the field characterization measurements, the depth of the Octavius in water was adjusted in steps of 2.5 mm over a width of 80 mm to fully cover the SOBP. For each 2DRM ($3 \times 3$ mm$^2$ pin base area, two identical versions), seven measurements were performed over a period of time of 10 weeks. The results for version 1 of the 2DRM can be seen in figure 8.

As can be seen in figure 8 (left), the data points agree with the Peakfinder signal very well. On the right, the one-dimensional lateral dose distributions across the x- and y-axes (in each case in the middle of the field) are shown for different depths.

As a value for the field’s homogeneity, the standard deviation of the dose values measured within a sphere with a 20 mm radius around the center of the 3D dose distribution (5164 data points) was calculated. The values for each measurement are given in table 3. The relative standard deviations are all below 1.1%, indicating a very flat and homogeneous irradiation field around the calorimetric measurement position.

As a criterion for the reproducibility of the relative dose distribution, the standard deviation between the signals of the repeated measurements from each was calculated for every single measurement point within the 20 mm sphere. Therefore the data was normalized before, as mentioned in section 2.4. On average this calculated standard deviation amounts to 0.26% for both versions of the 2DRM, which means that the field is also quite stable over the given period of time.

### 3.3. Monte Carlo simulations

For all FLUKA simulations, a pin base area of $3 \times 3$ mm$^2$ was used, as this is the pin base area of the selected 2DRM. For all results shown, 200 000 particles were simulated in each case.
Table 3. Relative standard deviations of doses measured within a sphere with a 20 mm radius around the calorimetric measurement position for each field characterization measurement.

| Measurement | Modulator vers. | Rel. std. dev. / % |
|-------------|-----------------|-------------------|
| 05-19-19    | 1               | 0.78              |
| 05-21-19    | 1               | 0.97              |
| 05-21-19    | 1               | 0.83              |
| 05-23-19    | 1               | 1.03              |
| 05-31-19    | 1               | 1.05              |
| 06-25-19    | 1               | 0.78              |
| 07-31-19    | 1               | 0.91              |
| 05-19-19    | 2               | 0.71              |
| 05-21-19    | 2               | 0.92              |
| 05-23-19    | 2               | 1.00              |
| 05-23-19    | 2               | 0.98              |
| 05-31-19    | 2               | 1.02              |
| 06-25-19    | 2               | 0.86              |
| 07-31-19    | 2               | 0.85              |

Figure 9. FLUKA simulation result: Depth dose distributions of 278 MeV/u 12C-beam in water, compared to Peakfinder measurement data; normalized to the SOBPs ($z = 85...141$ mm) mean value. $z$ is given as geometrical depth, as it is defined in the FLUKA geometry (figure 4).

Figure 9 shows the resulting depth dose distribution of this simulation setup for a beam in water compared to the depth dose distribution measured with the Peakfinder for the real 2DRM with a $3 \times 3$ mm$^2$ pin base area.

The simulated data is slightly noisier towards the end of the SOBP. The peak at the end of the SOBP given in the experimental data cannot be observed in the simulation, as the 2DRM’s inaccuracies are not implemented in the simulation. However, both data sets agree very well, especially in the region that is of interest for calorimetric measurements, the middle of the SOBP. This result shows that the implemented setup sufficiently maps the real setup when looking at the middle of the SOBP, even though simplifications had to be made due to computational constrains.

We tested the impact of the pins’ voxel resolution on the resulting depth dose distribution. For the smallest resolution ($59 \times 59 \times 56$ vx/pin), the distribution within the plateau region was very noisy, but becomes flatter with increasing resolution. Because the computational time increases as the pins’ voxel resolution increases, and due to a limitation of the voxel geometry within the FLUKA code, we were limited to a maximum resolution of $160 \times 160 \times 152$ vx/pin. We tested the resolution’s impact on the particle spectra obtained as a measure of the reliability of the results with a limited resolution. Comparing the particle spectra for the pins with $59 \times 59 \times 56$ vx/pin resolution to pins with a resolution of $127 \times 127 \times 121$ vx/pin, all discrepancies concerning dose, fluence and LET are below 1.5% for $Z \leq 6$. When the results for a resolution of $127 \times 127 \times 121$ vx/pin are compared to the highest resolution tested ($160 \times 160 \times 152$ vx/pin), even smaller deviations (below 1%) are given. This shows that even a resolution higher than $160 \times 160 \times 152$ vx/pin would not change the result significantly.
Figure 10. FLUKA simulation result: Distribution of dose and fluence in depth for a 278 MeV/u $^{12}$C-beam for the calorimeter setup. $z$ is given as geometrical depth, as it is defined in the FLUKA geometry (figure 4).

Table 4. Mean values for percentage of fluence and dose, and track-weighted LET per particle type at the measurement position for the 2DRM-modulated SOBP and for the active scanned SOBP in parentheses.

| Z  | $N_i/\sum N_i / \%$ | $D_i/D_{all} / \%$ | LET / keV/µm |
|----|---------------------|-------------------|--------------|
| 1  | 44.77 (47.66)       | 4.08 (4.49)       | 0.98 (1.00)  |
| 2  | 20.55 (19.37)       | 5.77 (5.72)       | 3.01 (3.12)  |
| 3  | 1.98 (1.83)         | 1.18 (1.16)       | 6.41 (6.68)  |
| 4  | 1.10 (1.00)         | 1.32 (1.22)       | 12.52 (12.90)|
| 5  | 2.48 (2.07)         | 4.57 (3.91)       | 19.85 (19.96)|
| 6  | 28.98 (27.97)       | 82.97 (83.39)     | 30.81 (31.56)|
| rest |                      | 0.11 (0.13)       |              |

As the result changes only slightly between a resolution of $127 \times 127 \times 127$ vx/pin and $160 \times 160 \times 152$ vx/pin, while the computational time dramatically increases, we decided to use a pin resolution of $127 \times 127 \times 121$ vx/pin for the simulation to obtain particle spectra for the whole calorimeter setup. The resulting absorbed dose to matter and fluence particle spectra are shown in figure 10. The dose distribution shows two very significant drops that appear at the calorimetric detector’s glass walls. They can be explained by a difference in the mass stopping power of glass compared to water. They will be taken into account when performing heat transport calculations to correct for heat conduction effects in the upcoming calorimetric measurements as described in Krauss (2006).

The dose, fluence and LET per particle type at the measurement position ($96.7 \text{ mm} \leq z \leq 96.8 \text{ mm}$ in figure 10) are given in table 4. For most of the particles at the measurement position, $Z = 1$ (protons, deuterons and tritons); only 30% of the fluence is carbon ions. Nevertheless, due to the difference in LET, the dose is mainly deposited by carbon ions (83%), whereas particles with $Z = 1$ only provide 4% of the total dose. Helium ions ($Z = 2$) make up 20% of the fluence, but only 6% of the dose. The percentage of lithium ($Z = 3$), beryllium ($Z = 4$), and boron ($Z = 5$) within the spectrum is below 2.5% each, together making up about 7% of the dose. Target fragments with $Z > 6$ are only 0.1% of the delivered dose.

We compared the results of this simulation setup with a simulation in which the SOBP is created by irradiating layers of different energies (i.e. by means of active scanning). The simulation showed only slight differences in the particle spectra of the actively scanned SOBP compared to the 2DRM-SOBP. The percentage of fluence for particles with $Z = 1$ was 3% higher; for the other particles, it was between 0.2% and 1.2% lower for the actively scanned SOBP; particles with $Z = 1$ and $Z = 6$ contributed 0.4% more to the total dose for the actively scanned SOBP. The maximum difference in LET was about 3%. The values for percentage of dose and fluence and for LET per particle type at the measurement position for the active scanned SOBP are given in parentheses in table 4.

4. Conclusion

The objective of this study was to develop and optimize an irradiation technique for water calorimetry in a SOBP for scanned carbon-ion beams, resulting in irradiation field parameters fulfilling certain requirements. To this end, we investigated the applicability of a 2D range modulator produced using rapid prototyping with a 3D printer. The 2DRM is very well suited to passively create a $^{12}$C-SOBP for time-critical applications. A 1.5 Gy dose cube of $6 \times 6 \times 6$ cm$^3$ was produced within 90 s. A relative standard deviation of $\leq 1.1\%$ for the measured values of the 3D dose distribution with a maximum distance of 20 mm from the calorimetric...
measurement position was achieved. A deviation of 0.26% of these values for repeated measurements over a period of 10 weeks was found, which shows that the relative dose distribution is stable over time.

Even for the identical design, the two versions of the 2DRM tested showed slight differences due to the limitation of the printing accuracy of the fine structures. It was therefore necessary to characterize each 2DRM individually.

The very low deviation in the simulated particle spectra for the passively modulated 2DRM-SOBP and an actively scanned SOBP gives a good rationale for also transferring the results concerning new $k_{0,Q}$ factors to irradiation fields created by active scanning. The next step will be to perform the calorimetric measurements under the given field parameters to determine experimental $k_{0,Q}$ factors in the passively realized SOBP of a $^{12}$C beam.

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