Water calorimetry-based $k_Q$ factors for Farmer-type ionization chambers in the SOBP of a carbon-ion beam

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Abstract
The dosimetry of carbon-ion beams based on calibrated ionization chambers (ICs) still shows a significantly higher uncertainty compared to high-energy photon beams, a fact influenced mainly by the uncertainty of the correction factor for the beam quality $k_Q$. Due to a lack of experimental data, $k_Q$ factors in carbon-ion beams used today are based on theoretical calculations whose standard uncertainty is three times higher than that of photon beams. To reduce their uncertainty, in this work, $k_Q$ factors for two ICs were determined experimentally by means of water calorimetry for the spread-out Bragg peak of a carbon-ion beam, these factors are presented here for the first time. To this end, the absorbed dose to water in the $^{12}$C-SOBP is measured using the water calorimeter developed at Physikalisch-Technische Bundesanstalt, allowing a direct calibration of the ICs used (PTW 30013 and IBA FC65G) and thereby an experimental determination of the chamber-specific $k_Q$ factors. Based on a detailed characterization of the irradiation field, correction factors for several effects that influence calorimetric and ionometric measurements were determined. Their contribution to an overall uncertainty budget of the final $k_Q$ factors was determined, leading to a standard uncertainty for $k_Q$ of 0.69%, which means a reduction by a factor of three compared to the theoretically calculated values. The experimentally determined values were expressed in accordance with TRS-398 and DIN 6801-1 and compared to the values given there. A maximum deviation of 2.3% was found between the experiment and the literature.

1. Introduction

Radiotherapy with carbon-ion beams offers the opportunity for a very accurate spatial dose deposition in the target volume while optimally sparing the healthy tissue (Schulz-Ertner et al 2004, Lodge et al 2007). However, the dosimetry in carbon-ion beams has not yet reached the same level of accuracy as for conventional high-energy photon beams. For the latter the standard uncertainty in terms of the absorbed dose to water measured with calibrated ionization chambers (ICs) is typically 1% (Andreo et al 2006, Mitch et al 2009, Van Dyk et al 2013), whereas it is about three times higher for carbon-ion beams (Andreo et al 2006). This high uncertainty is mainly caused by a high standard uncertainty of the correction factor $k_Q$.

The main quantity in radiotherapy dosimetry is the absorbed dose to water. The absorbed dose to water $D_{w,Q}$ is typically determined by help of ICs according to the following equation:

$$D_{w,Q} = M_Q \cdot N_{D_{w,Q}} \cdot k_{Q,W}$$  \hspace{1cm} (1)
where $M_Q$ denotes the IC reading corrected for different effects in a radiation beam with quality index $Q$ (Andreo et al 2006) and $N_{D,w,Q_s}$ the chamber-specific calibration factor for the beam quality $Q_s$, in which the chamber was calibrated (Palmans et al 2002). The correction factor $k_{Q,Q_s}$ corrects for the difference in the chamber’s response to the beam qualities $Q$ and $Q_s$. It is defined as the ratio of calibration factors for both beam qualities:

$$k_{Q,Q_s} = \frac{N_{D,w,Q_s}}{N_{D,w,Q}} = \frac{D_{w,Q_s}/M_Q}{N_{D,w,Q_s}}. \tag{2}$$

Due to a lack of experimental data, in practice, $k_{Q,Q_s}$ is determined via theoretical calculations. In the International Code of Practice for the Dosimetry of External Radiotherapy Beams TRS-398 (Andreo et al 2006) it is given by the following equation:

$$k_{Q,Q_s} = \frac{(s_{w,air})_Q (W_{air})_Q P_Q}{(s_{w,air})_{Q_s} (W_{air})_{Q_s} P_{Q_s}} \tag{3}$$

If $^{60}$Co is used as the reference beam quality $Q_s$ (as is usually the case (Palmans et al 2002)), $k_{Q,Q_s}$ is referred to as $k_Q$ (Andreo et al 2006). As this is the case for all values presented in this study, the notation $k_Q$ for the beam quality correction factor will be used in the following.

For the calculation according to equation (3), constant values are assumed for the stopping power ratio $(s_{w,air})_Q$, the mean excitation energy per ion pair $(W_{air})_Q$ and the perturbation factor $P_Q$ for the beam quality $Q$ with relative standard uncertainties of 2.0% ($(s_{w,air})_Q$), 1.5% ($(W_{air})_Q$) and 1.0% ($P_Q$), respectively (Andreo et al 2006). This results in a combined standard uncertainty of $k_Q$ of 2.8%. The DIN 6801-1 protocol (Germany) (DIN-Normenausschuss Radiologie (NAR) 2016) calculates the stopping power ratio for the beam quality $Q$, $(s_{w,air})_Q$, as a function of the residual range (defined as the difference between the measurement depth and the depth at which the value of the percentage depth dose distribution after the Bragg peak (100%) has dropped to 50%), leading to a somewhat lower standard uncertainty for $k_Q$ of 2.2%. Compared to this, the standard uncertainty for $k_Q$ in photon beams is 1.0% for calculated values in accordance with the TRS-398 (Andreo et al 2006) and even lower (0.6%) if experimentally determined values are also taken into account (Andreo et al 2020).

A direct, experimental determination of $k_Q$ values for ICs by means of water calorimetry is an established method for different types of radiation, like x-rays (Krauss et al 2012), high-energy photons (Krauss and Kapsch 2007, McEwen 2010, Krauss and Kapsch 2014), electron beams (Krauss and Kapsch 2018) and protons (Medin et al 2006, Medin 2010), whereas experimental data for carbon-ion beams are very rare. Water calorimetry-based absorbed dose to water values have been presented for example by Brede et al (2006) showing a discrepancy to IC-based values of 3%.

Especially for carbon-ion beams experimental determinations of $k_Q$ are needed in order to reduce their high standard uncertainty and thus the overall standard uncertainty of the dosimetry of carbon-ion beams. This was done for two Farmer-type ICs in the entrance channel of a monoenergetic carbon-ion by Oisinga-Blattermann et al (2017), who achieved a standard uncertainty of 0.8%. Based on this, $k_Q$ factors for a further eight different cylindrical ICs and three different plane-parallel ICs were determined by means of cross-calibration and showed a standard uncertainty of 1.1% (Oisinga-Blattermann and Krauss 2018).

Continuing this project, $k_Q$ factors were now determined in the spread-out Bragg peak (SOBP) of a carbon-ion beam. Although Jäkel et al (2004) recommend measurements at the entrance channel of a monoenergetic beam for the calibration of the beam monitoring system of scanning systems, as is done, for example, at the Heidelberg Ion-Beam Therapy Center (HIT) (Haberer et al 2004), an additional verification of the delivered dose using measurements of the SOBP is needed. Precise dosimetry is therefore indispensable in these type of fields as well. As the SOBP is characterized by a higher linear energy transfer (LET) compared to the entrance channel, possible dependencies of $k_Q$ on the LET could be observed.

For the experimental determination of $k_{Q,P}$ the absorbed dose to water was determined by means of water calorimetry as this is the most direct method (Karger et al 2010), measuring the irradiation-induced rise in temperature. To achieve a low overall uncertainty of the resulting $k_Q$ factors, the uncertainties of the quantities influencing the calorimetric experiment must be kept low. This can be best achieved by both detailedly investigating the influence quantities and keeping the corresponding corrections low; these quantities include e.g. heat conduction effects, perturbation effects caused by the calorimetric detector itself and volume effects of the ICs. To this end, it was necessary to apply a homogeneous irradiation field of sufficient size and dose within a short time. The evaluation of a suitable irradiation technique and parameters as well as the characterization of the resulting dose distribution have been presented by Holm et al (2020).

Based on this work, we determined $k_Q$ factors for two Farmer-type ICs by means of water calorimetry, as presented in the following sections.
2. Material and methods

2.1. Irradiation technique and dose distribution

All measurements were performed at the HIT (Haberer et al 2004) using pencil beam raster scanning (Haberer et al 1993). The SOBP was created via passive modulation using a so-called 2D range modulator (2DRM) as presented in Simeonov et al (2017). The entire irradiation technique and the characterization of the resulting dose distribution are described in detail in Holm et al (2020). Summarized briefly, the irradiation field consisted of four monoenergetic layers, each of which had $36 \times 36$ spots and a spot distance of 2 mm; the layers were shifted against each other by 1 mm in the $x$-, $y$- and $xy$-directions improving the lateral uniformity of the field; the layers were irradiated in a sequence. Each spot had a focus size of 8.2 mm full width of half maximum. A dose cube of $6 \times 6 \times 6$ cm$^3$ and a dose of about 1.5 Gy was optimized in terms of homogeneity and irradiated over about 90 s using the highest clinically used particle flux of $8 \times 10^7$ ions per second.

The beam had a pulsed structure with 2.6–4.6 s per spill (a spill being the length of the extraction pulse of the synchrotron) and a mean beam-off time (spill break) of 4.1 s; the mean irradiation time per spot was 9.3 ms; per spill between 288 and 504 spots were irradiated.

An initial beam energy of 278.29 MeV/u was chosen to enable measurements in the middle of the SOBP at about a 10 cm depth in water inside the calorimeter. The resulting dose distribution can be seen in figure 1. The depth coordinates ($z$-axis, coordinate system see figure 2) are given as water-equivalent depths from the isocenter as also done in Holm et al (2020).

Field characterization measurements were performed throughout the entire set of experiments, measuring the 3D dose distribution with an IC array (Octavius 1000p, PTW, Germany) that was remote controlled depth-adjusted inside a water phantom (see Holm et al (2020)) to assess the dose distribution’s stability. The IC array consisted of 977 ICs arranged in a $11 \times 11 \times 11$ cm$^3$ grid with 2.5 mm spacing in the inner $5 \times 5$ cm$^2$ and 5 mm spacing in the outer part of the detecting area.

In addition, dose measurements for a monoenergetic beam (i.e. without 2DRM in the beam path) with an IC inside a solid water slab phantom (RW-3, PTW, Germany) positioned in the isocenter were performed repeatedly to investigate the stability of the accelerator’s output. The standard deviation of these dose measurements was considered in the determination of the overall uncertainty budget of $k_Q$.

2.2. Experimental determination of $k_Q$ factors for different ICs

$k_Q$ factors were experimentally determined in accordance with equation (2). The chamber’s calibration factor $N_{D,w,Q}$ for $^{60}$Co radiation was determined beforehand at a $^{60}$Co source using the Physikalisch-Technische Bundesanstalt (PTB) primary standard for $D_w$ (Krauss 2006a). It is important to notice here that these factors did not include corrections for the chambers’ polarity, saturation and volume effect which were therefore considered in the determination of $M_Q$ using equation (8) (as later explained in detail) in accordance with the guidelines stated in TRS-398 (Andreo et al 2006).

The chamber’s calibration factor for the beam quality $Q$, $N_{D,w,Q}$, was determined by measuring the absorbed dose to water $D_{w,Q}$ for the given beam quality and comparing it to the corrected reading $M_Q$ of the IC of interest under the same irradiation conditions. For this purpose, four measurement campaigns were carried out in
accordance with the following procedure. First, $D_{w,Q}$ was determined by means of water calorimetry as described below at a water temperature of 4 °C at a measurement depth $z$. Then, the water was heated to about 18 °C, and the calorimetric detector was replaced with an IC. IC measurements were carried out with the IC’s reference point $p_{ref}$ positioned at the measurement depth $z$. Using equation (2), it was then possible to calculate a $k_Q$ factor for the IC used.

It should be noted that these experimentally determined $k_Q$ values cannot be directly compared to values given in the literature (e.g. TRS-398 or DIN 6801-1), as there, the IC positioning and the displacement effect in $^{60}$Co are treated differently: In both TRS-398 (Andre et al 2006) and DIN 6801-1 (DIN-Normenausschuss Radiologie (NAR) 2016), to use the tabulated $k_Q$ factors at radiation quality $Q$, the chamber’s reference point $p_{ref}$ (center of the chamber) is positioned 0.75 · $r_{IC}$ deeper than the measurement position $z$, with $r_{IC}$ denoting the chamber’s radius. For the determination of $N_{Dw,Q}$, $p_{ref}$ is positioned at $z$. To include this displacement, DIN 6801-1 introduces an additional IC-dependent factor $k_r$, whereas, in the TRS report, this effect is already included in the perturbation factor $p_{Q}$ (used for the theoretical calculation of $k_Q$, see equation (3)). Following these definitions, the $k_Q$ values following are given in accordance with DIN and TRS:

$$k_Q^{DIN} = \frac{k_Q}{k_r} \cdot (1 + 0.75r_{IC} \cdot \delta_{IC})^{-1}$$

$$k_Q^{TRS} = k_Q \cdot (1 + 0.75r_{IC} \cdot \delta_{IC})^{-1}$$

with $\delta_{IC}$ as the relative depth dose gradient of the irradiation field at the measurement position. Following the definition of $k_r$ in accordance with DIN 6801-1 (DIN-Normenausschuss Radiologie (NAR) 2016), a value of $k_r = 1.009$ for both ICs used within this study can be calculated.

2.3. Calorimetric determination of $D_{w,Q}$

The absorbed dose to water $D_{w,Q}$ was determined by means of water calorimetry. Measuring the radiation-induced rise in temperature $\Delta T$, $D_{w,Q}$ is given by

$$D_{w,Q} = \Delta T \cdot c_p \cdot k_c \cdot k_h \cdot k_l \cdot k_d \cdot k_p \cdot k_r,$$

with $c_p$ denoting the specific heat capacity of water; the correction factors applied are described in section 2.3.2. The water calorimetric measurements were performed using the portable PTB water calorimeter which is presented in the following.

2.3.1. The PTB water calorimeter

The portable PTB water calorimeter is described in detail in Krauss et al (2012) and can be seen in figure 2. Summarized briefly, it consists of an insulated cubic water phantom with an edge length of 30 cm surrounded by actively cooled aluminum plates. It is operated at a water temperature of 4 °C and designed for horizontal beams.
The calorimetric detector is placed inside the water phantom. It can be mounted at different depths in water relative to the entrance window with the central beam axis matching the cylinder axis. Here, we used a geometrical measurement depth of 10 cm relative to the inner water phantom’s wall (beam entrance window) which corresponds to the middle of the SOBP (11.1 cm water-equivalent depth from the isocenter). This distance between the detector and the entrance window was checked before each measurement campaign using a digital caliper which was positioned between the phantom wall and the detector offering a measurement accuracy of 0.05 mm; a time-dependent distance change over the course of one measurement campaign due to a bowing of the entrance window was found to be negligible.

The detector consisted of a thin-walled plane-parallel glass cylinder with a 95 mm outer diameter, a 41.4 mm outside length and wall thicknesses of 0.70 mm (flat walls) and 2.5 mm (cylinder walls) (Krauss et al. 2012). The glass cylinder was filled with purified water and saturated with hydrogen as described in Krauss (2006a), and pre-irradiated with a dose of about 50 Gy to ensure that the zero heat defect, shown in Klassen and Ross (1997) takes place. Two thermistors fused into glass pipettes were mounted inside the cylinder perpendicular to the cylinder axis and opposite each other, meaning that they both had a distance to the beam axis of about 3.5 mm. Each thermistor sensor had a diameter of 0.25 mm and a resistance of about 10 kΩ at 4 °C. The glass pipettes were conically shaped with a smallest outer diameter at the end sections between 0.51 and 0.61 mm, and a diameter of the tip in which the thermistor is fused between 0.56 and 0.69 mm (values valid for the detectors used within this study).

By measuring the thermistor’s resistance change $\Delta R$ via a 1.5 V DC-powered voltage divider circuit with a well-known fixed resistor of about 20 kΩ, the radiation-induced change in temperature $\Delta T$ was determined via

$$\Delta T = -\frac{1}{S} \cdot \frac{\Delta R}{R},$$

with $S$ denoting the thermistor’s sensitivity which was verified beforehand at PTB following the calibration procedure described in Krauss (2006a), and $R$ its resistance. Each thermistor’s resistance was measured individually with a resolution better than 1 mΩ (Krauss and Kapsch 2014). The calorimetric signal measured during a single irradiation is shown by the embedded picture in figure 3; four steps can be identified within the signal which reflect the four-fold rescanning of the field (as described in section 2.1). The resistance change for each irradiation $\Delta R$ was determined in the middle of the irradiation by fitting a linear function over 110 s of the signal’s course before the irradiation and over 110 s of the signal’s course starting 10 s after the irradiation (Krauss and Kapsch 2014). We performed ten irradiations of the complete beam plan with a break of two minutes between each irradiation, as can be seen in the figure (irradiation corresponds to a decrease in the signal). This group of ten irradiations was followed by mixing the water for five minutes with a remote-
controlled mixer inside the calorimeter and waiting for the temperature distribution to stabilize for about one hour (not shown in the picture).

In total, we performed four measurement campaigns over 16 months. During each measurement campaign, 65–88 calorimetric measurements were performed. We used two different calorimetric detectors (one for the first two measurement campaigns and one for the last two) with slightly different resistances and distances to the central axis of the thermistor probes to reduce a possible influence of the detector itself on the measurement result and thus to obtain a more reliable result.

2.3.2. Water calorimetric correction factors

To correct for several effects during the water calorimetric experiment, the following correction factors are applied in equation (6):

- $k_i$ corrects for the influence of heat transport effects on the dose distribution occurring during and after the irradiation. Heat conduction effects were modeled by performing finite-element calculations using COMSOL Multiphysics (vers. 5.4). The simulation of the heat transport (done in uniform water) was split into three separate calculations since modelling the thin structures of the glass cylinder and those of the glass pipettes enclosing the thermistors (as described in section 2.3.1) in a single calculation would require an extremely high spatial resolution requiring very long computation times and a lot of memory. Therefore, within the first calculation, only the influence of the actual dose distribution given during the experiments was simulated based on the data from the detailed and repeated field characterization measurements (Holm et al 2020), no additional geometry such as the detector was implemented. Within the second calculation, the water calorimetric detector’s glass cylinder was included in the simulation, excluding the glass pipettes with the thermistor probes; these were then included in the third calculation. Thereby, the effect of the dose distribution, the glass cylinder and the glass pipettes on the heat transport can be separated from each other; these effects can be considered independently (Krauss 2006a, de Prez et al 2016). Assuming that the mentioned heat conduction effects overlap without interference, the total heat conduction correction $k_i$ is calculated multiplicatively from the correction factors for the individual effects. Since 10 measurements were performed in sequence at a time (as described in section 2.3.1) followed by about one hour break, all heat transport correction factors were calculated as the mean value of the corrections for each of the 10 irradiations. Calculations were performed for different positions of the detector caused by positioning uncertainties and using different dose distributions to account for variations in the irradiation field. The correction factors are the mean value of the respective results; the measurement uncertainty reflects their variation range.

Whilst Krauss (2006b) implemented the temporal evolution of the irradiation by simulating the sequence of single beam spots, each as a Gaussian distribution, within this study, the irradiation was divided only into single spills, assuming that each part of the field per spill is irradiated at the same time. Therefore, an averaged spill/spill break sequence and irradiation pattern were used as it is described in section 2.1. The temporal evolution of the heat transport was simulated with a resolution of 1 μs for the smallest time step directly at the beginning of an irradiation and is varied up to a maximum time step of about 0.05 s during the irradiation and the selected maximum time step of 2 s for the post drift, as was also by Osinga–Blättermann et al (2017). Due to the fourfold re-scanning of the radiation field in the study here, a larger number of spots was irradiated compared to Osinga et al resulting in a shorter irradiation time per spot (as the total irradiation times are comparable). Therefore, for the field here, the procedure to model the time evolution according to Krauss (2006b) would require time steps of much smaller than 1 ms over the entire duration of the scan. In order to reduce the associated computational effort the approximation method described above was used. This approximation method is justified by the small heat conduction coefficient of water and the short duration of one spill of maximum 4.6 s for which only very small deviations between the heat conduction of a radiation field superimposed of single spots or a field permanently present over 4.6 s would appear are to be expected.

Simulations were also performed with the whole radiation field applied at the same time (instead of only single parts of the field for single spills), while still taking the beam-on/beam-off times of the pulsed irradiation into account, to evaluate the chosen approximation of the irradiation (as irradiation of full spills at once instead of single-spill irradiation). The deviation in the results of these two irradiation schemes was considered as the uncertainty contribution of this approximation within the overall uncertainty of $k_i$.

- $k_b$ denotes the correction factor correcting for the heat defect, that describes the possible difference between the absorbed radiation energy and the energy that appears as heat. The heat defect can be caused by the radiolyses of water triggering chemical reactions in the water. Klassen and Ross (1997) performed simulations of the radiolyses of water for several aqueous systems and showed that, for high-purified, H2-saturated water,
a steady state of the radiolyses’ products is reached after a small dose, which means a zero heat defect is present; this was also shown by Domen (1994). Experiments were performed with the PTB water calorimeter at a $^{60}$Co source showing that for our setup this assumption is reasonable within a relative standard uncertainty of 0.14% (Krauss 2006a). Calculations for a passively scattered (Palmans et al 1996) as well as a scanned proton beam (Sassowsky and Pedroni 2005) confirmed a zero heat defect for protons as well. Here, we pre-irradiated the calorimetric detector filled with hydrogen-saturated water with a dose of about 50 Gy before each measurement campaign. Since there are no hints to an LET dependence, $k_p$ was assumed to be unity also for carbon ions.

- $k_i$ corrects for the lateral displacement of the thermistor probes. Because of the non-uniformity of the dose distribution, the off-axis positions of the thermistor probes (see section 2.3.1) causes a difference in the measured $D_{\text{w},C}$ compared to that of the center position. To correct for this effect, $k_i$ is given by the ratio of dose values given at the center of the irradiation field and those at the thermistor probes’ positions. The data used for this purpose was taken from the three-dimensional field characterization measurements performed via an IC array. To determine the dose values at the thermistor’s positions, the discrete measurement points were interpolated in accordance with the Nyquist–Shannon sampling theorem (Maarks 1991, Bauer 2018). For each thermistor, a correction factor $k_i$ was determined from the field characterization measurement performed before the respective measurement campaign.

- $k_g$. Due to the temperature-dependent density of water, a difference in the water-equivalent measurement depth is given for the calorimetric measurements performed at 4 °C water temperature compared to the ionometric measurements performed at room temperature. The correction factor $k_g$ is given as the ratio between the dose value at the measurement position at 4 °C and at room temperature. The dose values are determined by a linear depth interpolation of the central dose values in the SOBP taken from the field characterization measurements.

- $k_p$ is the correction factor correcting for field perturbation effects that occur due to the presence of the glass cylinder of the calorimetric detector. It was determined using measurements obtained via an IC (PTW 30013) positioned inside a glass cylinder identical to that used for the calorimetric detector and comparing the result to measurements under the same conditions without the glass cylinder. In total, 22 (20) measurements were performed with (and without) the glass cylinder. In addition, Monte Carlo (MC) simulations were performed using the FLUKA code version 2011.2 × 0.5 (Ferrari et al 2005) with the settings and geometrical setup described in Holm et al (2020). Therefore, we implemented the full glass cylinder as a geometry as well as the glass pipettes approximated by means of solid glass cylinders with a diameter of 0.5 mm. We ran two different simulations with the region of the calorimetric detector’s glass components set to water and to glass. A USRBIN card was inserted as a detector with a thermistor’s dimensions; the output was compared for both geometries.

- $k_v$ was applied to correct for the influence of a possible temperature rise of the thermistor probes due to the change in the thermistors’ electrical power during the irradiation. It was calculated theoretically based on the thermal coupling between the thermistor and the water (known from the temperature calibration of the probes) as well as the setup of the resistance-measuring circuit.

### 2.4. Ionometric measurements

To determine chamber-specific $k_Q$ factors, IC measurements under the same irradiation conditions as those given for the calorimetric measurements were performed directly after the calorimetric measurements. To this end, the chambers’ reference point $p_{\text{ref}}$ was positioned at the same depth as the thermistor probes of the calorimetric detector, but at the central beam axis. In this study, two different Farmer type ICs were used: the PTW 30013 (PTW Freiburg) and the IBA FC65G (IBA Dosimetry). The characteristics of these chambers are listed in table 1.

The ionometric measurements were performed at 18 °C water temperature. Using a measurement system developed at PTB, the IC reading, the water temperature and the air pressure were recorded at a 1 Hz frequency, allowing a continuous correction of the IC measurement signal for the air density present. During each measurement campaign, we performed 20–30 measurements for each IC.

Based on these measurements, the corrected IC reading $M_Q$ in accordance with equation (2) is given by:

$$M_Q = M_{\text{corr}} \cdot k_p \cdot k_i \cdot k_v,$$

with $M_{\text{corr}}$ denoting the IC reading at a positive operating voltage that had been corrected for the air density present and the correction factors for the polarity effect $k_p$, ion recombination effect $k_i$, and volume effect $k_v$, all three of which stand for the respective ratios of the corrections for the radiation quality $Q$ and for $Q_0$ to take these
effects in both irradiation qualities into account (as they are not considered in $N_{DwQ,0}$, see section 2.2). Their determination is described in the following:

- $k_{pol}$: The polarity effect at beam quality $Q$, $k_{pol,Q}$, was determined via

$$k_{pol,Q} = \frac{|M_{pol}| + |M_{neg}|}{2 \cdot |M_{pol}|}.$$  

$M_{pol}$ and $M_{neg}$ are the corresponding IC readings (corrected for air density effects) at positive and negative operating voltages. The correction factors $k_{pol,Q}$ at beam quality $Q_0$ were taken from the IC’s calibration certificates.

- $k_v$: For the carbon-ion irradiation field, $k_{v,Q}$ at beam quality $Q$ was determined for each IC in accordance with DIN 6801-1 (DIN-Normenausschuss Radiologie (NAR) 2016), measuring at 10 different positive and negative voltages (5 times each). The inverse of the IC readings $M$ was plotted against the inverse of the corresponding voltage $U$. By fitting a second-order polynomial

$$1/M = a_0 + a_1 \cdot \left(\frac{1}{U}\right) + a_2 \cdot \left(\frac{1}{U}\right)^2,$$  

$k_{v,Q}$ is given by

$$k_{v,Q} = 1 + \frac{a_1}{a_0} \cdot \left(\frac{1}{U_G}\right) + a_2 \cdot \left(\frac{1}{U_G}\right)^2,$$  

with $U_G$ denoting the IC’s operating voltage. Equation (10) was fitted to the data by means of a Python routine using the Optimize module from the SciPy package (Jones et al). For $k_{v,Q_0}$ at beam quality $Q_0$ a value of 1.0010 was used (Derikum 2003).

- $k_v$: As the corrected $D_{w,Q}$ is a point-like quantity, it was necessary to correct the IC measurement for a volume effect. Simplified assumptions were made to account for this effect in beam quality $Q$, since the spatial dose response functions of the ICs, as presented for photon beams in Looe et al (2013) and for electrons in Ketelhut and Kapsch (2015), are not known for carbon-ion beams. On the data basis of the field characterization measurement performed before each measurement campaign, $k_{v,Q}$ was determined as the ratio of the relative dose at the IC’s reference point and the numerical integral across the IC’s cross section. This procedure was supported by the fact that the dose distribution within the volume of interest is smooth and has no steep gradients (Holm et al 2020). The flat dose distribution of the reference $^{60}$Co field made the volume effect almost negligible; therefore $k_{v,Q_0}$ was assumed to be one.

### Table 1. Ionization chambers for which $k_Q$ factors were experimentally determined. Data taken from (PTW Freiburg) and (IBA Dosimetry). The chamber voltage gives the positive voltage at which the chambers were operated during the calorimetric measurement campaigns, as well as the maximum absolute voltage allowed (in parentheses) as used for the determination of $k_{v,Q}$. The calibration factors $N_{DwQ,0}$ were determined at $^{60}$Co using the PTB’s primary standard water calorimeter (Krauss 2006a) with a relative standard uncertainty of 0.25%.

| Quantity | PTW 30013 | IBA FC65G |
|----------|-----------|-----------|
| Active medium | Air | Air |
| Active volume (Nominal values) | 0.60 cm$^3$ | 0.65 cm$^3$ |
| Reference point (dist. from chamber tip) | 13 mm | 13 mm |
| Chamber voltage | 400 V (500 V max.) | 300 V (500 V max.) |
| $N_{DwQ,0}$ | 5.369·10$^7$ Gy C$^{-1}$ | 4.811·10$^7$ Gy C$^{-1}$ |
3. Results

3.1. Calorimetric measurements and correction factors

In total, we performed 282 calorimetric measurements in four measurement campaigns following the measurement procedure describe in section 2.3.1. The resulting values of \( D_T \) from both thermistors and over all calorimetric measurements as well as their relative standard deviations are shown in figure 4.

The distribution of the single results of each measurement campaign shows no clear trends, which justifies the use of the mean values for each campaign and thermistor together with the corresponding individual correction factors to determine \( D_{w,Q} \).

The correction factors needed for the calorimetric measurements were determined as described in section 2.3 and are given in table 2.

The correction factor for heat transport effects \( k_c \) was determined as the product of the three factors determined from the individual calculations described in section 2.3.2. It should be noted here that the uncertainties of the three factors only reflect the range of variation resulting from the calculations based on the different dose distributions implemented. And at this point they do not include uncertainties of the material parameters, these were considered as an additional uncertainty contribution in the overall standard uncertainty of \( k_c \).

For the influence of the glass cylinder, a correction factor of 0.9996 was obtained with a standard uncertainty of 0.03%. The effect of the glass pipettes enclosing the thermistor probes resulted in a factor of 0.9972 with a standard uncertainty of 0.01%. Here, the mean diameter of the glass tips enclosing the thermistor probes was implemented. Knowing the dependence of the heat conduction on the diameter from earlier

Table 2. Correction factors determined for the calorimetric determination of \( D_{w,Q} \) and their relative standard uncertainties. If two values are given, different values for each of the two thermistors were found. For \( k_l \) and \( k_e \), different values for each measurement campaign have to be applied due to the different characteristics of the detectors used and small deviations in the measured dose distributions, their mean value is listed here. All other correction factors are valid for all measurements.

| Correction factor                        | Value     | Rel. standard uncertainty/% |
|------------------------------------------|-----------|----------------------------|
| Heat transport effects \( k_c \)         | 0.9979    | 0.40                       |
| Heat defect \( k_h \)                    | 1.0000    | 0.14                       |
| Lateral displacement \( k_l \)           | 1.0011; 1.0030 | 0.14               |
| Measurement depth at different water temperatures \( k_d \) | 1.0001   | 0.10                       |
| Perturbation effect \( k_p \)            | 1.0000    | 0.11                       |
| Influence of the thermistors’ electrical power \( k_e \) | 1.0003; 1.0003 | 0.01               |

Figure 4. Plot of the radiation-induced temperature rise \( \Delta T \) determined from the calorimetric measurement signal for each measurement point. The relative standard deviation of the given \( \Delta T \) values for each measurement campaign and each thermistor are listed in the legend.
For the PTW sensitivity, an additional uncertainty contribution of 0.08% was estimated to account for the maximum deviation of the thermistor probes’ diameter from the mean value used. Considering the dose distribution of the irradiated field, a factor of 1.0011 was determined as the mean value over each individual dose distribution measured. Its standard uncertainty of 0.10% included the uncertainty contribution due to fluctuations in the dose distribution. For the overall uncertainty of $k_p$, a contribution caused by the approximation of the irradiation’s time structure (irradiation of full spills at once instead of single-spill irradiation) of 0.15% and a contribution due to the different parameters used for the calculation were also taken into account. This results in a $k_p$ of 0.9979 with a standard uncertainty of 0.40%. Hereby, a value < 1 for the heat conduction correction factor means that taking the heat conduction effects into account reduces the measured temperature rise $\Delta T$ to obtain the correct value of $D_{\text{MC}}$, as it directly follows from equation (6).

As the calorimetric detector was filled with hydrogen-saturated water and pre-irradiated with about 50 Gy before each measurement campaign, a zero heat defect ($k_h = 1$) was assumed with a standard uncertainty of 0.14% (Krauss 2006a).

Both correction factors for the lateral displacement of the thermistor probes relative to the beam axis $k_l$ as well as for the difference in the measurement depth at 4 °C and at room temperature $k_d$ were based on the field characterization measurements.

$k_l$ was calculated for each thermistor position individually as these positions were different; the value given in table 2 is the mean of these values showing a relative standard deviation of 0.12%. The ratio of dose values at the measurement position and at the thermistor probes’ positions were calculated for each measurement campaign based on the respective field characterization measurement performed directly before the campaign. The measurement uncertainty of 0.14% was calculated as the standard deviation of a mean $k_l$ based on all field characterization measurements, addressing the influence of a possible fluctuation of the dose distribution. The influence of a positioning uncertainty is considered in an additional uncertainty contribution (see section 3.4).

For the determination of $k_h$, a linear function was fitted to the plateau region (90 mm $\leq z \leq 140$ mm) of the depth dose distribution taken from the field characterization measurements, showing a gradient of $-0.9$ mGy mm$^{-1}$. Based on this, a difference in dose values of 0.013% was found for a depth shift of 0.146 mm (due to a temperature-dependent water density). The standard uncertainty of 0.10% was estimated on the basis of the uncertainty of the linear fit and variations between the repeated field characterization measurements.

The perturbation effect caused by the glass cylinder was found to be of the same order as its uncertainty, which is mainly influenced by the standard deviation of repeated measurements, but also takes positioning uncertainties of the IC inside the calorimeter into account. The MC simulations performed supported this result. Therefore, $k_p$ was assumed to be unity with a standard uncertainty of 0.05%. As the glass pipettes of the detector were only approximated in the simulation (as described in section 2.3), an additional uncertainty contribution of 0.1% was assumed. This led to an overall uncertainty of 0.11% for $k_p$.

This very small field perturbation compared to values found for example for $^{60}$Co irradiation ($k_p = 1.0013$ (Krauss 2006a)) can be explained by the low scattering behavior of the heavy primary particles, which make up the majority of particles in the beam at the measurement position (Holm et al 2020). Therefore, only the very thin front walls of the cylinder played a role in the field perturbation, which was noticeable mainly via a change in the maximum range of the particles.

$k_l$ was calculated for each measurement campaign and each thermistor individually, as the measured resistance change differed slightly between the experiments, and as each thermistor showed a different thermal coupling between the thermistor and the water and has a different resistance. The mean value is given in table 2. The standard uncertainty of 0.01% is determined by the standard uncertainty of the measured temperature rise, the thermistors’ resistance and the change in this resistance as well as the uncertainty of the thermistors’ sensitivity.

### 3.2. Ionometric measurements and correction factors

For the PTW 30013, $M_{\text{ion}}$ showed a mean relative standard deviation of the measured values of 0.16%; for the IBA FC65G, this was 0.12%. The correction factors determined for the correction of the ionometric measurements as well as their relative standard uncertainties are given in table 3.

The correction factor for the polarity effect for the beam quality Q, $k_{\text{pol/Q}}$, was determined during each measurement campaign, resulting in a mean $k_{\text{pol/Q}}$ of 1.0006 for the PTW 30013 and 1.0010 for the IBA FC65G. The final values for $k_{\text{pol}}$ are given in table 3. Their standard uncertainty was determined based on the standard deviation of the repeated measurements performed at beam quality Q of 0.06% and an assumed standard uncertainty of $k_{\text{pol/Q}}$, of 0.05%, yielding an overall standard uncertainty for $k_{\text{pol}}$ of 0.08%.

To determine the correction factor for the saturation effect $k_{\text{s/Q}}$, the inverse of the mean measured values, $1/M$, was plotted against the inverse voltages, $1/U$, and fitted in accordance with equation (10) as shown in figure 5. When equation (11) was applied, $k_{\text{s/Q}}$ was found to be 1.0018 for the PTW 30013 and 1.0046 for the IBA FC65G showing a relative standard uncertainty of 0.20%, which was determined via the uncertainty of the
yielded fitting parameters, while taking the standard deviation of the repeated measurements into account. The resulting $k_v$ is given by the ratio of $k_{v,Q}$ and $k_{v,Q} = 1.0010$ at beam quality $Q_0$. Taking an uncertainty contribution of 0.05% for $k_{v,Q}$ into account, this results in an overall standard uncertainty of $k_v$ of 0.20%.

The correction factor for the volume effect $k_{v,Q}$ for beam quality $Q$ was calculated by numerically integrating the dose distribution across the IC’s cross section and dividing the dose value at the chamber’s reference point by the integration result. For the numerical integration, we tested two determination methods: simply by summing up all measurement points measured with the IC array inside the IC’s volume, and by first interpolating the dose values and then integrating the resulting dose distribution. It was found that the determined values for $k_{v,Q}$ based on the two methods differed by only 0.004%. Values for $k_{v,Q}$ were determined for every field characterization measurement performed before a measurement campaign; the mean of these values is given in table 3 with a relative standard deviation of 0.16%. In addition, $k_{v,Q}$ was calculated based on the field characterization measurements performed in Holm et al (2020); the standard deviation of 0.21% of all $k_{v,Q}$ values found was considered as $k_{v,Q}$’s standard uncertainty which takes possible dose fluctuations into account. Due to the influence of a possible positioning uncertainty of the IC as well as the assumptions made due to the lack of the IC’s spatial dose response function in carbon-ion beams, an additional uncertainty for the determination method of $k_{v,Q}$ of 0.1% was assumed. As $k_{v,Q} = 1$ was assumed for beam quality $Q_0$ (see section 2.4), $k_v = k_{v,Q}$.

The value for $k_v$ is given in table 3. As both ICs have nearly the same active volume, the $k_v$ determined are identical for both ICs due to the IC array’s spatial resolution with which the integrated dose distribution had been measured.

### 3.3. Determination of $k_Q$-factors

$k_Q$ was calculated from the measured data for both ICs in accordance with equation (2) while taking all correction factors for the influencing quantities presented into account. The resulting $k_Q$ values for each measurement campaign are shown in figure 6. Unfortunately, in the first measurement campaign, only the IBA FC65G chamber could be used.

For a better comparison of the $k_Q$ values determined, the error bars indicate an overall uncertainty based on the uncertainties of influencing quantities that depend on the given measurement situation; this uncertainty is 0.4% for all measurement campaigns and ICs. Quantities that stay constant between the single measurements, such as $N_{D_{w,Q}}$ and $c_p$, are not included in the uncertainty indicated by the error bars.

Further, the experimental $k_Q$ values were expressed in accordance with TRS-398 and DIN 6801-1 (see section 2.2) for a direct comparison with the calculated $k_Q$ factors given in the protocols. The result is shown in table 4.
an uncertainty of the measurement of temperature and air pressure, was considered, together with the uncertainty contributions of the different correction factors described above (section 3.2). Two positioning

3.4. Uncertainty budget for \( k_Q \)

An uncertainty budget for the entire determination procedure was estimated for an overall standard uncertainty for \( k_Q \). The budget was calculated in accordance with the Guide to the Expression of Uncertainty in Measurement (GUM) (Joint Committee for Guides in Metrology 2008) using the GUM workbench (Metrodata GmbH 2017). The majority of the stated quantities refer to type B uncertainties except for values which were determined from repeated measurements such as the uncertainty contribution of the temperature rise \( \Delta T \) or the air-density corrected IC reading \( M_{corr} \). The combined standard uncertainty budget is given in table 5. As the uncertainties were quite similar, this budget is valid for both ICs and all measurement campaigns.

The standard uncertainty for the absorbed dose to water \( D_{w,kQ} \) is determined by the temperature rise \( \Delta T \) and the different correction factors applied. The uncertainty of \( \Delta T \) is based on the uncertainties of the measured quantities \( \Delta R (0.20\%) \) and \( R (0.02\%) \), and the thermistors’ sensitivity \( S (0.07\%) \). A contribution to the uncertainty of \( \Delta T \) due to the determination method for \( \Delta R \) of 0.08\% as well as the influence of a possible temperature background drift (0.24\%) was also included. The uncertainty of the determination method for \( \Delta R \) was determined by varying the time window for the linear interpolation of the signal before and after the irradiation by ±2 s (see section 2.3.1) and comparing the resulting values for \( \Delta R \); the uncertainty was conservatively estimated as the maximum deviation from the actual \( \Delta R \) value that was found within all measurements. Analyzing the influence of a possible change of the calorimeter’s background drift, the calorimetric signal was linearly interpolated over a course of 60 s at varying positions directly before a new group of irradiations. The standard deviation of the slopes’ values obtained was found to be \( 0.1 \cdot 10^{-4} \Omega \text{ s}^{-1} \) leading to deviations in the extrapolation to the mid run middle of an irradiation (where \( \Delta R \) was obtained, 45 s after starting the irradiation) of \( 4.5 \cdot 10^{-4} \Omega \). This results in a relative deviation from the mean \( \Delta R \) of 0.24\%. This was taken as the uncertainty contribution of the temperature background drift.

As the calorimetric detector (and thus the thermistors) is tightly fixed in place inside the calorimeter, only a positioning uncertainty of the calorimeter itself relative to the beam of 0.5 mm was considered. Its influence on the correction factors \( k_i \) which are based on the dose distribution, was estimated as the uncertainty contribution.

For the overall standard uncertainty of the ionometric measurements, the standard uncertainty of the corrected IC reading, which resulted from the standard deviation of repeated IC measurements as well as from an uncertainty of the measurement of temperature and air pressure, was considered, together with the uncertainty contributions of the different correction factors described above (section 3.2). Two positioning

### Table 4. Comparison of experimental \( k_Q \) factors (This work) with values for \( k_Q \) given in TRS-398 (Andreos et al 2006) and DIN 6801-1 (DIN-Normenausschuss Radiologie (NAR) 2016) (Literature). Relative standard uncertainties are given in parentheses; for the experimental values these are explained in detail in the section 3.4 below.

|            | This work | PTW 30013 | Literature | Δ/% | This work | IBA FC65G | Literature | Δ/% |
|------------|-----------|-----------|------------|-----|-----------|-----------|------------|-----|
| TRS        | 1.016 (0.69\%) | 1.032 (2.8\%) | 1.55 | 1.018 (0.69\%) | 1.042 (2.8\%) | 2.31 |
| DIN        | 1.007 (0.69\%) | 1.014 (2.2\%) | 0.70 | 1.009 (0.69\%) | 1.012 (2.2\%) | 0.29 |

Figure 6. Values for \( k_Q \) calculated for each measurement campaign for the PTW 30013 (left) and the IBA FC65G (right). The respective mean value is indicated by the dashed lines. Error bars show the uncertainty of each \( k_Q \) value due to possible deviations between each experiment.
uncertainties, one of the calorimeter itself (0.5 mm) and one of the IC inside the calorimeter (another 0.5 mm) were also taken into account. Their uncertainty contribution of 0.03% describes the influence on the ionometric correction factor $k_v$ which is based on the dose distribution.

The overall standard uncertainty for $k_Q$ of 0.69% is mainly influenced by the uncertainty of the determined absorbed dose to water $D_{w,Q}$ as well as the corrected IC reading $M_Q$ of 0.32%. The uncertainty of the chamber-specific calibration factor $N_{D,w,Q}$ determined at the PTB primary standard also contributes to the overall standard uncertainty. As both $N_{D,w,Q}$ and $D_{w,Q}$ are based on water calorimetry, the uncertainty contributions specific for the water calorimetric experiment (marked with a *) to the overall uncertainty are correlated, as it can be also concluded from equation (2). Taking this correlation into account, the contribution of the standard uncertainty of $D_{w,Q}$ to the overall standard uncertainty of $k_Q$ is reduced to 0.53%. For the uncertainty contribution of $N_{D,w,Q}$, a reduced value of 0.20% has to be considered.

An additional uncertainty contribution due to temporal fluctuations in dose application, that can appear during the each measurement campaign, was also included. It is given by the relative standard deviation of the repeated IC measurements in the monoenergetic beam at the isocenter (as described in section 2.1) from each other.

### 4. Discussion and conclusion

In this work, we have shown that it is possible to determine $k_Q$ in the SOBP of a carbon-ion beam with a standard uncertainty below 1%. Here, the quantity that has the greatest influence on the overall uncertainty is the correction for the heat conduction (with a relative standard uncertainty of 0.4%) as well as the temperature rise measured (0.3%).

Comparing the experimental result with values for $k_Q$ taken from the literature (table 4, figure 7), differences of up to 2.3% can be found. These differences could be explained by the values for the stopping power ratio

| Quantity | Rel. standard uncertainty/\% |
|----------|-----------------------------|
| Calorimetric measurements |                           |
| Absorbed dose to water $D_{w,Q}$ | 0.55 |
| Temperature rise $\Delta T$ | 0.33 |
| Specific heat capacity of water $c_p$ | 0.03* |
| Correction for heat conduction effects $k_c$ | 0.40 |
| Correction for heat defect $k_h$ | 0.14* |
| Correction for lateral displacement $k_l$ | 0.14 |
| Correction for measurement depth at $4 ^\circ C$ $k_d$ | 0.10 |
| Correction for field perturbation by the detector $k_p$ | 0.11 |
| Correction for thermistor’s electrical power $k_e$ | 0.01 |
| Positioning uncertainty of the calorimeter | 0.06 |
| Ionometric measurements |                     |
| Corrected IC reading $M_Q$ | 0.32 |
| Air-density corrected IC reading $M_{corr}$ | 0.04 |
| Uncertainty of the measurement of temperature and air pressure | <0.01 |
| Correction for polarity effect $k_{pol}$ | 0.08 |
| Correction for saturation effect $k_{s,Q}$ | 0.20 |
| Correction for volume effect $k_v$ | 0.21 |
| Uncertainty of the determination method for $k_v$ | 0.10 |
| Positioning uncertainty of the calorimeter and the IC | 0.03 |
| Calibration factor for IC $N_{D,w,Q}$ | 0.25* |
| Time stability of $N_{D,w,Q}$ | 0.10 |
| Uncertainty contribution due to temporal fluctuations in dose application | 0.21 |
| Correction factor for beam quality $k_Q$ | 0.69 |
\( W_{\text{air}} Q \) and the mean excitation energy per ion pair \( W_{\text{air}} Q \) in the carbon-ion beams applied for the theoretical calculation of \( k_Q \) (equation (3)) differing from the experimental situation. Furthermore, it is possible that the assumption of a perturbation factor \( p_Q \) of unity (as stated in both TRS-398 and DIN 6801-1) is insufficient.

Based on the key data for stopping power ratios and \( W_{\text{air}} Q \) presented in the ICRU 90 report (Seltzer et al 2016), a change in \( k_Q \) compared to the values stated in TRS-398 of \(-0.5\%\) can be concluded. This would reduce the differences to the experimental values presented here to 1.04\% for the PTW 30013 and 1.80\% for the IBA FC65G. Nonetheless, more experimental data is needed for a comprehensive comparison of the experiment and the literature.

For the entrance channel, Osinga-Blättermann et al (2017) determined an experimental \( k_Q \) factor of 1.036 ± 0.8\% for the PTW 30013 and 1.030 ± 0.8\% for the IBA FC65G (values in accordance with TRS-398). Compared to the factor found for the SOBP, a difference of 1.9\% for the PTW 30013 and 1.1\% for the IBA FC65G is given (see figure 7). These differences might be explained by a possible LET dependence of \( k_Q \), which needs to be investigated further. We calculated and compared stopping power ratios as a function of the residual range in accordance with the equation stated in DIN 6801-1 (DIN-Normenausschuss Radiologie (NAR) 2016) for both situations. Though, for this calculation, we used the parameter values derived by Burigo and Greilich (2019), as they are based on the newer key data from ICRU 90 (Seltzer et al 2016). This gives a 0.3\% larger stopping power ratio for the SOBP compared to the entrance channel. If one assumes \( W_{\text{air}} Q \) and \( p_Q \) to remain constant between SOBP and entrance channel (as also stated in DIN6801-1 (DIN-Normenausschuss Radiologie (NAR) 2016)), this would predict a 0.3\% larger \( k_Q \) for the SOBP. In contrast, in this study, the \( k_Q \) values found for the SOBP decreased by up to 1.9\%.

A possible dependence on the primary energy of the ions, as stated for the stopping power ratio in pristine Bragg peaks by Lühr et al (2011), should also be examined, as this differed in the experiments mentioned.

These measurements have made experimental \( k_Q \) values available for the SOBP for the first time. The use of such experimental \( k_Q \) factors as they were presented here would substantially reduce of the uncertainty in dosimetry for carbon-ion beams. However, an enlargement of the data base is still needed. In principle, it is confirmed that water calorimetry is excellently suited for the experimental determination of \( k_Q \) factors with low measurement uncertainties also in carbon-ion beams.

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