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### Consistency in quality correction factors for ionization chamber dosimetry in scanned proton beam therapy

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**Purpose:** The IAEA TRS-398 code of practice details the reference conditions for reference dosimetry of proton beams using ionization chambers and the required beam quality correction factors ( $k_Q$ ). Pencil beam scanning (PBS) systems cannot approximate reference conditions using a single spot. However, dose distributions requested in TRS-398 can be reproduced with PBS using a combination of spots. This study aims to demonstrate, using Monte Carlo (MC) simulations, that  $k_Q$  factors computed/measured for broad beams can be used with scanned beams for similar reference dose distributions with no additional significant uncertainty.

**Methods:** We consider the Alfonso formalism<sup>13</sup> usually employed for nonstandard photon beams. To approach reference conditions similar as IAEA TRS-398 and the associated dose distributions, PBS must combine many pencil beams with range or energy modulation and shaping techniques that differ from those used in passive systems (broad beams). In order to evaluate the impact of these differences on  $k_Q$  factors, ionization chamber responses are computed with MC (Geant4 9.6) in three different proton beams, with their corresponding quality factors (Q), producing a 10 × 10 cm<sup>2</sup> field with a flat dose distribution for (a) a dedicated scanned pencil beam ( $Q_{pbs}$ ), (b) a hypothetical proton source ( $Q_{hyp}$ ), and (c) a double-scattering beam ( $Q_{ds}$ ). The tested ionization chamber cavities are a 2 × 2 × 0.2 mm<sup>3</sup> air cavity, a Roos-type ionization chamber, and a Farmer-type ionization chamber.

**Results and Discussion:** Ranges of  $Q_{pbs}$ ,  $Q_{hyp}$ , and  $Q_{ds}$  are consistent within 0.4 mm. Flatnesses of dose distributions are better than 0.5%. Calculated  $k_{Qpbs}^{f_{pbs},f_{ref}}$  is 0.999  $\pm$  0.002 for the air cavity and the Farmer-type ionization chamber and 1.001  $\pm$  0.002 for the Roos-type ionization chamber. The quality correction factors  $k_{Qpbs,Q_{ds}}^{f_{pbs},f_{ref}}$  is 0.999  $\pm$  0.002 for the Farmer-type ionization chamber. The numbers and 1.001  $\pm$  0.002 for the Farmer-type and Roos-type ionization chambers and 1.001  $\pm$  0.002 for the Farmer-type and Roos-type ionization chambers and 1.001  $\pm$  0.002 for the Roos-type ionization chamber.

**Conclusion:** The Alfonso formalism was applied to scanned proton beams. In our MC simulations, neither the difference in the beam profiles (scanned beam vs hypothetical beam) nor the different incident beam energies influenced significantly the beam correction factors. This suggests that ionization chamber quality correction factors in scanned or broad proton beams are indistinguishable

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within the calculation uncertainties provided dose distributions achieved by both modalities are similar and compliant with the TRS-398 reference conditions. © 2017 American Association of Physicists in Medicine [https://doi.org/10.1002/mp.12434]

Key words: beam quality correction factors, pencil beam scanning, proton therapy, reference dosimetry

#### 1. INTRODUCTION

Absorbed dose must be determined with high accuracy for successful radiotherapy. Dosimetry methods applied at any radiotherapy facility must be consistent or traceable with those at other facilities to compare clinical data.<sup>1</sup> Today, most scattered-beam proton therapy centers are following dosimetry guidelines of the IAEA TRS-398 Code of Practice<sup>2</sup> (CoP) or ICRU 78,<sup>1</sup> which are equivalent, except for a few details. Both rely on an absorbed dose-to-water based formalism. TRS-398 provides reference conditions for reference dosimetry of most types of external radiotherapy beams. While calorimeters are generally regarded as the only instruments that measure absorbed dose directly, they are not practical for routine use in the clinic and no proton center has one available on a permanent basis. Typically, dosimeters used for reference dosimetry as well as in clinical daily routines are ionization chambers since they provide fast, reliable, and reproducible readout. For reference dosimetry, ionization chambers are calibrated under well-defined reference conditions in a calibration beam quality  $Q_0$  (typically a <sup>60</sup>Co beam). A correction factor,  $k_{Q,Q_0}$ , specific to the ionization chamber is applied to take into account differences in ionization chamber response between the user beam quality Q and the reference beam quality  $Q_0$ .

For a majority of ionization chambers in clinical use, the  $k_{Q,Q_0}$  factors are calculated based on theoretical assumptions. Some experimental values have also been published in the literature.<sup>3,4</sup> Quality correction factors  $k_{Q,Q_0}$  proposed in TRS-398 have been validated for broad beams only, as from the start of proton beam therapy until early 2000s, most of proton therapy centers were using broad beam techniques to control the shape and the depth of penetration (range) of proton beams. Newly built proton therapy centers, however, use an active scanning technique, the pencil beam scanning (PBS),<sup>5</sup> spot scanning,<sup>6</sup> or raster scanning.<sup>7</sup> With these modalities, reference conditions cannot be reproduced with a single beam to deliver a homogeneous dose distribution over a sufficient distance perpendicular to the beam axis.

There is at present no consensus on what the best way is to calibrate scanned proton beams; the methods implemented in hospitals can be divided in three categories<sup>8,9</sup>:

- the use of a Faraday cup to calibrate the beam monitor directly in terms of the number of protons in a single spot.<sup>6,10</sup>
- the use of a large-area plane-parallel ionization chamber in the entrance plateau of a single static spot to calibrate the beam monitor directly in terms of dose-area-product.<sup>11</sup>

• the use of a cylindrical or plane-parallel reference ionization chamber in the entrance plateau of a single energy layer scanned field to calibrate the beam monitor indirectly in terms of dose-area-product of a single spot.<sup>4,5,12</sup>

The first approach, involving a Faraday cup, may seem logical since the pencil beam dose calculation algorithms in planning systems are based on the proton fluence of each spot. However, the uncertainty on the stopping powers used, combined with the uncertainty on the exact spectrum of charged particles (primary protons + protons produced in nuclear interactions), makes that the uncertainty of this approach is substantial. In the other two approaches, dose-area-product has to be divided by the stopping power at the depth of measurement to derive the number of protons in a spot, but this divider is highly correlated with the stopping power with which the fluence is multiplied in the dose calculation. Pseudomonoenergetic calibration might be better to minimize the errors in the calibration at low-energy layers. These lowenergy layers will have a low weight, and an error on these energy layers might be diluted. The limitation of the Faraday cup approach is also suggested by Pedroni et al.,<sup>6</sup> who performed dosimetry according to IAEA TRS-398 in  $10 \times 10 \times 10$  cm<sup>3</sup> box irradiations to determine correction factors to the entire, energy-dependent Faraday cup-based calibration curve. These types of box fields are delivered using a complex sequence which is very clinic like and which provides a homogeneous dose distribution within the box volume. Such field fulfills also the criteria of a plan-class-specific reference (pcsr) field according to the dosimetry formalism developed by Alfonso et al.,<sup>13</sup> a nonstandard field for IAEA TRS-398.

The formalism described by Alfonso et al.<sup>13</sup> introduces additional correction factors to link the reference dosimetry of nonstandard fields to current CoPs. We propose to apply this formalism to PBS delivery in order to evaluate the consistency of quality correction factors  $k_{Q,Q_0}$  between broad and scanned beams. In other words, our aim is to isolate and quantify the impact in quality correction factors  $k_{Q,Q_0}$  of using scanned beams instead of broad beams for comparable reference conditions. We will rely on Monte Carlo simulations, as they have proven in past studies in photon therapy their capability to compute ionization chamber dose responses for standard<sup>14–16</sup> and nonstandard beams.<sup>17,18</sup>

#### 2. METHODS

Reference conditions for proton beam therapy as recommended by the TRS-398 CoP are detailed in Section 2.A. Both broad and scanned therapy beam differences are described in Section 2.B. Using the analogy to photon beams, Section 2.C proposes an application of the Alfonso formalism for nonstandard proton beams. A description of Monte Carlo simulation is given in Section 2.D. Ionization chamber specifications are described in Section 2.E.

#### 2.A. Background theory

The TRS-398  $\text{CoP}^2$  provides guidelines for user-specific beams based on the absorbed dose-to-water formalism. These recommendations are based on the use of ionization chamber dosimeters having calibration factors of absorbed dose-towater in a reference beam quality Q<sub>0</sub> (<sup>60</sup>Co). The absorbed dose-to-water at the reference depth  $z_{\text{ref}}$  in a proton beam quality Q is given by

$$D_{w,Q} = M_Q N_{D,w,Q_0} k_{Q,Q_0}$$
(1)

where  $M_Q$  is the ionization chamber reading corrected for different influence quantities such as temperature, atmospheric pressure, polarity, electrometer calibration, and ion recombination. The coefficient  $N_{D,w,Q_0}$  is a calibration coefficient of the dosimeter in terms of absorbed dose-to-water in a beam quality  $Q_0$  and  $k_{Q,Q_0}$  is a correction factor specific to the ionization chamber to take into account differences between the user beam quality Q and the reference beam quality  $Q_0$ . The measurement is performed in a water phantom at the position  $z_{ref}$ , usually the middle of a Spread Out Bragg Peak (SOBP) or the plateau region for single energy beam applications. The recommended field size at phantom surface is  $10 \times 10 \text{ cm}^2$ , or that used for normalization of the output factors whichever is larger.

Since no primary standards of absorbed dose-to-water for proton beam quality are available,  $k_{Q,Q_0}$  values provided in TRS-398 code of practice are calculated using MC simulations of Spencer-Attix stopping power ratios.<sup>19,20</sup> These calculations are for broad monoenergetic proton beams. Ionization chamber perturbations in proton beams are assumed to be negligible.

#### 2.B. Proton beam therapy systems

A number of the proton therapy centers still use the passive scattering technique to control the shape and the range of proton beams. The proton beam coming from the accelerator through the beam line is a few millimeters wide until it reaches the treatment head nozzle. Scatter material is then used to broaden the beam and range-shifting material ensures the adjustment of the proton range modulation. Nowadays, proton therapy centers are progressively shifting toward an active scanning technique, sometimes referred to as PBS. The pencil beam coming from the beam line is deflected using scanning magnets in the nozzle. The target volume can be scanned with a few millimeters wide proton beams in three dimensions. Each position of a scanned pencil beam, defined as the terminal end of a beamlet around which most of its dose is deposited, is commonly called "spot" and the dose of each spot might be adjusted so that all beamlets combined

result in the prescribed dose, e.g., cover uniformly the targeted tumor volume(s). Passive scattering and PBS may present differences in beam qualities for a similar dose distribution (e.g., a  $10 \times 10 \times 10$  cm<sup>3</sup> homogeneous box). First, the PBS technique uses a composition of small, magnetically focused beams while passively scattered beams are broad beams. Second, the technologies to control range coverage are also different, potentially resulting in a different proton energy spectrum within the target volume. These differences may affect the dosimetric response of ionization chambers. Finally, passive scatter materials are producing contamination under the form of low-energy protons due to grazing-incidence in the collimator, secondary protons, and neutrons from nuclear interactions in the beam shaping components.

### 2.C. Application of Alfonso formalism for reference dosimetry of nonstandard beams to PBS

Alfonso formalism introduces a machine-specific reference field ( $f_{msr}$ ) for treatment machines that cannot deliver the static conventional reference field.<sup>13</sup> This is typically used for nonstandard reference photon fields, e.g., TomoTherapy or CyberKnife. This formalism can be used to extend Eq. 1 to be applicable to an msr field of a proton PBS-dedicated machine, e.g., a static pencil beam. Then, the absorbed doseto-water is given by the following:

$$D_{w,Q_{msr}}^{f_{msr}} = M_{Q_{msr}}^{f_{msr}} N_{D,w,Q_0} k_{Q,Q_0} k_{Q_{msr},Q}^{f_{msr},f_{ref}}$$
(2)

where  $f_{ref}$  is the reference field compliant with TRS-398 reference conditions. The quality  $Q_{msr}$  is the machine-specific reference quality delivered by the machine-specific reference field  $f_{msr}$ .

As discussed in Section 1, the use of a machine-specific reference field for reference dosimetry in PBS might not be appropriate for this study. The type of reference field (a spot) is not able to cover an ionization chamber uniformly, while the reference box fields described in TRS-398 CoP are very clinic like and fulfill the criteria of plan-class-specific reference field described by Alfonso et al.<sup>13</sup> In the case of absorbed dose-to-water in a composite field, like in PBS, instead of using a machine-specific reference field (pcsr). In that case,  $f_{msr}$  is replaced by  $f_{pcsr}$ ,  $Q_{pbs} \equiv Q_{pcsr}$  and Eq. 2 becomes

$$D_{w,Q_{pesr}}^{f_{pesr}} = M_{Q_{pesr}}^{f_{pesr}} N_{D,w,Q_0} k_{Q,Q_0} k_{Q_{pesr},Q}^{f_{pesr},f_{ref}}$$
(3)

The three calibration methods listed in the introduction, all establish a calibration curve as a function of energy. Calibration in "pcsr" fields, which are multi-energy layer fields, aims at establishing a correction for the entire calibration curve, similar to what Pedroni et al.<sup>6</sup> have done, so as to provide a calibration curve for conditions that are representative for a clinical field.<sup>9</sup>

The correction factor  $k_{Q_{pesr},Q}^{f_{pesr},f_{ref}}$  accounts for differences in beam qualities between a broad proton beam (i.e., using

passive scattering) of quality Q and a PBS quality  $Q_{pcsr}$ , for a similar dose distribution.

Geometrical and fluence dissimilarities in proton beam delivery, stated in Section 2.B, can be treated following two options:

1. According to Alfonso et al.,<sup>13</sup> Q could be a hypothetical broad beam quality  $Q \equiv Q_{hyp}$ . Henceforth, the beam quality Q will be replaced by  $Q_{hyp}$  and  $f_{ref}$  by  $f_{hyp}$ in the following equations. The hypothetical field with beam quality Q<sub>hyp</sub> is a standard reference beam according to IAEA TRS-398 (so that we can take  $k_{Q_{hvp},Q_0}$  from that report) but which cannot be realized at the machine that is being calibrated. In the context of this article, this hypothetical field has the spectrum of a scanned field (pcsr) but is delivered as a broad beam. It is distinct from the double-scattering field with beam quality Q<sub>ds</sub>, which has a different spectrum because of the scatterers, collimators, and other beam shaping components, i.e.,  $Q_{hyp} \neq Q_{ds}$ . The qualities  $Q_{hyp}$  and  $Q_{pcsr}$ are simulated so that dose distributions have the same range modulation within 0.5 mm and are in agreement within  $\pm$  0.5% in the SOBP. TRS 398 mentions that the magnitude of the displacement correction factor (p<sub>dis</sub>) is unlikely to exceed 0.5%. TRS-398 estimated an uncertainty of 0.2% on p<sub>dis</sub>. Then, the correction factor  $k_{Q_{pesr},Q_{hyp}}^{f_{pesr},f_{hyp}}$  is introduced, so that:

$$D_{w,Q_{pesr}}^{f_{pesr}} = M_{Q_{pesr}}^{f_{pesr}} N_{D,w,Q_0} k_{Q_{pesr},Q_{hyp}}^{f_{pesr},f_{hyp}} k_{Q_{hyp},Q_0}^{f_{hyp}}$$
(4)

$$k_{Q_{pcsr},Q_0|1} = k_{Q_{pcsr},Q_{hyp}}^{f_{pcsr},f_{hyp}} k_{Q_{hyp},Q_0}^{f_{hyp}}$$
(5)

Here, the fields  $f_{pcsr}$  and  $f_{hyp}$  are producing similar (within  $\pm~0.5\%$ ) dose distribution in the SOBP region and have an identical incident energy set. Therefore, the quality correction factor  $k_{Q_{pcsr},Q_{hyp}}^{f_{pcsr},f_{hyp}}$  accounts only for the different spatial distributions of the protons at the nozzle exit (composite versus broad beam). It is expected that  $k_{Q_{pcsr},Q_{hyp}}^{f_{pcsr},f_{hyp}}$  is close to unity under the above assumption.

2. One can check if different incident beam energy sets and beam shaping items have to be taken into account under the same assumptions stated earlier (similar range modulation and dose distribution). Then,  $k_{Q_{pest},Q_{ds}}^{f_{pest},f_{ds}}$  is directly evaluated and

$$D_{w,Q_{pesr}}^{f_{pesr}} = M_{Q_{pesr}}^{f_{pesr}} N_{D,w,Q_0} k_{Q_{pesr},Q_{ds}}^{f_{pesr},f_{ds}} k_{Q_{ds},Q_0}^{f_{ds}}$$
(6)

$$k_{Q_{pesr}Q_{0}|2} = k_{Q_{pesr},d_{ds}}^{f_{pesr},f_{ds}} k_{Q_{ds},Q_{0}}^{f_{ds}}$$
(7)

where  $Q_{ds}$  is the beam quality of a double-scattering machine delivering a conventional reference field  $f_{ref} = f_{ds}$ . The fields  $f_{ds}$  and  $f_{pcsr}$  reproduce a same range modulation within 0.5 mm and are in agreement within  $\pm$  0.5% at ionization chamber position  $z_{ref} \pm 5$  mm but do not have the same incident energy set.

#### It is important to note here that we do not attempt to compute $k_{Q_{hyp},Q_0}^{f_{hyp}}$ and $k_{Q_d,Q_0}^{f_d}$ . Because both $f_{hyp}$ and $f_{ds}$ comply to IAEA TRS-398 reference conditions, both $k_{Q_{hyp},Q_0}^{f_{hyp}}$ and $k_{Q_d,Q_0}^{f_d}$ can be directly derived from IAEA TRS-398 tables or experimental/computed values previously determined under IAEA TRS-398 reference conditions in broad beams.

Using Monte Carlo simulations, we will compute  $k_{Q_{pesr},Q_{hyp}}^{f_{pesr},f_{ds}}$  under the above reference conditions (i.e., same energy range modulation and same spatial dose distributions). As mentioned earlier,  $k_{Q_{hyp},Q_0}^{f_{hyp}}$  and  $k_{Q_{ds},Q_0}^{f_{ds}}$  are TRS-398 compliant and can be looked up in the TRS-398 table. If  $k_{Q_{pesr},Q_{hyp}}^{f_{pesr},f_{hyp}} = k_{Q_{pesr},Q_{ds}}^{f_{pesr},f_{ds}} = 1$ , it is safe to assume that neither the geometry of the beam nor spectral differences significantly influence the ionization chamber response and that consequently,  $k_{Q_{pesr}Q_0|1} = k_{Q_{pesr}Q_0|2}$ . A graphical representation of the methodology is given in Fig. 1.

#### 2.D. Monte Carlo simulations

MC simulations are widely used to compute ionization chamber response in radiation beams. Sterpin et al.<sup>21</sup> showed that Geant4 is reliable for ionization chamber proton dose calculation using appropriate settings. Quality correction factors could be measured or obtained from MC simulations as follow<sup>22</sup>:

#### REFERENCE DOSIMETRY PROTON SCANNED BEAM



FIG. 1. Schematic representation of the application of Alfonso et al. formalism to PBS. The field  $f_{ref}$  is the conventional reference field. The field  $f_{pcsr}$  is the PBS field that approximates the dose distribution of  $f_{ref}$  in the SOBP region. The quality correction factor  $k_{Q_{pcsr},Q_{hpp}}^{f_{pcsr},f_{hpp}}$  takes into account the way incident protons are spatially distributed keeping the same incident energies and  $k_{Q_{pcsr},Q_{ds}}^{f_{pcsr},f_{ds}}$  takes into account geometrical differences and energy spectral differences.

$$k_{Q_A,Q_B} = \frac{\left(\frac{D_w}{D_{air}}\right)_{Q_A}}{\left(\frac{D_w}{D_{air}}\right)_{Q_B}} \frac{\left(\frac{W_{air}}{e}\right)_{Q_A}}{\left(\frac{W_{air}}{e}\right)_{Q_B}}$$
(8)

If  $Q_A$  and  $Q_B$  are proton beams, the mean energy to create an ion pair in air,  $W_{air}/e$  can be simplified and

$$k_{Q_A,Q_B} = \frac{\left(\frac{D_w}{D_{air}}\right)_{Q_A}}{\left(\frac{D_w}{D_{air}}\right)_{Q_B}}$$
(9)

Verhey et al.<sup>23</sup> estimated that the variation of  $W_{air}$ /e with the energy is less than 1% for proton energies greater than 10 MeV. Therefore, it is a reasonable assumption to simplify  $W_{air}$ /e for proton beam qualities that have similar energy spectra.

In order to determine  $k_{Q_{pcsr},Q_{hyp}}^{f_{pcsr},f_{hyp}}$  and  $k_{Q_{pcsr},Q_{ds}}^{f_{pcsr},f_{ds}}$ , simulations were setup as follow:

 The fields with beam qualities Q<sub>pcsr</sub> and Q<sub>hyp</sub> are simulated using the Geant4 9.6 Monte Carlo code<sup>24</sup> and the Gate v6.2 platform.<sup>25</sup> The pcsr beam quality  $Q_{pcsr}$  is that of a full pencil beam scanning simulation using an optical beam model tuned on the Gantry 4 beam-line model of the Essen proton therapy facility (Germany).<sup>26</sup> Every spot of the field f<sub>pcsr</sub> is simulated. The field with hypothetical beam quality Qhyp is constructed as a broad beam delivering a similar dose distribution to the actual Q<sub>pcsr</sub> simulation, including therefore a small divergence. To simulate the divergence in the hypothetical reference field, the sinus of the polar angle  $\theta$  is sampled from a uniform distribution within the interval [0,  $\sin(\theta_{max})$ ], with  $\theta_{max}$  the maximum polar angle  $\theta$  in order to simulate (Q<sub>hyp</sub>, f<sub>hyp</sub>). The azimuthal angle is uniformly distributed taking into account an averaged angular spread of the source. The angular spread of the spots in the field with beam quality Q<sub>pcsr</sub> is slightly different in the X and Y directions due to beam optics adjustment in the beam line. Therefore, angular spreads of protons in the hypothetical reference field are small but slightly different in the X and in Y directions to achieve the same field size as the field with beam quality  $Q_{pcsr}$  at the depth  $z_{ref}$ . To first approximation, as the beam quality  $Q_{hyp}$  is that of a point source, X and Y angular spreads can be averaged to a mean angular spread in both directions (Fig. 2).

• The scattered broad beam with beam quality  $Q_{ds}$  is simulated using TOPAS<sup>27</sup> (TOPAS beta9 based on Geant4 9.6) for the Massachusetts General Hospital (MGH) Gantry 1 beam line in double-scattering mode.<sup>28</sup> All components of the treatment head nozzle are simulated. Phase space data are scored at the nozzle exit. Those phase space data are then used in a second step to simulate the ionization chamber's response using the same physics list as for the Geant4 v9.6 simulations of the fields with beam qualities  $Q_{pcsr}$  and  $Q_{hyp}$ .

The phantom geometry is a  $40 \times 40 \times 40$  cm<sup>3</sup> water volume. The scoring voxel size is  $1 \times 1 \times 1$  mm<sup>3</sup> in the water phantom. The same phantom geometry is used throughout all simulations. The scoring of dose is performed inside air cavity of the ion chamber geometry.

The field size is  $10 \times 10 \text{ cm}^2$ . The set of energy layers of  $Q_{pcsr}$  is optimized to get a uniform SOBP within 0.5% and ranges at 80% dose values ( $R_{80}$ ) close to the distal  $R_{80}$  of the quality  $Q_{ds}$ . TRS-398 recommends less than 0.5% of fluctuations. Flatness is evaluated at  $z_{ref} \pm 5 \text{ mm using}^1$ :

$$Flatness = \frac{d_{max} - d_{min}}{d_{max} + d_{min}} *100$$
 (10)

For the double-scattering machine, MGH nozzle-specific settings are automatically chosen in order to achieve the desired field size, range, and modulation width.<sup>29</sup> For PBS range modulation, the flatness of the SOBP is sensitive to the choice of the energy layer spacing. Several tests on energy layer spacing were performed in order to optimize flatness. Simulations of the  $10 \times 10 \text{ cm}^2$  scanned fields were performed for each energy separately. Then, each single energy field was weighted using an 1-BFGS optimization algorithm (Limited-memory Broyden–Fletcher–Goldfarb–Shanno algorithm, implemented using Matlab©). This method does not rely on the optimizer of a treatment planning system (TPS).



Fig. 2. Schematic representation of the hypothetical field with beam quality  $Q_{hyp}$  which is a point source, simulated in a 40  $\times$  40  $\times$  40 cm<sup>3</sup> water phantom to achieve the same field size of the field with beam quality  $Q_{pcsr}$  at  $z_{ref}$ .

For GATE and TOPAS Geant4 simulations, multiple-scattering algorithms of charged particles are used. Electron and hadron ionization processes are added to the physics list. Production thresholds of secondary particles were set through SetCutInRegion function in a  $4 \times 4 \times 4$  cm<sup>3</sup> box around the ionization chamber model. The limitation of the particle step is controlled by a step function algorithm. The algorithm limits the step according to the constraint Step/Range < dRoverRange and decreases smoothly the step size until it becomes lower than the finalRange value. The skin controls the activation of single scattering in a region close to boundaries within a distance equivalent to the skin parameter times the mean free path for elastic events. The settings of step limitation algorithms are reported in Table I. Note that Table I parameters are more strict than Geant4 emstandard opt3 usually defined for applications requiring higher accuracy of electrons, hadrons, and ion transport without magnetic field.<sup>30</sup> More conservative values for protons setCutInRegion and finalRange parameters are chosen from previous work on the Fano test<sup>21</sup> that has evaluated Geant4 proton transport in a small cavity of low-density material. Concerning Geant4 electron transport, Elles et al.<sup>31</sup> reported improvements and performances of multiple-scattering algorithm on the Fano test for electrons. The parameters values in Table I are values reported by Elles et al.<sup>31</sup> giving a dose computed over theory ratio of 0.995, mentioning that a more recent Geant4 version is used in this study. It should be mentioned that the work by Elles et al.<sup>31</sup> on the adequacy of the combined photonelectron transport in Geant, and its compliance with Fano's theorem, remains to be demonstrated on the same grounds as it has been done with MC codes like EGSnrc and Penelope, where electron transport and boundary crossing are treated accurately. For proton nuclear inelastic interactions, the Geant4 Binary Cascade Model is used.<sup>32,33</sup> Elastic scattering cross-sections of nucleons are taken from SAID experimental

TABLE I. Settings for various parameters of particles simulations.

Particles	setCutInRegion (mm)	dRoverRange	finalRange (mm)	Skin
Protons	0.005	0.2	0.01	1
Electrons/positrons	0.005	0.2	0.1	1
Photons	1	_	_	_
Other ions	1	0.1	0.02	1

Table II. Ionizat	ion chamber	specifications.
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data.<sup>34</sup> For inelastic interaction of incident neutrons with energy below 20 MeV, the G4NeutronHPInelastic model is used. G4NeutronHPInelastic is based on a set of parameterizations of inelastic scattering data. For neutrons of energy higher than 20 MeV, the Precompound model is used. For other deuterons, tritons, and alphas, G4BinaryLightIonReaction, the G4LEDeuteronInelastic, and G4LEAlphaInelastic models are used through IonInelastic process. For other ions, the default IonInelastic process is defined. Decay, radioactive decay, neutron capture, and fission processes are also added to the physics list.

#### 2.E. Ionization chambers

The cavity geometries tested are an idealized  $2 \times 2 \times 0.2 \text{ mm}^3$  air cavity, a Roos-type chamber, and a Farmer-type chamber. The size of the idealized air cavity is selected to approach point dose measurement in the beam direction in a homogeneous dose area of the proton fields with sufficient statistics. The use of an air cavity of the size of a typical chamber is directly calculated using ion chamber models. Ionization chamber specifications<sup>2,35,36</sup> are reported in Table II.

Simplified models of the ion chambers are used. The geometry of the plane-parallel chamber is a succession of slabs of accurate dimensions in the direction of the beam. This simplification remains valid since the chamber has a guard ring.<sup>37</sup> For the cylindrical chamber, a geometry including details from user manual with a spherical top and the stem is simulated. In photon beams, Muir et al.<sup>35</sup> published a comparison between simulations performed using three models yields a spread in  $k_{Q,Q_0}$  values of less than 0.2% with a relative statistical uncertainty on the values of 0.1% for the cylindrical chambers. It is noteworthy that perturbation factors in photon beams are dominated by electrons; however,

tors in photon beams are usual the ratio of perturbation factors  $\frac{\frac{P_{Q_{hyp}}}{P_{Q_{pesr}}}}{\frac{P_{Q_{ds}}}{P_{Q_{pesr}}}}$  due to electrons is of lower order of magnitude in proton beams. Moreover, the

range of secondary electrons in proton beams is much small than in high energy photon beams.

For plane-parallel chambers, the reference point is on the inner surface of the window at its center. For cylindrical chambers, the reference point is on the central axis at the center of the cavity volume.<sup>2</sup> Ion chambers are oriented

	Window and electrode	Window thickness (mg.cm <sup>-2</sup> )	Sensitive volume	Cavity material	Wall material	Electr. material	Electr. radius (mm)	Guard-ring width (mm)	Water-proof
Roos	1 mm PMMA 0.02 mm C 0.1 mm PMMA	132	Volume 0.35 (cm <sup>3</sup> ) Height 2 mm Radius 7.5 mm	Air	_	Gr	7.8	4	Y
FC65-G	Cavity radius (mm) 3.1	N/A	0.65	Air	Gr	Al	0.5	_	Y



Fig. 3. Simulated depth dose profiles in a 10  $\times$  10 cm<sup>2</sup> field delivered by a pencil beam scanning quality,  $Q_{pcsr}$  and a double-scattering quality  $Q_{ds}$ . The depth dose  $Q_{hyp}$  refers to a dose distribution using an hypothetical broad beam quality that mimics the pencil beam scanning composite field,  $f_{pcsr}$ .

perpendicular to the beam as it is usually when positioning ion chamber for dosimetry in a water phantom.

#### 3. RESULTS AND DISCUSSION

Figure 3 provides depth dose profiles for each beam quality producing a flat 6-cm modulation width in a large water phantom.  $R_{80}$  is 16.35 cm for  $Q_{pcsr}$ , 16.35 cm for  $Q_{hyp}$ , and 16.31 cm for  $Q_{ds}$ . The flatness of the SOBP is 0.08 % for  $Q_{pcsr}$ , 0.07% for  $Q_{hyp}$ , and 0.3% for  $Q_{ds}$  at ionization chamber position  $z_{chamber} \pm 5$  mm. Figure 4 shows the lateral profile for the three beam qualities at the ionization chamber position in depth ( $z_{chamber} \equiv z_{ref}$ ). The ionization chamber is



Fig. 4. Simulated lateral dose profiles in a 10  $\times$  10 cm<sup>2</sup> field delivered by a pencil beam scanning quality,  $Q_{pcsr}$ , and a double-scattering quality,  $Q_{ds}$ . The dose profile  $Q_{hyp}$  refers to a dose distribution using an hypothetical broad beam quality that mimics the pencil beam scanning composite field,  $f_{pcsr}$ .

TABLE III. Quality correction factors (incl. type-A standard uncertainty) between  $Q_{pcsr}$ ,  $Q_{hyp}$ , and  $Q_{ds}$  qualities for a residual range of 3 g cm<sup>-2</sup>.

	$k_{Q_{pcsr},Q_{hyp}}^{f_{pcsr},f_{hyp}}$	$k_{Q_{pcsr},Q_{ds}}^{f_{pcsr},f_{ds}}$
Air cavity $(2 \times 2 \times 0.2 \text{ mm}^3)$	$0.999 \pm 0.002$	$1.001 \pm 0.001$
Roos type	$1.001\pm0.002$	$0.999\pm0.002$
FC65-G	$0.999\pm0.002$	$0.999 \pm 0.002$

placed at the center of the field. The flatness of lateral profile is 0.3% for  $Q_{pcsr}$ , 0.3% for  $Q_{hyp}$ , and 0.5% for  $Q_{ds}$  at ionization chamber position  $z_{chamber} \pm 5$  mm.

tion chamber position  $z_{chamber} \pm 5$  mm.  $k_{Q_{pesr},Q_{hyp}}^{f_{pesr},f_{ref}}$  and  $k_{Q_{pesr},Q_{ds}}^{f_{pesr},f_{ref}}$  with their statistical uncertainty are reported in Table III for an air cavity of  $2 \times 2 \times 0.2$  mm<sup>3</sup>, a Roos type and a cylindrical chamber (FC65-G). Each  $k_{Q_{pesr},Q_{hyp}}^{f_{pesr},f_{ds}}$  value is close to unity. These results confirm our first intuition that for similar dose distributions, stopping powers are similar and therefore so are quality correction factors.

This method relies strongly on the flatness of the dose distributions. Variations in the SOBP can lead to fluence variations that will scale the quality correction factors. In that case, the latter can differ from unity. Those variations can be simulated as any set of energy layers can be optimized in PBS. The impact on  $k_{Q_{pesr},Q_{hyp}}$  value is evaluated depending on the SOBP flatness achieved by the optimization. For a flatness of 0.55% (~TRS-398 recommendation),  $k_{Q_{pesr},Q_{hyp}}$  is 1.002 × 0.001. For a flatness of 1.4% and 5%, ripples are present in the SOBP and calculated  $k_{Q_{pesr},Q_{hyp}}$  is 1.031 × 0.001 and 1.022 × 0.001, respectively. These larger corrections are attributed to gradient perturbation factors. Note that all uncertainties here and in the remainder of this article are standard uncertainties (k = 1).

The choice of MC simulations parameters is important to get realistic dose deposition in small air cavities. Results of previous work on the Fano test<sup>21</sup> drove the choice of setCutIn-Region, dRoverRange, and finalRange parameters for protons. The setCutInRegion parameter is sensitive to get accurate stopping power ratios at  $z_{ref}$ , especially for protons and electrons. Variations up to 10% are observed in stopping power ratio if setCutInRegion is too high regarding the cavity size.

It is important to mention that the Fano test described by Sterpin et al.<sup>21</sup> only addressed the case of protons. Electrons have been tested previously<sup>31</sup> but not for more recent versions of Geant4. Parameters in Table I provide simulation of electrons with a strong step limitation. An uncertainty estimates on the  $k_{Q_{pesr},Q_d}^{f_{pesr},f_{ds}}$ , based on the error in the electronic term of the dose computed in the cavity, evaluate the uncertainty very close to zero (within 0.002%) considering 1% error in the Fano cavity test (consistent with publications on the Fano cavity test related to Geant4) and 20% of dose from the electrons.<sup>38</sup>

Uncertainties in the nuclear cross-sections are significant (of order of 5–10% as reported in ICRU 63). Moreover, the dose distributions are sensitive to the model used in the simulation (here binary cascade<sup>32</sup>). These uncertainties may also impact the determination of  $k_{Q_{pesr},Q_{hyp}}^{f_{pesr},f_{hyp}}$  and  $k_{Q_{pesr},Q_{ds}}^{f_{pesr},f_{ds}}$ .

However, by construction, the effect is supposed to be negligible for  $k_{Q_{pcsr},Q_{hyp}}^{f_{pcsr},f_{hyp}}$  because both  $f_{hyp}$  and  $f_{pcsr}$  use an incident beam with protons only. Thus, by-products of nuclear reactions are produced in the phantom and should be similar because the dose distributions are similar. The impact of nuclear reactions may be higher for  $k_{Q_{pcsr},Q_{ds}}^{f_{pcsr},f_{ds}}$  because  $f_{ds}$  correspond to a double-scattered beam with an incident beam contaminated with by-products of nuclear reactions in the treatment head. However, a significant impact of these nuclear reactions should reflect in the correction factor itself. Thus, it can be safely assumed that the uncertainty in  $k_{Q_{pcsr},Q_{ds}}^{f_{pcsr},f_{ds}}$  due to the uncertainties in the nuclear reactions is a percentage of the deviation of  $k_{Q_{pcsr},Q_{ds}}^{f_{pcsr},f_{ds}}$  from unity, which is thus negligible.

The total uncertainty for the determination of the absorbed dose-to-water in a clinical proton beam is estimated in TRS-398 around 2% and 2.3% for a cylindrical and a plane-parallel ionization chamber, respectively.<sup>2</sup> In this total uncertainty, beam quality correction factor  $k_{Q,Q_0}$  accounts for 1.7% and 2%, respectively. The determination of  $k_{Q,Q_0}$  involves changes in  $W_{air}/e$  for air which accounts for most of the uncertainty. In the present work, we have quantified the contribution to the uncertainty in the total quality correction factor due to the delivery modality chosen considering the same dose distribution. Both  $k_{Q,exr,Q_{hyp}}^{f_{pesr},f_{hyp}}$  and  $k_{Q,exr,Q_{ds}}^{f_{pesr},f_{ds}}$  equal unity within type-A uncertainty due to the particular design of the simulation. Thus, the uncertainties specific to beam delivery mechanics ( $k_{Q,pesr,Q_{hyp}}^{f_{pesr},f_{ds}}$ ) in the total quality correction factor for scanned beams is at most 0.2% (statistical uncertainty) for the three ionization chambers, well below the total uncertainty.

As mentioned in the introduction, there is no consensus on the best method to calibrate scanning proton beams, but for the same reference conditions (in terms of residual range), beam quality corrections factors are not influenced by the modality (scanned or broad) of proton beams.<sup>37,39,40</sup>

Proton therapy and ion therapy centers might have, in the future, access to clinical dedicated calorimeters to determine the absorbed dose-to-water<sup>41,42</sup> to avoid additional uncertainty on the ion chamber charge measurement (e.g., due to large ion recombination effects<sup>43</sup>). Dedicated calorimeters would also avoid the need to determine beam quality correction factors.

Finally, MC has been used efficiently to compute  $k_{Q_{pcsr},Q_{hyp}}^{f_{pcsr},f_{hyp}}$ and  $k_{Q_{pcsr},Q_{ds}}^{f_{pcsr},f_{ds}}$  values. This opens the possibility to calculate quality correction factors using MC simulation of ionization chamber dose–response irradiated by user proton beam quality  $Q_{pcsr}$ . Nevertheless, in dose-to-water determination, other large sources of uncertainty than  $k_Q$  have to be addressed with other methods than those described here, e.g., correction of ion chamber reading  $M_Q$  for ion chamber recombination, polarity, and other effects.

#### 4. CONCLUSION

The Alfonso formalism<sup>13</sup> was applied to scanned proton beams. In our MC simulations, neither the difference in the

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geometry of the beam (scanned beam vs. hypothetical beam) nor the different incident beam energies influenced significantly the beam quality correction factors. This suggests that ionization chamber quality correction factors in scanned or broad proton beams are indistinguishable within the calculation uncertainties provided dose distributions achieved by both modalities are similar and comply with TRS-398 reference conditions<sup>2</sup>.

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