

An approximate analytical formula for 3D dose deposition in water by a Gaussian proton beam

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ABSTRACT

A proton linear accelerator named TOP-IMPLART, developed as a prototype of a full linear machine for proton therapy, is currently in operation at the ENEA laboratories of the Frascati Research Center in Italy. In anticipation of test irradiations of volumes or, more specifically, simulated treatment plans to check the linac's performance, it is desirable to have a streamlined tool for calculating dose deposition in three spatial dimensions and for designing volumetric spread-out Bragg peaks. To this end, a preliminary quick approach to 3D dose calculation that avoids lengthy Monte Carlo simulations would be quite convenient. Here, we present the derivation of an analytical formula for the approximate calculation of the dose volume deposited in water by a Gaussian proton beam. The formula combines Bortfeld's Bragg curve model with Preston-Koehler's model for the widening of pencil beams. Example tests are shown.

1. Introduction

Accelerated protons deposit energy in matter such that most of their kinetic energy is released almost at the end of their trajectories, where the so-called Bragg peak forms [1]. The depth of this peak increases almost quadratically with the initial energy of the protons. These characteristics are useful in proton therapy, because by careful designing the irradiation parameters, a suitable superposition of Bragg peaks can be obtained at the location of the tumor mass, while simultaneously limiting the amount of radiation absorbed by the adjacent healthy organs. This superposition of peaks consists of suitably weighted contributions of different energies, ensuring that the entire volume of the tumor mass is covered by a so-called spread-out Bragg peak (SOBP) [1]. Indeed, the typical depth-width of a single Bragg peak alone would be too narrow for that task. Because the tumor mass typically extends also transversally to the direction of the proton beam, the beam must also be moved laterally for the superposition of translated Bragg peaks to cover its entire volume. Therefore, the SOBP needs to be designed in three dimensions, considering that the component proton beams gradually widen during propagation in matter due to multiple Coulomb scattering (MCS) [1].

Generally, the design of SOBPs in three dimensions is primarily achieved using specialized software and Monte Carlo (MC) simulations, as these methods can produce reliable representations of dose deposition in matter. In the literature, several papers have addressed the problem of calculating 3D dose deposition in water and designing

SOBPs using alternative approaches. Separating central-axis and off-axis contributions, Lee and coauthors introduced an empirical method to design a proton SOBP in water by modeling the lateral spread of the beam with a Gaussian function and integrating range-energy table data [2] for calculating the monochromatic Bragg curves composing the SOBP [3]. Hong and coworkers proposed an analytical model, also extended to the case of a broad beam, to calculate dose deposition in water by a proton beam traversing various elements before reaching the patient, where the central-axis contribution is deduced from depth-dose measurements in a water phantom, while the off-axis one is described by a Gaussian function [4]. Using a Gaussian approximation for the radial coordinate, Hollmark and colleagues presented an analytical pencil beam model, based on the generalized Fermi-Eyges' theory, to calculate the effects of MCS and energy-loss straggling on the dose deposited in water by light-ion beams [5]. In [6], Pedroni and coauthors presented a model to calculate the 3D dose in proton therapy, used at the Paul Scherrer Institute in Switzerland. This model is based on the stopping power formula of Bethe and Bloch and a double-Gaussian representation of the transverse dose distribution, also including a halo correction for the nuclear interaction effects. In another paper, Ulmer and Matsinos, emphasizing the importance of using accurate representations of the Bragg curve in proton therapy, examined three different theoretical models for calculating the 3D dose deposited in water by an almost monochromatic proton beam, including contributions from

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primary and secondary protons [7]. In [8], an algorithm for 3D dose was presented by Westerly and coauthors for a collimated Gaussian proton beam, which combined depth-dose profiles obtained by MC simulations at 100, 160, and 220 MeV with analytical expressions for the fluence widening based on different 2D scaling models. In [9], the MONET computational code, which combines Molière's theory for MCS and Bethe-Bloch's formula for longitudinal stopping power, was presented by Embriaco and colleagues for dose calculation in three dimensions in the presence of a Gaussian energy spectrum and validated by comparison with MC simulations.

Here, we present an alternative approximate model to calculate 3D dose deposition in water by a proton beam with a Gaussian transverse shape. The model has been developed within the framework of the TOP-IMPLART project (Terapia Oncologica con Protoni—Intensity Modulated Proton Linear Accelerator for RadioTherapy), aimed at realizing a prototype of a radio-frequency pulsed active-modulation proton linear accelerator (linac) for cancer treatment using proton therapy [10, 11]. The linac is actually in operation in the Frascati Research Center with a maximum proton energy of 71 MeV.

During the commissioning of the linac, simulated treatment plans involving SOBP designing and, more generally, tests encompassing 3D irradiations of volumes are planned. For these purposes, a tool for dose deposition in 3D space that is lighter and quicker than the inevitably lengthy MC simulations, such as one using analytical or semi-analytical formulas, is very convenient.

In the model presented in this paper, the beam can be collimated or slightly divergent, with the slopes of the particle momenta being approximately proportional to the distance of the protons from the beam's central axis. These characteristics can be considered to represent typical beam behaviors in phase space. For simplicity, only contributions to dose from primary protons are considered. The model combines our implementation of Bortfeld's analytical Bragg curve model [12] for the on-axis component of the 3D dose, and Preston-Koehler's fluence analytical formula [13–15] for the beam lateral spreading caused by MCS. The Preston-Koehler's formula was selected among those available in the literature due to its intrinsic simplicity, which allows, as will be shown, obtaining an approximate analytical formula for the 3D dose.

It should be noted that our tests will not involve clinical applications, allowing for a certain degree of approximation to be tolerated. In cases where more accuracy is needed, the approximate results obtained with the analytical model could serve as starting parameters for subsequent refinement using MC simulations.

2. Bortfeld's Bragg curve formula

A formula for the approximate calculation of the dose delivered in water by accelerated protons was proposed in 1997 by Bortfeld [12]. The result of the formula is the transversally integrated dose per unit primary particle as a function of depth penetration (depth-dose curve), also known as the proton Bragg curve in water. Besides dose deposition by ionization, the formula includes the effect of gradual fluence decrease caused by inelastic nuclear interactions (INIs) and the consequent dose contribution from a fraction (60%) of the protons lost in that way.

In our implementation of Bortfeld's formula, after a number of comparisons with MC simulations run in FLUKA [16–18] with its graphical user interface Flair [19], we have modified a few details with respect to the original model formulation given in [12]: (a) the values of the parameters α and p of the Bragg-Kleeman (BK) formula for the proton range, $R_0 = \alpha E_0^p$ —where R_0 and E_0 are the range and the proton energy, respectively—have been replaced with those found by best fitting the ranges obtained with MC simulations from 5 to 160 MeV; (b) a polynomial correction is applied to the BK formula for better accuracy (see Appendix A for this and the previous point); (c) as shown in [20], an alternative approach to the calculation of the INI-induced variation of fluence along the propagation axis is used; (d) although in

what follows we formally keep the parameter γ of Bortfeld's formula, representing the fraction of protons, lost due to INIs, that contribute to the dose ($\gamma = 0.6$ in [12]), in our calculations it will be set to zero. Even though this last setting is unlikely to be fully realistic because the products of INIs are known to participate in dose deposition [21], the applied changes provided more satisfying matches with the monochromatic Bragg curves simulated in FLUKA in many tests we conducted, compared to using the original approach and parameter values found in [12]. Additionally, for simplicity, we consider the low-energy tail that Bortfeld adds to the Gaussian main component of the energy spectrum to be negligible. Nonetheless, it is important to point out that the theory presented in the following sections of this paper retains its formal validity even if one uses Bortfeld's original analytical formula without our implementation changes.

For the moment, we do not consider the effects of range straggling, which is due to the statistics of interactions between protons and water, and possible non-monochromaticity of the energy spectrum (energy straggling). Under these conditions, as reported in Eq. (3) in Bortfeld's paper, a preliminary expression $\hat{D}_B(z)$ of the dose, where z is the propagation distance, is

$$\hat{D}_B(z) = -\frac{1}{\rho} \left[\phi_N(z) \frac{dE}{dz}(z) + \gamma \frac{d\phi_N}{dz}(z) E(z) \right]. \quad (1)$$

In this equation, ρ is the material density, $\phi_N(z)$ is the z -dependent fluence (including the effect of INIs), and $E(z)$ is the z -dependent energy of the protons. In Bortfeld's paper, Eq. (1) is convolved with a Gaussian distribution, whose standard deviation σ includes the effects of both range straggling and energy straggling, thereby obtaining an expression $D_B(z)$ for the absorbed dose—Eq. (26) in [12]. The same convolution operation is applied in our implementation of Bortfeld's formula to obtain an expression for the absorbed dose. An example of our implementation of Bortfeld's formula, however applied to a different material, is reported in [22].

As mentioned earlier, for better comparability with a number of MC simulated Bragg curves, our implementation assumes $\gamma = 0$, a different calculation of the effects of INIs, and includes some differences in the application of BK's formula, as shown in Appendix A. Nonetheless, to keep our notation simple, we also label the absorbed dose calculated with our changes as $D_B(z)$. As already stated, the following theory is formally valid in either case.

3. Preston-Koehler's fluence formula

As a consequence of multiple Coulomb scattering, described by Molière's theory [23], an accelerated proton propagating inside a material is subjected to a series of random angular deviations from its path. The global effect on an initially collimated proton beam is that of a gradual increase in its transversal size during propagation. Some mathematical models have been introduced to describe the gradual enlargement of a pencil proton beam [4,8,13–15,24–26]. For its simplicity, one of the most convenient models for our purposes is Preston-Koehler's model [13–15], which describes the transversal section of the beam with a single Gaussian,

$$\phi_{PK}(x, y, z) = \frac{1}{2\pi\sigma_{PK}^2(z)} \exp \left[-\frac{x^2 + y^2}{2\sigma_{PK}^2(z)} \right], \quad (2)$$

whose standard deviation σ_{PK} depends on the penetration depth z according to

$$\sigma_{PK}(z) = \sigma_{PK}(R_0) \left[2(1-t)^2 \ln \left(\frac{1}{1-t} \right) + 3t^2 - 2t \right]^{1/2}, \quad (3)$$

where $t = z/R_0$. Eq. (2) is written for a beam whose transversal size is zero at $z = 0$.

In the original Preston-Koehler's theory [13], the standard deviation at the average range distance ($z = R_0$) is $\sigma_{PK}(R_0) \approx 0.0217R_0$. This value was slightly modified to $\sigma_{PK}(R_0) \approx 0.0225R_0$ in Gottschalk's

revision of the theory [15], which is the value we use in this paper. Table I in Gottschalk's paper [15] lists a series of $\sigma_{PK}(R_0)/R_0$ values for various materials.

It should be stressed that Preston-Koehler's model is a basic single-Gaussian approximation of the transversal fluence per particle, which mainly neglects the presence of a peripheral halo corresponding to a small fraction of the whole fluence. For this reason, other authors have proposed more complex models consisting of two concentric Gaussians [24], one for the main distribution and the other for the peripheral halo, or even of three Gaussians [25,26]. This three-Gaussian model has shown to be especially effective for the case of carbon ions [25]. Even more complex models have been proposed by other authors [4,8,9,26–29]. A summary—updated to 2015—of the main types of available models is reported in [26]. For our purposes, we believe the single-Gaussian Preston-Koehler's model to be sufficiently accurate.

3.1. Initially collimated Gaussian beam

Preston-Koehler's model describes the propagation of the transversal fluence distribution per particle assuming an initial infinitesimal beam size in $z = 0$. Let us now consider the case of a wider proton beam whose fluence per particle, $\phi(x, y, z)$, has an initial transversal shape which is a Gaussian function having standard deviations w_x and w_y along the x and y axes, respectively,

$$\phi(x, y, 0) = \frac{1}{2\pi w_x w_y} \exp \left[-\frac{1}{2} \left(\frac{x^2}{w_x^2} + \frac{y^2}{w_y^2} \right) \right]. \quad (4)$$

Assuming the momenta of the beam protons are all parallel to the z -axis in $z = 0$, one can see this Gaussian beam as a continuum superposition of weighted elementary Preston-Koehler contributions originating from each point on the Oxy plane. Therefore, the propagation of the fluence per particle along z ($z \geq 0$) can be written as

$$\phi(x, y, z) = \iint_{\mathbb{R}^2} \phi(\xi, \eta, 0) \phi_{PK}(x - \xi, y - \eta, z) d\xi d\eta. \quad (5)$$

This integral admits the analytical solution

$$\phi(x, y, z) = \frac{1}{2\pi\sigma_x(z)\sigma_y(z)} \exp \left\{ -\frac{1}{2} \left[\frac{x^2}{\sigma_x^2(z)} + \frac{y^2}{\sigma_y^2(z)} \right] \right\}, \quad (6)$$

where

$$\sigma_\mu^2 = w_\mu^2 + \sigma_{PK}^2(z) \quad (\mu = x, y). \quad (7)$$

In case of cylindrical symmetry of the beam at $z = 0$, Eq. (6) can be rewritten in polar form,

$$\phi(r, z) = \frac{1}{2\pi\sigma_r^2(z)} \exp \left[-\frac{r^2}{2\sigma_r^2(z)} \right], \quad (8)$$

where $r^2 = x^2 + y^2$, $w = w_x = w_y$, and

$$\sigma_r^2(z) = w^2 + \sigma_{PK}^2(z). \quad (9)$$

3.2. Initially slightly diverging Gaussian beam

Let us consider a proton beam with the fluence per particle described by Eq. (4) in $z = 0$, but with the beam particles at $z = 0$ diverging from the beam central axis as explained below. In a small-angle approximation, let us denote with x' and y' the slopes of the momentum-vector projections onto the Oxz and Oyz planes, respectively. Under the hypothesis that these slopes are proportional to the projected distances of the particles from the z -axis, one can write $x' = m_x x$ and $y' = m_y y$, where m_x and m_y are positive parameters. Still under a small-angle approximation, this situation corresponds to the typical phase-space behavior of particle beams experiencing scattering events while traversing material elements before reaching the plane at $z = 0$.

Under these assumptions, Eq. (5) modifies as

$$\phi(x, y, z) = \iint_{\mathbb{R}^2} \phi(\xi, \eta, 0) \phi_{PK} [x - (1 + m_x z)\xi, y - (1 + m_y z)\eta, z] d\xi d\eta. \quad (10)$$

The solution of this integral is still Eq. (6), however with the following expression for the standard deviations $\sigma_x(z)$ and $\sigma_y(z)$:

$$\sigma_\mu^2 = (1 + m_\mu z)^2 w_\mu^2 + \sigma_{PK}^2(z) \quad (\mu = x, y). \quad (11)$$

For cylindric symmetry of the fluence at $z = 0$, also in this case Eq. (8) holds true, with $r^2 = x^2 + y^2$, $w = w_x = w_y$, $r' = x' = y' = mr$, $m = m_x = m_y$, and

$$\sigma_r^2(z) = (1 + mz)^2 w^2 + \sigma_{PK}^2(z). \quad (12)$$

4. Approximate 3D dose computation

Neglecting for now any effect of range straggling and energy straggling, the results reported in the previous sections make it possible to write an approximate formula for the dose in 3D space. Such a formula can be obtained by replacing $\phi_N(z)$ with $N_p \phi(x, y, z) \phi_N(z) / \phi_N(0)$ in Eq. (1), where N_p is the number of protons, and the factor $\phi_N(z) / \phi_N(0)$ is needed to retain the effect of the INIs. Division by $\phi_N(0)$ ensures both normalization to unity at $z = 0$ of the INI factor $\phi_N(z) / \phi_N(0)$ and correct dimensionality of the obtained formula for the dose.

The term containing $d\phi_N/dz$ in Eq. (1) concerns the contribution to dose coming from protons removed from the beam due to INIs, while the z -variation of $\phi(x, y, z)$ is caused by the beam widening due to MCS. Therefore, $\phi(x, y, z)$ should not be included in the derivative operation with respect to z . Taking this into account, our pre-straggling formula for the 3D dose is

$$\hat{D}(x, y, z) = N_p \frac{\phi(x, y, z)}{\phi_N(0)} \hat{D}_B(z), \quad (13)$$

with $\hat{D}_B(z)$ and $\phi(x, y, z)$ given by Eqs. (1) and (6)—or (8) for cylindrical symmetry—respectively.

At this point, the effects of range straggling and energy straggling can be introduced. Applying a Gaussian convolution as in Bortfeld's paper [12], the mathematical expression for the 3D dose is

$$\begin{aligned} D(x, y, z) &= \frac{1}{\sqrt{2\pi}\sigma} \int_{-\infty}^{R_0} \hat{D}(x, y, \zeta) \exp \left[-\frac{(z - \zeta)^2}{2\sigma^2} \right] d\zeta \\ &= \frac{N_p}{\sqrt{2\pi}\sigma\phi_N(0)} \int_{-\infty}^{R_0} \phi(x, y, \zeta) \hat{D}_B(\zeta) \exp \left[-\frac{(z - \zeta)^2}{2\sigma^2} \right] d\zeta, \end{aligned} \quad (14)$$

where the standard deviation σ of the Gaussian function contains the contributions due to range straggling and energy straggling, and it is calculated with Eq. (19) in [12].

If $\phi(x, y, \zeta) \approx \phi(x, y, z)$ within the interval in which the Gaussian function is not negligible, say within $z - 3\sigma \leq \zeta \leq z + 3\sigma$, then $\phi(x, y, z)$ can be taken out of the integral and the following approximate result is obtained:

$$\begin{aligned} D(x, y, z) &\approx N_p \frac{\phi(x, y, z)}{\sqrt{2\pi}\sigma\phi_N(0)} \int_{-\infty}^{R_0} \hat{D}_B(\zeta) \exp \left[-\frac{(z - \zeta)^2}{2\sigma^2} \right] d\zeta \\ &= N_p \frac{\phi(x, y, z)}{\phi_N(0)} D_B(z). \end{aligned} \quad (15)$$

This equation states that the 3D dose is approximately equal to the fluence of the Gaussian beam multiplied by the dose calculated either with Bortfeld's formula [12] or with our implementation of it. In case of cylindrical symmetry around the z -axis, Eq. (15) can be written in radial form as

$$D(r, z) = N_p \frac{\phi(r, z)}{\phi_N(0)} D_B(z). \quad (16)$$

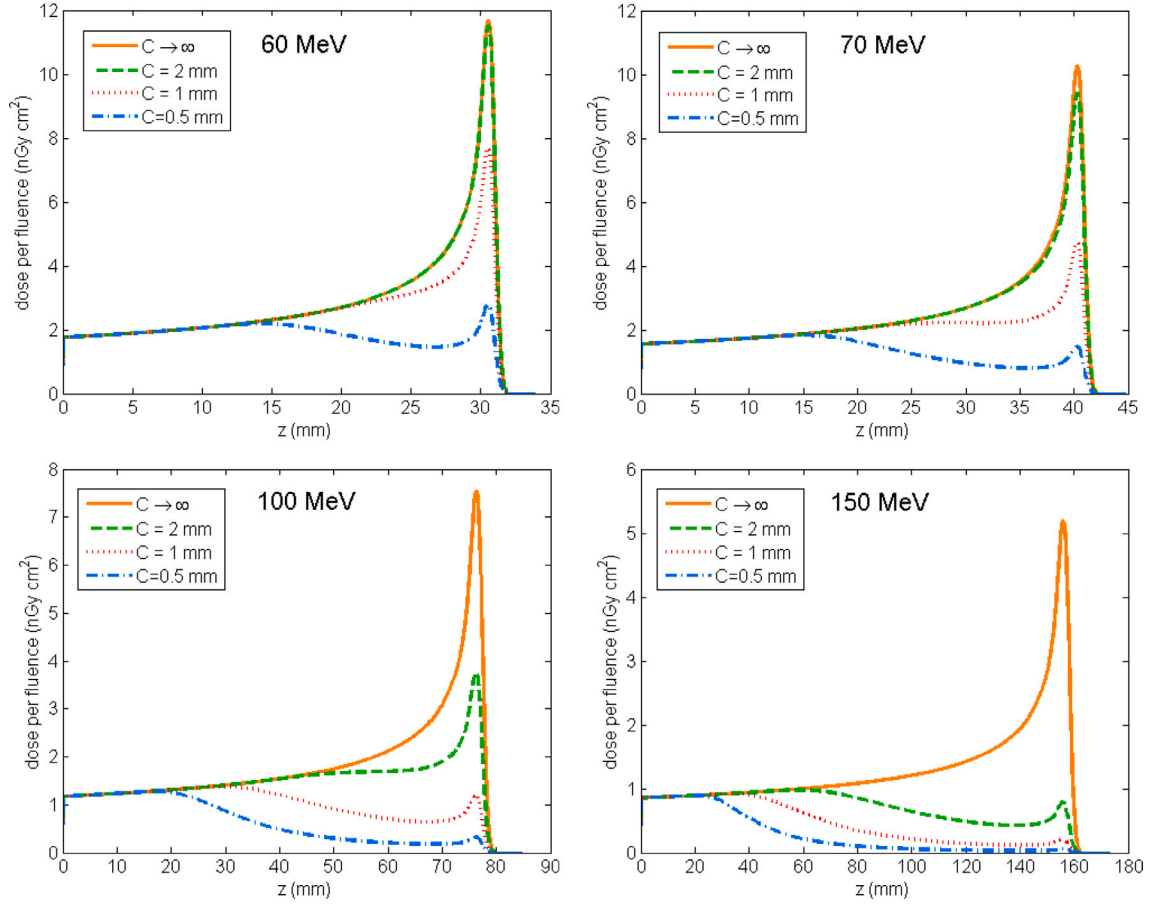


Fig. 1. Dose per fluence deposited in water inside cylinders of radius C , coaxial to the beams and the z -axis, by collimated pencil proton beams with four representative energies. The curves are calculated using Eq. (17). See the text for more details.

Taking $\phi(x, y, \zeta)$ out of the integral in Eq. (14) to obtain Eq. (15)—even though typically justified by the relatively small variation of the fluence along z in presence of not too broad energy spectra, as shown with an example in Appendix B—is a delicate step, whose feasibility should be verified in doubtful cases, for instance by comparison with MC simulations.

4.1. Bragg curve in the axial region

A significant consequence of the proton beam widening in water is a gradual decrease, compared to a standard Bragg curve, in the average dose deposited inside the axial region, which is a narrow area surrounding the z -axis, during propagation. This effect gets increasingly significant for narrower pencil beams, that is, as $w \rightarrow 0$.

To understand the relevance of this phenomenon, we evaluated the dose per fluence, $D_{cyl}(C, z)$, that is absorbed in water inside a cylinder coaxial to the z -axis for various values of the cylinder radius C . We considered four example energies for the proton beam: 60, 70, 100, and 150 MeV. In the case of collimated beams of fluence per particle as in Eq. (8), the following analytical expression for $D_{cyl}(C, z)$ is found by integrating $D(r, z)/N_p$ over the circle of center $(0, 0)$ and radius C on the Oxy plane:

$$D_{cyl}(C, z) = \frac{2\pi}{N_p} \int_0^C r D(r, z) dr = \left\{ 1 - \exp \left[-\frac{C^2}{2\sigma_r^2(z)} \right] \right\} \frac{D_B(z)}{\phi_N(0)}. \quad (17)$$

Limiting, for simplicity, the reported examples to pencil beams with $w = 0$, Fig. 1 shows plots of $D_{cyl}(C, z)$ for some selected values of C , including the standard Bragg curve $D_B(z)$ corresponding to $\lim_{C \rightarrow \infty} D_{cyl}(C, z)$. Note how the Bragg peaks become increasingly less

visible at the higher energies for smaller values of C . Conversely, at 60 MeV, the two curves for $C \rightarrow \infty$ and $C = 2$ mm are practically indistinguishable.

In the literature, similar axial distributions were reported by Hong and coworkers through simulations using their pencil-beam algorithm for dose deposition in water by 160 MeV proton beams passing through the beam delivery line at the Harvard Cyclotron Laboratory [4]. In that paper, Fig. 10 shows how the size of the collimating aperture influences the height of the axial Bragg peak and the overall shape of the central-axis Bragg curve.

We were not able to find experimental depth-dose distributions in the literature to compare with the ones analytically calculated using Eq. (17). Nonetheless, aiming to compare the analytical depth-dose curves with curves obtained using a more established method, we performed a few FLUKA simulations of dose deposition in water inside a cylinder of radius C by collimated pencil proton beams. These confirmed the good reliability of Eq. (17), as shown in Fig. 2 for two example curves at 100 MeV, although they showed a slight overestimation of the Bragg peak height, something that will be discussed in Section 5.2. The two simulated curves in Fig. 2 were calculated using FLUKA's basic default settings and 2.5×10^6 particles, with a sampling of 500 equispaced points along the z -axis from 0 to 90 mm.

5. Test comparisons with MC simulations

To verify the reliability of the analytical formulas derived in the previous sections, we made a few comparisons of test cases with MC simulations for selected energy values. As a first step, we checked the standard-deviation formula shown in Eq. (9) regarding the generalization of Preston-Koehler's fluence to a Gaussian beam with cylindrical

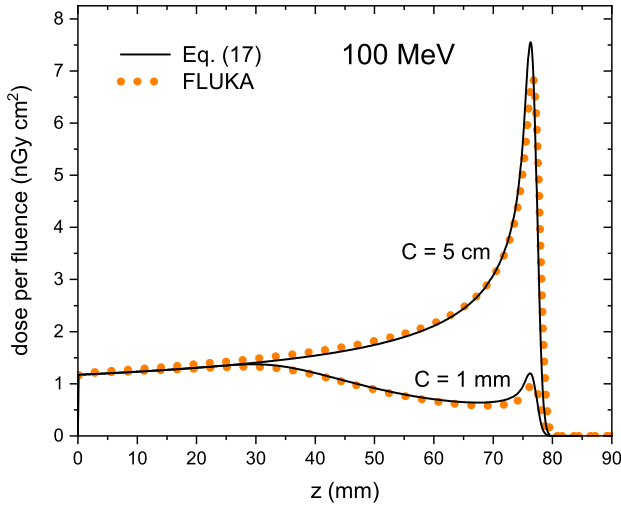


Fig. 2. Dose per fluence deposited in water inside cylinders of radius $C = 5$ cm and $C = 1$ mm, coaxial to the beam and the z -axis, by a 100 MeV collimated pencil proton beam: comparison between calculations with Eq. (17) and FLUKA simulations.

symmetry. Then, we checked the formula shown in Eq. (16) for the approximate computation of 3D dose in water for a slightly diverging beam.

5.1. Fluence of an initially collimated Gaussian beam

We considered a cylindrical-symmetry collimated proton beam with a Gaussian section of standard deviation $w = 7.30$ mm at $z = 0$. Four cases were checked at the monochromatic energies of 50, 60, 70, and 80 MeV. Using FLUKA, beam fluences per particle in water were simulated at the penetration depths $z_n = n/(10 R_0)$, with $n = 0, 1, \dots, 10$. The transversal shape of each of these fluences was detected in FLUKA using $R_0/200$ -thick USRBIN virtual detectors operating in BEAMPART and R- Φ -Z mode. The radius of each detector was set equal to $5\sigma_r(z_n)$ and was sampled with 250 points. In FLUKA, the PRECISIO setting was chosen for the physics defaults, with the following additional option: a FLUKAFIX card was added with Ekin frac set equal to 0.005 for the water material. Each simulation was performed launching 10^7 virtual protons from $z = 0$. The simulation uncertainties at the n^{th} detector were typically lower than 0.05% of the corresponding fluence values for $r \leq 3\sigma_r(z_n)$.

Using Mathematica [30], the transversal shapes of the simulated fluences were best fitted with Gaussian functions for the four considered energies, after averaging them around the polar angle to obtain radial curves. The standard deviations of the best-fitting Gaussians are plotted in Fig. 3 (dots with error bars) along with the corresponding curves calculated using Eq. (9) (solid lines).

For all four energies, the distances between the standard deviations of the simulated fluences (dots with error bars) and those calculated analytically (solid lines) are quite small, corresponding to relative differences lower than 1%. The largest differences, found at $z = 0.9 R_0$, can be attributed to the fact that the radial distributions obtained from the FLUKA simulations are not exact Gaussian curves. Indeed, they consist of a core Gaussian component paired with a very light external halo that becomes more pronounced with increasing depth. This halo is caused by long-range scattering and non-electromagnetic effects. On the other hand, the main approximation in the Preston-Koehler theory is that the beam maintains its transverse Gaussian shape along the propagation direction. As this shape should match the Gaussian core component of the actual beam, the presence of the external halo is likely to cause Gaussian fits of the FLUKA simulated fluences to overestimate the standard deviations. However, the detected

Table 1

Mean and standard deviation of the phase-space parameters from LINAC+SRIM (12,955 phase-space points) and Mathematica (5×10^5 phase-space points).

	LINAC+SRIM		Mathematica	
	Mean	Std. dev.	Mean	Std. dev.
Energy (MeV)	69.83	0.2165	69.83	0.2168
x (mm)	-3.633×10^{-3}	5.634	-4.769×10^{-3}	5.632
y (mm)	5.657×10^{-3}	5.389	5.880×10^{-3}	5.386
x' (mrad)	-18.57×10^{-3}	3.533	-23.90×10^{-3}	3.530
y' (mrad)	9.812×10^{-3}	3.424	13.86×10^{-3}	3.426

differences are minor, at least for the examined cases.

To visually illustrate how minor the above differences are, let us compare the simulated and calculated radial fluences for the worst case among those represented in Fig. 3: 80 MeV. In this case, the maximum difference between the two approaches amounts to 0.00978 at $z = 0.9 R_0$. Fig. 4 shows these two radial fluences, both normalized to one. The two curves overlap quite well. Neglecting the region close to the axis ($r < 8$ mm), which appears to be influenced by a light simulation noise, one finds that the largest relative difference between the two curves is about 0.7% at the radial distance $r \approx 13$ mm, as more clearly visible in the figure inset.

5.2. 3D dose deposited by an initially slightly diverging Gaussian beam

Here, we address the case of a slightly diverging Gaussian proton beam. A file was generated with phase-space coordinates of 12,955 protons emitted by the TOP-IMPLART linac using LINAC beam dynamics software [31]. The mean energy of these protons was 71 MeV. Then, using SRIM software [32], the protons were virtually propagated through a sequence of materials: a Ti window (thickness of 25 μm), air (17 cm), an aluminized-mylar window (20 μm of mylar + 2 μm of Al), He (170.8 cm), another aluminized-mylar window (20 μm of mylar + 2 μm of Al), and air (60 cm). This configuration represents the experimental setup of the beam delivery line following the accelerator.

Subsequently, the obtained phase-space file was analyzed in Mathematica. First of all, the distribution of the particle positions on the Oxy plane exhibited a cylindrical symmetry to a good degree, as shown in Fig. 5. Then, the covariance matrix of the obtained file and statistical distributions of energy and position on the Oxy plane were evaluated. The distributions of all these quantities were found to be Gaussian. Regarding the slopes of the momenta, the majority were found, on average, to be approximately proportional to the distance of the particles from the beam axis, with slope signs matching the coordinate signs, as shown in the phase-space diagrams in Fig. 6. This allowed using the model developed in Section 3.2.

Our purpose was that of comparing the dose deposited by this beam, calculated with Eq. (16), with that obtained from an MC simulation using the phase-space data. These data, however, needed to be increased in number to obtain good statistics in the MC simulation. To do so, we used the covariance matrix to generate with Mathematica 5×10^5 virtual protons having the same statistical characteristics of the original 12,955 ones. In Table 1, the main parameters of the extended distributions generated by Mathematica are compared with those of the original distributions from LINAC and SRIM.

As far as the parameters needed to evaluate dose deposition with Eq. (16) are concerned, the previous findings, summarized in Figs. 5 and 6 and in Table 1, justified the assumption of an approximately cylindrical-symmetry Gaussian beam centered around $(x, y) = (0, 0)$ with a standard deviation $w = 5.509$ mm and $\sigma_r = 3.478$ mrad. This latter quantity is the standard deviation of r' , whose mean value is approximately $r' = 0$. These values of r' and σ_r are averages of the mean values and standard deviations reported in the Mathematica columns in Table 1 for the parameters x' and y' .

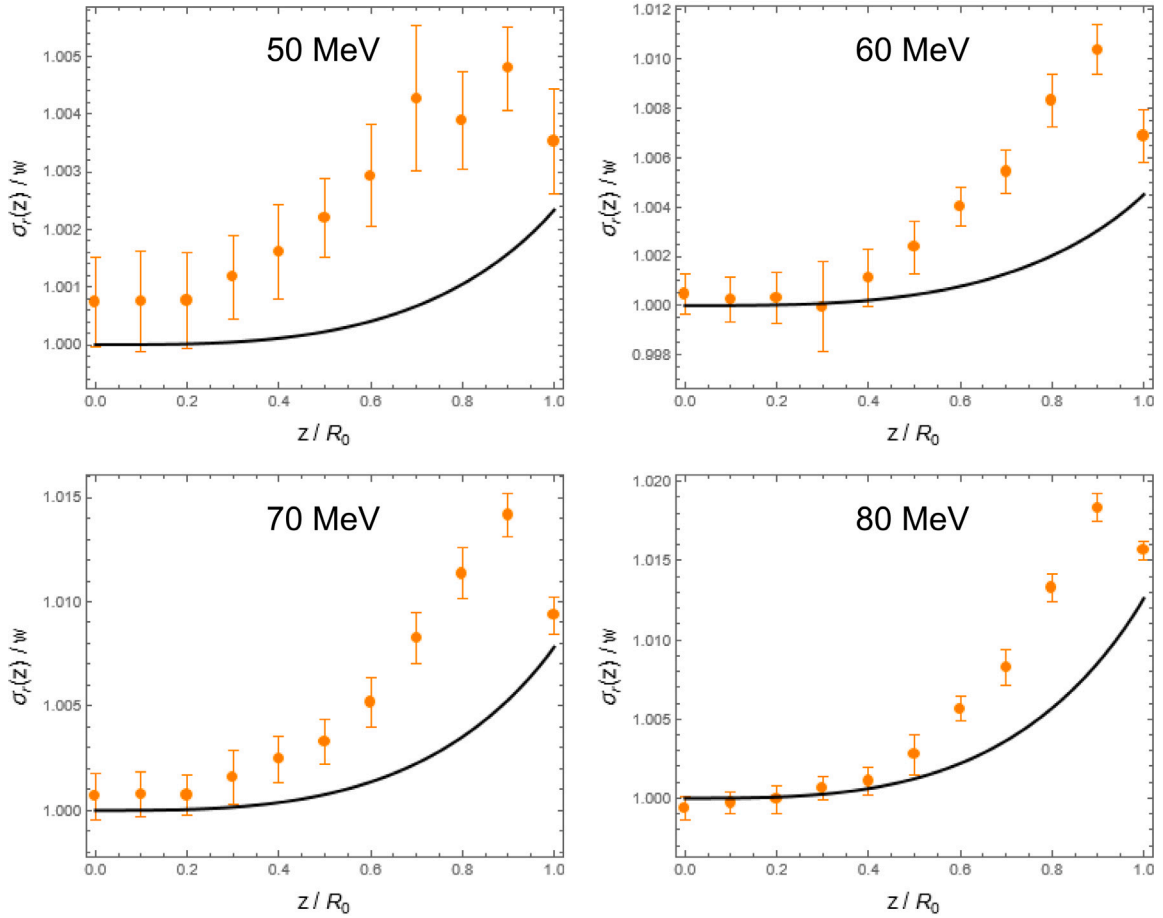


Fig. 3. Standard deviations $\sigma_r(z)$ of the fluences of four monochromatic collimated Gaussian beams at the penetration depths $z_n = n/(10 R_0)$ ($n = 0, 1, \dots, 10$) in water: values obtained from MC-simulated radial shapes (dots with error bars) and calculations with Eq. (9) (solid lines). The standard deviations are normalized to the nominal value w they possess at the beginning of the propagation. The propagation depth z is normalized to the average range R_0 for each energy.

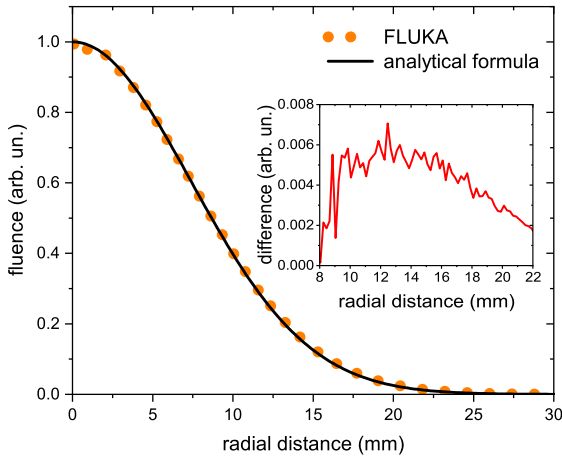


Fig. 4. Radial fluence in water of a collimated proton beam of energy 80 MeV and starting transversal Gaussian shape of standard deviation $w = 7.30$ mm at the penetration depth $z = 9R_0/10$: comparison between FLUKA simulation (dots) and analytical curve calculated using Eqs. (8) and (9) (solid line). The inset shows the difference between the two curves in the radial range $8 \text{ mm} \leq r \leq 22 \text{ mm}$.

The value of the beam-divergence parameter m —see Section 3.2—was estimated from the phase-space diagrams in Fig. 6 as $m = \tan \Psi$, where Ψ is given by Eq. (45) of [15]. By averaging between the x -plane and y -plane results, $m = 0.5446$ mrad/mm was obtained. Finally,

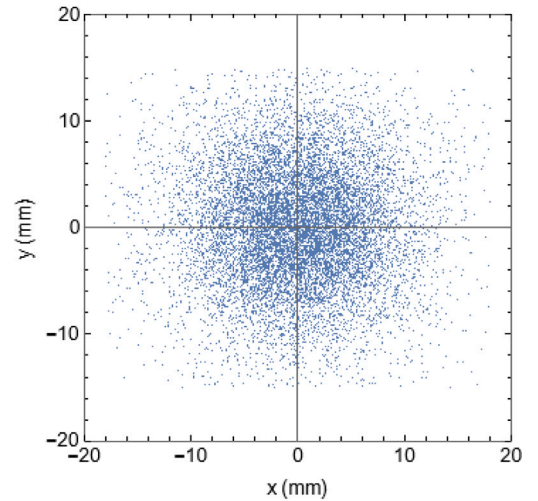


Fig. 5. Distribution on the Oxy plane at $z = 0$ of 12,955 virtual protons generated and propagated using LINAC and SRIM software. See the text for more details.

still referring to the Mathematica columns in Table 1, the beam energy spectrum at $z = 0$ was assumed to be Gaussian-shaped with mean value $E_0 = 69.83$ MeV and standard deviation $\sigma_{E_0} = 216.8$ keV.

To run the MC simulation of dose deposition in water, we used the Mathematica-generated phase-space file as the input source in FLUKA.

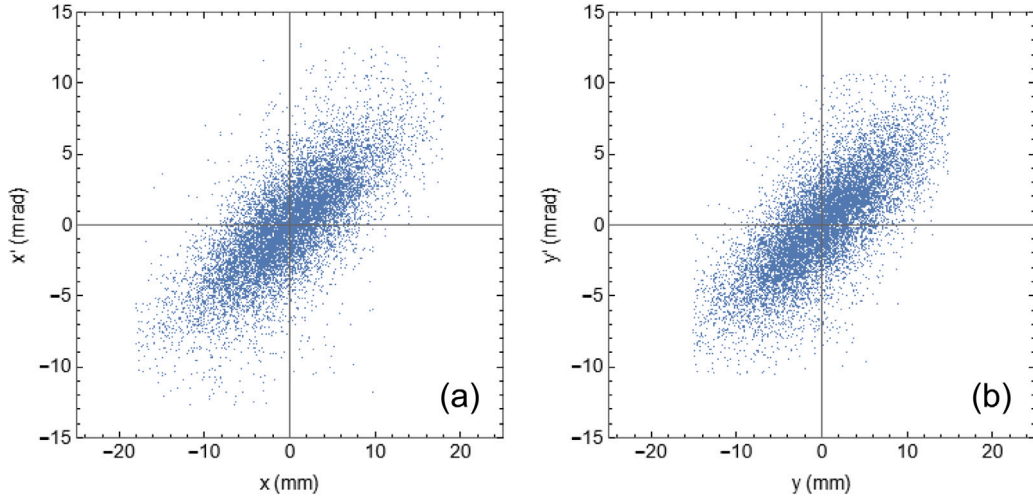


Fig. 6. Phase-space diagrams: slopes (a) x' and (b) y' at $z = 0$ of the particle-momentum projections of 12,955 virtual protons, generated and propagated using LINAC and SRIM software, as functions of the x and y coordinates, respectively.

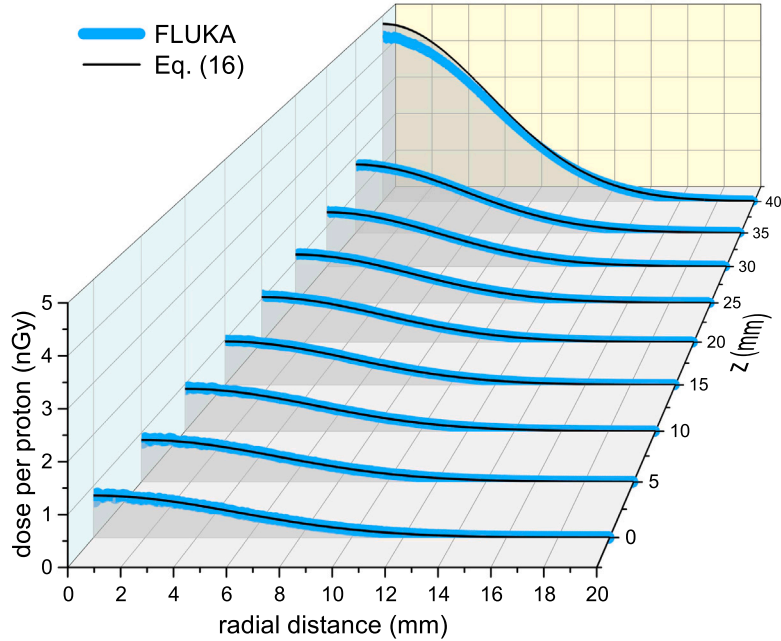


Fig. 7. Depth-radial distribution of dose deposited in water by a slightly diverging proton beam of Gaussian energy spectrum with mean 69.83 MeV and standard deviation 216.8 keV. Comparison between FLUKA simulations, using an externally generated phase-space source, and calculations performed with Eq. (16). See the text for more details.

In this software, the `PRECISIO` setting was chosen for the physics defaults, with the following additional option: a `FLUKAFIX` card was added with `Ekin frac` set equal to 0.01 for the water material. The dose was detected using a virtual `USRBIN` detector operating in `BEAMPART` and `R-Φ-Z` mode. This detector, with a radius of 3 cm sampled with 300 points, was coaxial to the beam propagation axis. Its extension along the z -axis ranged from $z = 0$ to $z = 5$ cm with a sampling of 500 points. To gain good statistics, the 5×10^5 virtual protons of the input phase-space source were launched 50 times by FLUKA, for a total of 2.5×10^7 particles entering the target. The radial distributions of dose were detected at discrete depths from $z = 0$ to $z = 40$ mm with a step of 5 mm. At each sampled depth, considering doses higher than 1/100 of their maximum value, the relative average simulation uncertainties were below 0.25%.

At the aforementioned discrete depths, Fig. 7 compares the radial distributions of dose per primary proton calculated using Eq. (16) with those simulated by FLUKA. The agreement between the curves

obtained with the two methods is very good, with the exception of a near-axis slight overestimation at $z = 40$ mm by the formula in Eq. (16) compared to the MC-simulated curve: ~ 4.78 nGy instead of ~ 4.48 nGy. By comparison with a FLUKA simulation of fluence vs. penetration depth, we have identified the origin of this difference in the calculation of $\phi_N(z)$ with the method reported in [20]. Indeed, at least for the parameters of this example, this method slightly overestimates the fluence in the region of the Bragg peak, located at a depth of about 40 mm. We have verified that a similar overestimation is found even when using the original Bortfeld's formula for fluence [12]. As seen in Fig. 7, this overestimation of fluence becomes an overestimation of the dose in the proximity of the Bragg peak.

A similar Bragg-peak dose overestimation was also reported in [33] by comparing Bortfeld's analytical formula with Geant4 simulations. In [33], Zhang and coworkers ascribed this overestimation to the fact that Bortfeld's formula applies to dose deposition along the proton tracks rather than on the axis. This means that Bortfeld's formula

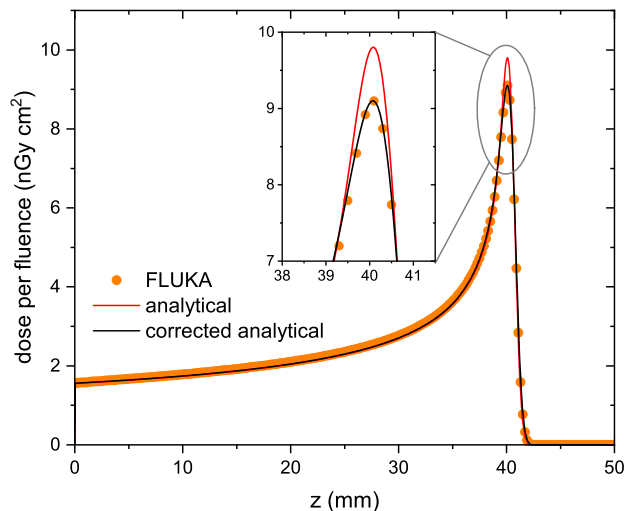


Fig. 8. Bragg curves corresponding to the 3D plot in Fig. 7: comparison among FLUKA simulation, analytical calculation, and analytical calculation with SSTA correction [33]. See the text for details.

does not account for peak smudging effects due to lateral scattering of the protons. However, a more reliable on-axis Bragg curve can be calculated as the superposition of curve projections calculated using Bortfeld's formula along the off-axis tracks. Under the approximation that the proton tracks can be assumed to be straight lines (SSTA, straight scattering track approximation) and that their slopes k follow a Gaussian distribution of standard deviation σ_k , Zhang and coworkers provided a correction to Bortfeld's formula consisting of averaging a continuum of scaled versions of it weighted by the aforementioned Gaussian.

While implementing this correction of the analytical Bragg curve formula into our 3D dose model is theoretically possible, its numerical nature would significantly slow down the calculations. This would defeat our purpose of having a quick and lightweight tool for preliminary optimizations of beam delivery lines via best fitting of target dose volumes. However, out of curiosity, we applied the correction to the analytically calculated monodimensional Bragg curve, $D_B(z)$, corresponding to the 3D distribution shown in Fig. 7, and compared it to a FLUKA simulation performed with the same previously used settings. The comparison is shown in Fig. 8. In this figure, the peak of the SSTA corrected curve (black line) matches almost exactly the FLUKA simulated one (orange dots). The difference with the uncorrected Bragg curve (red line) is clearly visible. The SSTA correction was applied with $\sigma_k = 0.11$ and assuming a mean energy of 70.05 MeV. Our value of σ_k is slightly larger than the one that could be expected from Fig. 6(a) in [33], very likely because the beam considered in our case is slightly divergent at the beginning of the propagation in $z = 0$. Regarding the slightly larger value of the mean energy compared to that reported in Table 1, it is easily justified by the fact that the projections onto the beam axis of the sloped Bragg curves entering the correction formula give rise to an average Bragg peak shifted to a slightly lower value of z . Consequently, a marginally higher energy is required to align it with the position given by the uncorrected analytical formula.

6. Discussion

As previously mentioned, the analytical calculation of 3D dose deposition in water presented in this paper is not meant for clinical applications. Instead, it can be used as a quick tool for preliminary irradiation design applications, which can be refined, if necessary, in a subsequent MC simulation stage. While we currently have no

experimental feedback about this two-stage design process, future tests are being planned.

For instance, the analytical model is going to be utilized to design beam delivery lines for the TOP-IMPLART linac for both pristine and SOBP test irradiations. The availability of such an analytical computation method will allow it to be included in efficient optimization codes and best fit the desired 3D dose target by varying the parameters—thicknesses of the materials, distances in air, etc.—of the beam delivery line, something that would be not feasible in reasonable times using an MC simulation-based process. The optimal values found in the first analytical stage, although possibly approximate, should be close enough to the most efficient ones. This will enable refinement in MC simulations aimed at optimizing the beam delivery line design without starting from an untested configuration. The results of the analytical stage will also provide strong confidence in choosing the spatial sampling and positioning of the virtual detectors to be used in the refinement MC simulations.

The extent to which computation times are shortened using the analytical 3D dose calculation compared to an MC simulation cannot be precisely quantified. It clearly depends on the computer and software being used, the complexity of the beam delivery line, as well as the desired spatial resolution and confidence level in the MC simulation. To provide a rough idea of the typical differences encountered in our workstation (Dell Precision 3660, 12th gen. Intel Core i9-12900K, 3200 MHz, 16 core, 24 logical processors, 64 GB RAM, Microsoft Windows 11 Pro build 26100.2894), consider the case examined in Section 5.2. To obtain the results shown in Fig. 7, our Mathematica code for Eq. (16) took about 0.28 s—including writing the nine calculated radial distributions to output ASCII files—while the FLUKA simulation—run under Ubuntu Linux hosted in WSL (Windows Subsystem for Linux, version 1) environment under Microsoft Windows—took about 40 min.

Finally, it is evident that incorporating an analytical computation routine into an optimization program will offer significant advantages, not only in terms of much shorter computation times but also in the practicality of utilizing a self-contained code.

7. Conclusions

Starting with two analytical models regarding proton beams—Bortfeld's model for Bragg curves in water [12], with a few modifications in our implementation, and Preston-Koehler's model for beam gradual widening due to MCS [13–15]—we have combined them to obtain an approximate analytical formula for 3D dose deposition in water by a Gaussian proton beam. The key steps to obtain this formula were: (a) generalizing Preston-Koehler's formula to the case of a finite-size Gaussian beam, either initially collimated or slightly diverging; (b) inserting the resulting fluence expression into Bortfeld's formula for dose deposition; (c) extracting this fluence from the integral used to incorporate range straggling and energy straggling into the dose formula.

Test comparisons of the developed model with MC simulations were performed. First, for four example proton energies (50, 60, 70, and 80 MeV), the transverse standard deviation of the 3D fluence of an initially collimated Gaussian beam was successfully compared with FLUKA simulations at selected penetration depths in water. Second, the radial distribution of dose of an initially slightly diverging ~ 70 MeV proton beam, whose coordinates in the phase space were generated using LINAC and SRIM software, was compared with FLUKA simulations at various penetration depths in water with good results.

In this second test, the axial dose value in the vicinity of the Bragg-peak depth was slightly overestimated by the analytical formula compared to the FLUKA simulation. We have ascribed this difference to the calculation of fluence, which, at least for the presented case,

is slightly overestimated near the Bragg peak even when using the original Bortfeld's formula. An example of how this difference could be corrected has been provided, even though it would involve numerical integrations that would significantly slow down our 3D dose computation. Nonetheless, it is worth recalling that the proposed formula for the 3D dose is meant to be used as a preliminary step in the design of test SOBPs for the commissioning and tests of the TOP-IMPLART linac. If necessary, the results of this preliminary step, which are not intended for actual clinical applications, will be checked and refined using MC simulations, for which they will provide a good starting point in setting the parameters.

CRedit authorship contribution statement

E. Nichelatti: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **C. Ronsivalle:** Writing – review & editing, Validation, Supervision, Software, Resources, Project administration, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used Microsoft CoPilot in order to only review and enhance certain English grammar and sentence structures. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Implementation of Bragg–Kleeman's formula

A.1. Values of α and p

For each energy E_0 in the set ranging from 5 to 100 MeV in 5 MeV increments, and from 100 to 160 MeV in 10 MeV increments, MC simulations of proton fluence versus the propagation distance z in water were run in FLUKA, considering a collimated proton beam of infinitesimal size. From these simulations, range values R_0 were estimated by fitting with a Gaussian function the z -derivative of the ending part of the fluence curves and setting R_0 , including its uncertainty, equal to the fitted value and uncertainty of the Gaussian center.

The values of R_0 obtained with this method are plotted in Fig. A.1 along with their best fitting curve using the BK function $R_0 = \alpha E_0^p$. The values of α and p obtained from the fit are listed in Table A.2 and compared with the original ones reported in [12].

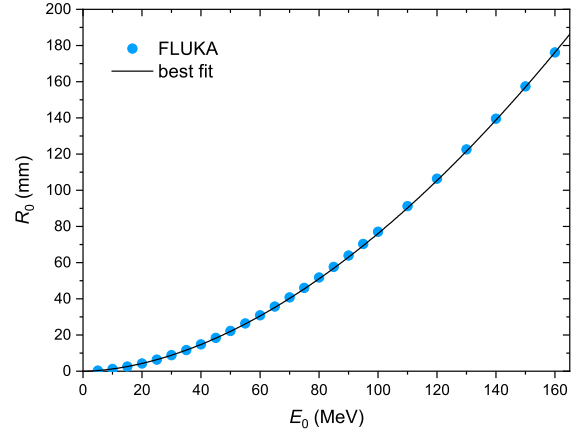


Fig. A.1. Range values R_0 versus proton energy E_0 as resulting from FLUKA simulations of fluence in water (points). The best fitting curve (solid line) is the BK function $R_0 = \alpha E_0^p$, whose parameter values are reported in Table A.2.

Table A.2

Values of α and p resulting from the fit of the points in Fig. A.1 along with those reported in [12].

	This paper	Ref. [12]
α ($\mu\text{m}/\text{MeV}^p$)	20.24 ± 0.10	22
p	1.7876 ± 0.0018	1.77

Table A.3

Values of the polynomial coefficients for the correction of the BK formula.

a_1 ($\mu\text{m}/\text{MeV}$)	a_2 ($\mu\text{m}/\text{MeV}^2$)	a_3 ($\mu\text{m}/\text{MeV}^3$)	a_4 ($\mu\text{m}/\text{MeV}^4$)	a_5 ($\mu\text{m}/\text{MeV}^5$)
-8.79671	0.20812	0.00181	-2.64611×10^{-5}	5.62779×10^{-8}

A.2. Polynomial correction

To gain better accuracy in the analytical evaluation of the range R_0 , we have fitted the difference between the values obtained from the FLUKA simulations and those of the best fitting curve in Fig. A.1 with a fifth-degree polynomial $P_5(E_0)$. In this way, our modified formula for the range is

$$R_0(E_0) = \alpha E_0^p + P_5(E_0) = \alpha E_0^p + \sum_{n=0}^5 a_n E_0^n. \quad (\text{A.1})$$

The values of the polynomial coefficients a_n are reported in Table A.3. Note that because a_0 must be zero to ensure a zero range for null energy, this coefficient is not shown in the table.

Appendix B. Approximation of Eq. (14)

Here, we seek a criterion to determine under what conditions the fluence $\phi(x, y, \zeta)$ can be taken out of the integral in Eq. (14) to obtain Eq. (15). Let us consider Eq. (14). In the vicinity of z , $\phi(x, y, \zeta)$ can be approximated using its first-order Taylor expansion,

$$\phi(x, y, \zeta) \approx \phi(x, y, z) + (\zeta - z) \left[\frac{\partial \phi}{\partial \zeta}(x, y, \zeta) \right]_{\zeta=z}. \quad (\text{B.1})$$

The Gaussian function in Eq. (14) assumes non-negligible values within a finite interval around z , for example, $z - 3\sigma \leq \zeta \leq z + 3\sigma$ to fix the ideas. This means that the integration limits can be approximated as $z \pm 3\sigma$, yielding:

$$D(x, y, z) \approx \frac{N_p}{\sqrt{2\pi} \sigma \phi_N(0)} \int_{z-3\sigma}^{z+3\sigma} \left\{ \phi(x, y, z) + (\zeta - z) \left[\frac{\partial \phi}{\partial \zeta}(x, y, \zeta) \right]_{\zeta=z} \right\} \times \hat{D}_B(\zeta) \exp \left[-\frac{(z - \zeta)^2}{2\sigma^2} \right] d\zeta. \quad (\text{B.2})$$

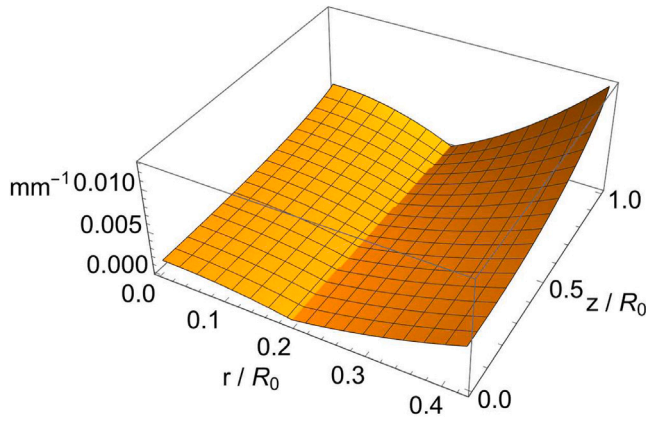


Fig. B.1. Map of the function $\left| \frac{\partial \phi}{\partial z}(r, z) / \phi(r, z) \right|$ for the considered example case.

If $\left| (\zeta - z) \left[\frac{\partial \phi}{\partial \zeta}(x, y, \zeta) \right]_{\zeta=z} \right|$ is much smaller than $|\phi(x, y, z)|$ for all ζ within the integration domain, the first-order term in Eq. (B.1) can be neglected, thus obtaining Eq. (15). Unfortunately, a general criterion to apply this simplification is not available. However, one can test its validity in a specific case as an example.

To this end, we consider the case of the slightly diverging proton beam discussed in Section 5.2, which has Gaussian shape and cylindrical symmetry (therefore, we use polar coordinates). The radial size of this beam at $z = 0$ is characterized by a standard deviation $w = 5.509$ mm. Its energy spectrum is Gaussian with an average energy of 69.83 MeV—corresponding to an average range in water $R_0 = 40.5$ mm—and a standard deviation of 216.8 keV. Preston–Koehler’s standard deviation at $z = R_0$ is $\sigma_{PK}(R_0) \approx 0.0225 R_0 = 0.911$ mm. The slope parameter has been evaluated to be $m \approx 0.5446$ mrad/mm, resulting in a radial standard deviation of the beam at $z = R_0$, as given by Eq. (12), $\sigma_r(R_0) \approx 5.704$ mm.

To test the feasibility of neglecting the first-order expansion term in Eq. (B.1), we used Mathematica [30] to map the function $\left| \frac{\partial \phi}{\partial z}(r, z) / \phi(r, z) \right|$ in the domain $(r, z) \in \{0 \leq r \leq 3\sigma_r(R_0)\} \times \{0 \leq z \leq R_0\}$. Considering values of r larger than $3\sigma_r(R_0)$ would be unnecessary due to the transverse Gaussian shape of the beam. We do not report the explicit analytic expression of $\left| \frac{\partial \phi}{\partial z}(r, z) / \phi(r, z) \right|$ because it would be too lengthy and not useful for our purposes. The map of this function is shown in Fig. B.1. Its maximum value is $M = 0.0126$ mm^{−1}, found at $(r, z) = (3\sigma_r(R_0), R_0)$. Because in Eq. (B.1) the maximum value $|\zeta - z|$ can assume is 3σ , the condition that allows us to neglect the first-order term in the Taylor expansion shown in Eq. (B.1) is $3M\sigma \ll 1$ or, equivalently, $\sigma \ll M^{-1}/3 = 26.5$ mm. For the considered case, the value of the total straggling, obtained by summing in quadrature the range straggling and the energy straggling [12], is $\sigma \approx 498$ μm, which abundantly satisfies the required condition.

Data availability

Data will be made available on request.

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