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A comparison between approximate solutions of the Bethe equation for clinical-energy-range proton beams

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ABSTRACT

Proton therapy is an alternative to conventional radiotherapy, especially for treating localized tumors near important and/or sensitive parts of the human body. Protons, due to their electric charge and mass, interact with the propagating media in such a way that a well localized maximum - known as the Bragg peak - is observed if a depth dose deposition curve is plotted. Since the Bragg peak location depends on the initial proton energy beam, by adjusting this parameter it can be placed over the tumor to be treated. In addition, because the dose deposition goes to zero right after this peak, the health tissue after the tumor is spared if proton therapy is adopted. However, despite the aforementioned advantages, many issues prevent a wider adoption of proton therapy over radiotherapy. In addition to the very high implementation cost, unsolved technical issues, such as, the uncertainty in the proton beam range within the medium, or the correct dose prediction at the Bragg peak, must be addressed. This research aims to investigate the validity of theoretical approximations for the solution of Bethe equation. Such approaches are compared to results from Monte Carlo simulations, executed with the MCNPX code, and reference values from the literature as well for the proton beam range, the energy deposition in the medium, and the unrestricted LET (linear energy transfer). A parameter is proposed and adopted to quantify the global difference between the theoretical approximations evaluated in this work with respect to the Monte Carlo simulation results.

Keywords: proton beam, Bethe equation, theoretical approaches, Monte Carlo simulation.

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1. INTRODUCTION

Proton therapy is a radiotherapeutic modality, originally proposed by Robert R. Wilson in 1946 [1], that allows for a high depth dose deposition near the maximum range attained by the proton beam in a medium. Moreover, proton therapy has the advantage of better maximizing the dose to the tumor tissue and minimizing the dose to organs at risk, if compared to conventional radiotherapy with photons [2], as shown in Figure 1. It is worth noting that Figure 1 depicts the energy deposition of a theoretical proton beam, with a well-defined, low-spread initial energy distribution. In clinical applications, less-focused proton beams with a larger initial energy spread are applied to tissue, resulting in a higher entrance skin dose, an attenuation in the Bragg peak amplitude, as well as a less steeper decrease after the tumoral tissue. Even though these effects may mitigate the proton therapy efficiency for some cancer modalities, gains in therapeutic ratio [3] are expected if the treatment with protons is compared to the treatment with photons [4,5].

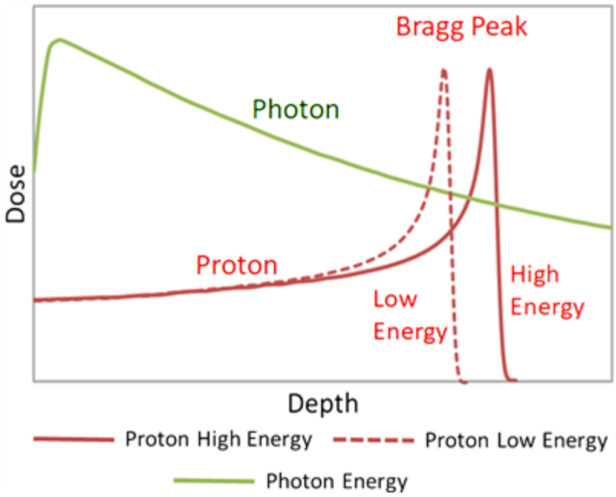

Figure 1 - *Schematic representation of depth dose deposition for a photon beam (conventional radiotherapy), and two proton beams, with low and high energies, respectively. Source: Adapted from Liao, Lim and Zhang* (2019) [6].

Assuming the typical energy range for clinical treatments, the predominant mechanisms of proton interaction with the medium corresponds to the Coulombian interaction with the electronic cloud [7]. The theory related to the energy transfer rate of a charged particle propagating in a material medium refers to the works of Rutherford (1909) [8], Bohr (1915) [9], Bethe (1930) [10], Bloch [11], remaining an active object of research [12-17]. This work aims to compare the existing semi-analytical and numerical solutions for the Bethe equation, here named as the theoretical results, obtained by considering different approaches given in the literature. Particularly, an analytical form to the inverse integral exponential function is used. The predictions for the proton range and energy deposition of a clinical proton beam (100-250 MeV) are analyzed. These theoretical results are compared with reference values from ICRU-49 [18], and with Monte Carlo simulation results as well. In section 2, a brief introduction to the modeling of this problem is presented, resulting in the so-called Bethe equation. In section 3, some approaches for the solution of this equation are presented, particularly an analytical form proposed in this work. In section 4, a brief description of the Monte Carlo simulation code is presented, and in section 5 the simulation results are compared with the theoretical predictions. Finally, in section 6, the conclusions are presented.

2. THE MODEL

To start modeling this problem, we consider a beam particle with charge $q = z\,e$ where z is an integer and e is the elementary charge, which propagates in a straight line within the medium with velocity v. In addition, electrons in the medium are assumed to be free and at rest in the laboratory reference frame. Then, if the smallest distance between a beam particle and an electron in the material is given by the impact parameter b, the distance $r(t)$ between this particle and that electron is given by the expression $r^2(t) = b^2 + (\gamma v t)^2$, where $\gamma = (1-\beta^2)^{-1/2}$ is the Lorentz relativistic factor, $\beta = v/c$, and c is the speed of light in vacuum, as schematically represented on Figure 2.

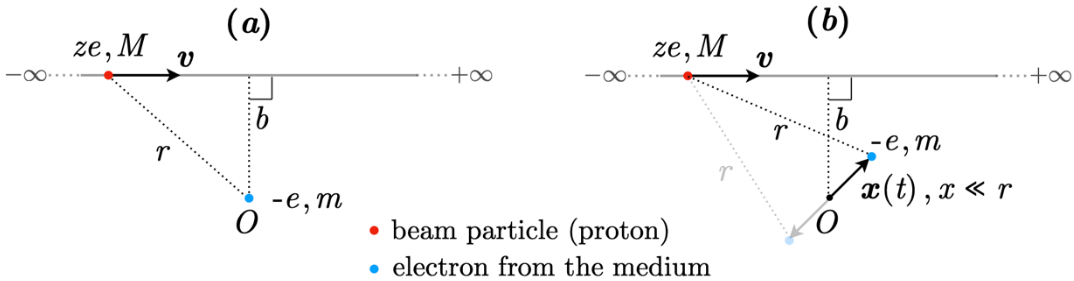

Figure 2: *Schematic representation of a charged particle of mass M and total charge $q = ze$ with velocity v passing close to an electron from the medium, and b is the impact parameter [19]. Panel (a) depicts the case in which the electron is at rest; In panel (b), the electron is at motion, with a displacement much smaller than its distance to the beam particle (x(t) << r).*

In a collision between a beam particle and an electron at rest from the medium, as shown in Figure 2(*a*), the modulus of the momentum Δp transferred to this electron is given by the following expression,

$$\Delta p = \int_{-\infty}^{+\infty} e\, \mathbb{E}_{\perp}(t) dt = \int_{-\infty}^{+\infty} \frac{\gamma b z e^2}{r^3(t)} dt = \frac{2ze^2}{b\, v}, \tag{1}$$

where $\mathbb{E}_{\perp}(t)$ is the transverse component of the electric field generated by the particle beam [19]. The assumption of the electron being at rest in the collision is plausible if the beam particles are sufficiently faster and heavier. From equation (1), the electron energy gain ΔE is given by

$$\Delta E(b) = \frac{(\Delta p)^2}{2m} = \frac{2z^2 e^4}{mv^2}\left(\frac{1}{b^2}\right), \tag{2}$$

where m is the electron mass. The divergence in eq. (2) can be removed assuming that there is a minimum value for the impact parameter, which can be obtained from the expression for the maximum electron energy gain, achieved for the case where the electron momentum is inverted ($p \to -p$) in the rest reference frame of the heavy beam particle,

$$\Delta E(b_{min}) = \Delta E_{máx} = 2\, m\, \gamma^2 v^2, \tag{3}$$

and by comparing equations (2) and (3),

$$b_{min} = \frac{z\, e^2}{\gamma\, m\, v^2}. \tag{4}$$

If the collision time is very long in comparison to the electron orbital period, then the electron will interact adiabatically with the incident particle, with no net energy transfer. This situation defines the maximum value for the impact parameter,

$$b_{max} = \frac{\gamma\, v}{\omega}, \tag{5}$$

where ω is the electron angular frequency. Considering all electrons situated between b_{min} and b_{max}, at a given depth Δx around a position x in the medium,

$$\Delta E \simeq n \int_{b_{min}}^{b_{máx}} \Delta E(b)\, 2\pi\, b\, db\, \Delta x, \tag{6}$$

where *n* is the electron density of the medium, here assumed as uniform. Then,

$$\frac{dE}{dx} \simeq 4\pi n \frac{z^2 e^4}{m v^2} ln(\frac{\gamma^2 m v^3}{z e^2 \omega}), \tag{7}$$

which represents the energy gain by unit length of a free electron gas. However, in general, electrons are not free in the target atom. Hence, in a simpler approach, this interaction could be approximated by some harmonic potential plus some dissipative term. Under this condition, the electron can be assumed to be oscillating around a fixed position, as shown in Figure 2(*b*). In the presence of a particle from the incident beam, the electron experiences the electric field generated by such a particle, gaining energy according to the following expression,

$$\Delta E = e\int_{-\infty}^{+\infty} \boldsymbol{v}.\mathbb{E}\, dt. \tag{8}$$

After some additional algebraic steps, by considering the complete expression for the electric field generated by a relativistic charged particle, $\mathbb{E}$(t) [19], one finds that

$$\frac{dE}{dx} = 4\pi n \frac{z^2 e^4}{m v^2} [ln(\frac{2 e^{-\lambda} \gamma^2 m v^3}{z e^2 <\omega>}) - \frac{v^2}{2c^2}], \tag{9}$$

where $<\omega>$ is the average electron angular frequency, obtained from $Z\, ln <\omega> = \sum_j f_j\, ln\, \omega_j$, with $\sum_j f_j = Z$, where *Z* is the atomic number from the target atom, and λ is the Euler constant [20]. Equation (9) was initially derived by Bohr in 1915, in its seminal work [9], and more recently [17], by using a distinct approach. If the beam particles are not fast enough in comparison to the target particles, or if the target density is sufficiently high, quantum effects need to be considered [11]. In particular, the minimum value for the impact parameter, b_{min}, must obey Heisenberg's uncertainty principle [21]. Considering this constraint, and following the previous derivation steps, one can show that

$$\frac{dE}{dx} = 4\pi n \frac{z^2 e^4}{m v^2} [ln(\frac{2\gamma^2 m v^2}{<I>}) - \frac{v^2}{c^2}], \tag{10}$$

where $<I>$ is the average excitation potential of the medium, which can be either theoretically derived or obtained from standard references [18, 22]. Equation (10) was initially presented by Bethe (1930) [10], and later corrected by Born [11], in order to consider other quantum effects. Assuming that the electron energy gain, ΔE corresponds exactly to the energy transferred by the beam particle ΔE^*, i.e., $\Delta E = -\Delta E^*$, the beam linear stopping power *S* is given by

$$S = -\frac{dE^*}{dx} = \frac{dE}{dx}, \tag{11}$$

which under this condition corresponds to the unrestricted beam linear energy transfer (LET). Since the mass stopping power is defined by $S_\rho = S/\rho$, where ρ is the mass density of the medium, in Bethe's approach,

$$S_\rho = C_0 \frac{Zz^2}{A}\frac{1}{\beta^2}[ln(\frac{2mc^2}{<I>}) + ln(\frac{\beta^2}{1-\beta^2}) - \beta^2], \tag{12}$$

where $C_0 = 4\pi N_A {r_e}^2 mc^2$, $r_e = \frac{e^2}{mc^2}$ is the classical electron radius, N_A is the Avogadro's constant, and A is the relative atomic mass of the target atom. In this work the equation (12) is solved, by different approaches, for a monoenergetic proton beam propagating in a water phantom, and compared with Monte Carlo simulation results, and with data obtained from standard references [18, 22].

3. APPROXIMATE SOLUTIONS FOR THE BETHE EQUATION

From the relativistic energy of a beam particle $E^* = (\gamma - 1)Mc^2$, where M is the mass of such a particle, it is possible to derive the energy per unit length transferred from the beam particle to the medium,

$$\frac{dE^*}{dx} = Mc^2\frac{d\gamma}{dx} = Mc^2\frac{\beta}{(1-\beta^2)^{3/2}}\frac{d\beta}{dx}, \tag{13}$$

and, if it is assumed that all this energy is transferred to the electrons in the medium, the eqs. (12) and (13) can be compared, such that,

$$\frac{d\beta}{dx} = -C_1\frac{(1-\beta^2)^{3/2}}{\beta^3}[ln(\frac{C_2\beta^2}{1-\beta^2}) - \beta^2], \tag{14}$$

where $C_2 = \frac{2\,m\,c^2}{<I>}$, $C_1 = \rho C_0 \frac{Z\,z^2}{A\,M\,c^2}$, $C_0 = 0.30707\ MeV\ cm^2\ mol^{-1}$. Assuming a proton beam, $(m\,, M) = (0.511\,, 938.272)\ MeV/c^2$, pointing to the resting masses of the electron and the proton, respectively. The differential equation (14) when solved offers the proton range in the medium,

$$R_{CSDA} = \frac{1}{C_1}\int_0^{\beta_0} \frac{\beta^3(1-\beta^2)^{-3/2}}{ln(\frac{C_2\beta^2}{1-\beta^2})-\beta^2}\,d\beta, \tag{15}$$

where (CSDA) refers to the continuous slowing down approximation, which means that the beam particle continuously transfers energy along its path inside the material [4]. The integral given in eq. (15) has no analytical solution. However, approximate solutions can be found in literature [23-24]. In particular, Grimes et al. (2017) [15] proposed an alternative in which, by using a series expansion in powers of β for the logarithm in the Bethe equation (12), the proton range can be written in the following parametric form,

$$R_{CSDA} = \int_0^{R'} [1-\beta^2(x')\,]^{-3/2} dx', \tag{16}$$

with $\beta^2(x')$ given by,

$$\beta^2(x') = \frac{1}{C_2} Exp\{\frac{1}{2}\ \varepsilon_i^{-1}[2{C_2}^2 C_1(R'-x')]\}, \tag{17}$$

and,

$$R' = \frac{\varepsilon_i[ln({C_2}^2{\beta_0}^4)]}{2{C_2}^2 C_1}, \tag{18}$$

where $\varepsilon_i(x)$ is the exponential integral function,

$$\varepsilon_i(x) = \int_{-\infty}^{x} \frac{e^{x'}}{x'}\,dx'. \tag{19}$$

Equations (16-18) present a solution for the Bethe equation, and ${\varepsilon_i}^{-1}(x)$ refers to the inverse exponential integral function, to be obtained numerically [15]. In this work, by considering the asymptotic behavior of $\varepsilon_i(x)$,

$$\lim_{x\to\infty} \varepsilon_i(x) = \frac{e^x}{x}, \tag{20}$$

an alternative way to determine the function ${\varepsilon_i}^{-1}(x)$ is presented by iteratively solving [25] the following equation,

$$x = e^{{\varepsilon_i}^{-1}(x)} / {\varepsilon_i}^{-1}(x). \tag{21}$$

By proposing the initial ansatz ${\varepsilon_i}^{-1}(x) \approx ln\, x$, after some iterations one can find its asymptotic form,

$${\varepsilon_i}^{-1}(x) \simeq A\, ln(x\, ln(x\, ln(x))), \tag{22}$$

where A is a constant which allows for adjusting the theoretical initial beam energy.

The approximation for ${\varepsilon_i}^{-1}(x)$ given by Eq. (22), labeled as "XLOGX" in the upcoming figures, is used to determine the proton range, and energy deposition in the medium. The same quantities are obtained by using the predictions of [15], labeled as "Grimes" in the upcoming figures, and then both approaches are compared to Monte Carlo simulation results.

4. MONTE CARLO SIMULATIONS

The Monte Carlo code MCNPX 2.7.0 [26] is used to simulate a monoenergetic beam of protons propagating in a rectangular phantom composed of liquid water, with average ionization potential $< I >= 75\ eV$, in agreement with the ICRU-49 reference [18]. A monoenergetic beam was chosen to match the reference [15]. The initial beam energies adopted in the simulations range from 100 MeV to 250 MeV. The deposited energy in the phantom is detected along its central axis, with detectors (tally F6) longitudinally spaced in order to cover the expected proton beam range [18]. For each simulation, a pencil beam of 2 x 10^9 protons originated from a monodirectional disk source propagating in a z direction. For this number of particles, the relative errors associated with the deposited dose are under 0.009%. To describe the transport of incident particles, the following parameters were used: elastic scattering for protons, pre-equilibrium model after intranuclear cascade, Bertini model for intranuclear cascade, and other parameters were set to their default value, according to the MCNPX manual [26]. Although newer, enhanced intranuclear models are available [27], recent works still use Bertini's model, in the MCNPX and in GEANT4 as well, to compare simulation results with experimental data [28].

5. RESULTS AND DISCUSSION

In figure 3, the proton beam range, obtained by using both theoretical approaches (XLOGX, Grimes), is compared with the reference values given in ICRU-49 [18]. The average error of the deviations between the theoretical and reference values are 0.07% and 0.04% for the XLOGX and the Grimes approximation, respectively. Regarding the computation time to generate both curves shown in Figure 3, while the XLOGX approximation required a computational time of 2.8 s, the Grimes method required 27.1 s under the same computational conditions in Mathematica 10.

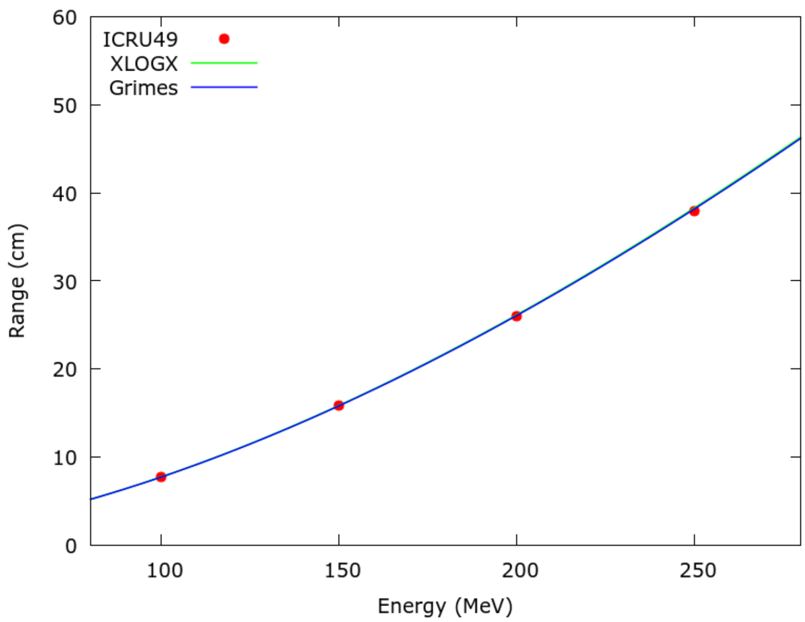

Figure 3 - Proton beam *range as a function of the initial beam energy, obtained by using both XLOGX and Grimes approaches, through the eqs.* (16)-(18)*, compared with ICRU-49* [18] *reference values.*

In Figure 4, the average beam energy is plotted as a function of depth for each initial energy E_0: 100 MeV, 150 MeV, 200 MeV, and 250 MeV. $E(x)$ points to the theoretical energy predictions (XLOGX, Grimes) and $E_{MC}(x)$ to the Monte Carlo simulation results (MCNPX).

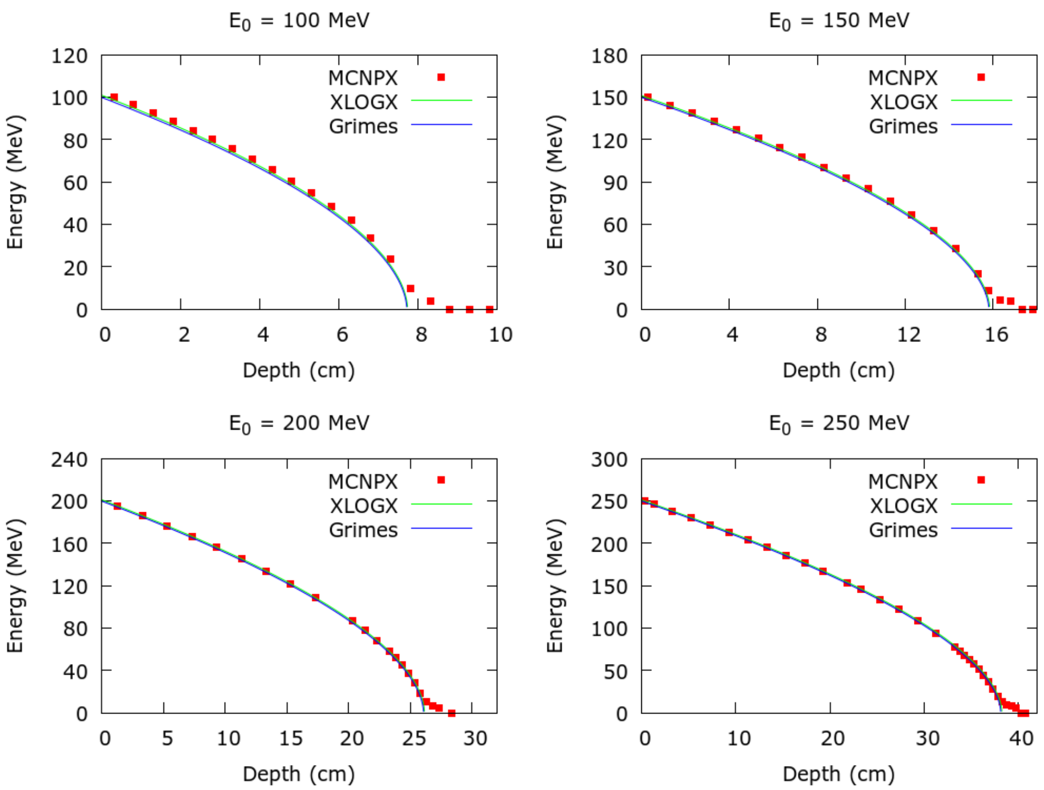

Figure 4 - *Average beam energy as a function of depth, obtained from Monte Carlo simulation results (MCNPX), compared to the theoretical predictions, obtained by integrating eq.* (13) *using eq.* (17)*, for both XLOGX and Grimes approaches.*

In order to quantify the differences between the XLOGX and Grimes approaches, the following quantity is defined,

$$\sigma^2(E_0, x) = \{ [E(x) - E_{MC}(x)] \,/\, E_0\}^2 \quad . \tag{23}$$

Figure 5 shows values of $\sigma(E_0, x)$ calculated all along the depth, for each of the previously presented simulations.

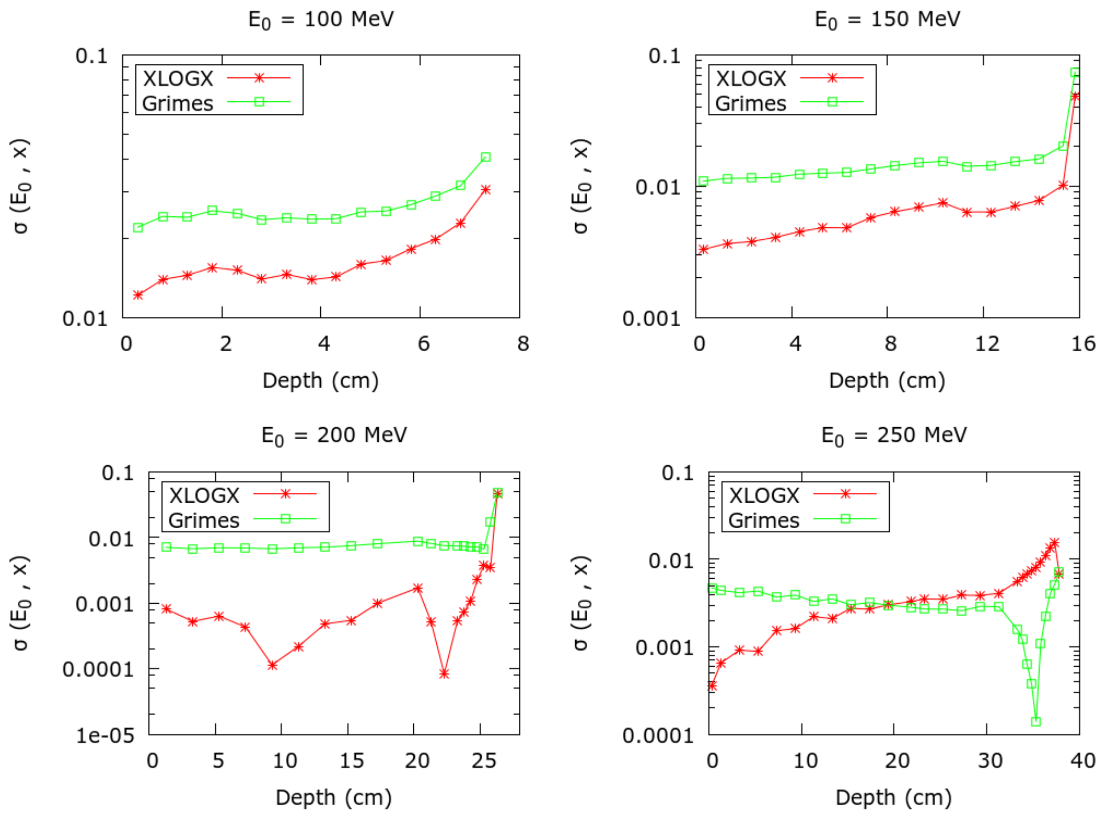

Figure 5 - *Deviation between the proposed theoretical approaches (XLOGX, Grimes) and Monte Carlo simulation results (MCNPX), obtained by the parameter defined in eq.* (23).

From Figure 5 one can see that, for lower energies (up to 200 MeV), the XLOGX approach shows a lower deviation from the Monte Carlo simulation results, if compared to the Grimes approach. For the 250 MeV proton beam, although the deviation calculated for the XLOGX is initially lower, it grows with the depth, becoming higher than that of the Grimes approach after approximately half of the proton range. In order to better elucidate the difference between the XLOGX and Grimes predictions in comparison to the Monte Carlo simulation results (MCNPX), the global deviation can be quantified as follows,

$$\sigma^2(E_0) = \int_0^{R_I(E_0)} \sigma^2(E_0, x)\, dx, \qquad (24)$$

where $\sigma\ (E_0)$ is analog to the statistical standard deviation for each initial energy E_0, and $R_I(E_0)$ is the theoretical proton beam range. Figure 6 shows the values of $\sigma\ (E_0)$ calculated for all investigated energies, for both approaches (XLOGX, Grimes).

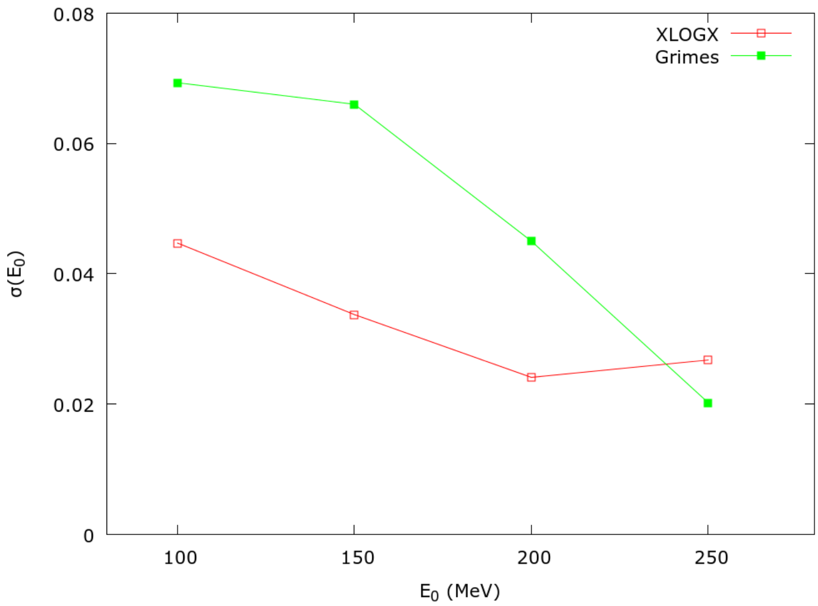

Figure 6 - *Global behavior of the approximations as a function of the initial beam energy, measured by the parameter* $\sigma(E_0)$ *defined on eq.* (24).

6. CONCLUSION

Despite the nuclear interactions not being taken into account in Bethe equation, Figure 4 shows that the results obtained from approximate solutions of this equation, for both investigated approaches (XLOGX and Grimes), are in agreement with the Monte Carlo simulations, which include such nuclear interactions. Figure 6 shows that, for energies up to ~240 MeV, spanning the typical clinical energy range for proton beams, the XLOGX approach has a better agreement with the simulation results, providing an average total deviation of approximately 3%, while the Grimes approach provides an average total deviation of 5%. In addition, the computational time required to obtain the theoretical curves by using the XLOGX approach is approximately nine times faster than that required if the Grimes approach is adopted. In future works, these theoretical approaches will be extended for non-homogeneous media, non-monoenergetic beams, and other treatment modalities. In addition, the impact of using existing newer, enhanced intranuclear cascade models in Monte Carlo simulations will be evaluated.

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