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FULL PAPER

Standardizing Monte Carlo simulation parameters for a reproducible dose-averaged linear energy transfer

1WEI YANG CALVIN KOH, 2HONG QI TAN, 2KHONG WEI ANG, 2SUNG YONG PARK, 1WEN SIANG LEW and 1,2JAMES CHEOW LEI LEE

1Division of Physics and Applied Physics, Nanyang Technological University, Singapore, Singapore
2Division of Radiation Oncology, National Cancer Centre Singapore, Singapore, Singapore

Address correspondence to: Mr Wei Yang Calvin Koh
E-mail: calvin.kohwy@gmail.com

Objective: Dose-averaged linear energy transfer (LETD) is one of the factors which determines relative biological effectiveness (RBE) for treatment planning in proton therapy. It is usually determined from Monte Carlo (MC) simulation. However, no standard simulation protocols were established for sampling of LETD. Simulation parameters like maximum step length and range cut will affect secondary electrons production and have an impact on the accuracy of dose distribution and LETD. We aim to show how different combinations of step length and range cut in GEANT4 will affect the result in sampling of LETD using different MC scoring methods.

Methods: In this work, different step length and range cut value in a clinically relevant voxel geometry were used for comparison. Different LETD scoring methods were established and the concept of covariance between energy deposition per step and step length is used to explain the differences between them.

Results: We recommend a maximum step length of 0.05 mm and a range cut of 0.01 mm in MC simulation as this yields the most consistent LETD value across different scoring methods. Different LETD scoring methods are also compared and variation up to 200% can be observed at the plateau of 80 MeV proton beam. Scoring Method one has one of the lowest percentage differences compared across all simulation parameters.

Conclusion: We have determined a set of maximum step length and range cut parameters to be used for LETD scoring in a 1 mm voxelized geometry. LETD scoring method should also be clearly defined and standardized to facilitate cross-institutional studies.

INTRODUCTION

In radiation therapy, dose is used an indicator for inducing cell death and thus tumour control. However, in proton therapy, LETD is one of the independent variables required for the calculation of relative biological effectiveness (RBE)\(^1\). In fact, McMahon et al\(^1\) had reported that there is a better correlation between cell survival curve and both dose and dose-averaged linear energy transfer (LETD) as compared to solely dose in proton irradiation. This further exemplifies that LETD affects the biological effective dose calculation and it should be determined meticulously.

LET values are difficult to measure experimentally\(^4,5\) and thus they are often determined analytically\(^6\) or via simulation\(^7,8\). Monte Carlo (MC) simulation is usually used for this purpose as it is regarded as the gold standard in radiation transport simulation\(^8\). Although MC simulation is used extensively in various applications (Medical, Space and Radiation Protection), the results depend heavily on the physics models and the parameters incorporated in the simulation.

Despite the known importance of LET values and its effect on cell killing\(^9,10\), there is still a lack of studies investigating the credibility of the methods to obtain LETD values from MC simulation. The reproducibility of LET values will depend on the definition of LETD: (a) track-averaged LET (LET\(_{T}\)) and (b) dose-averaged LET (LET\(_{D}\)) as represented by analytical equations discussed in Wilkens and Oelfke\(^6\). Furthermore, in MC simulation, parameters such as the choice of physics model, maximum step length (upper limit of a particle's tracking step length), range cut limits (minimum energy of secondary particles in inelastic interaction) and voxel dimensions can also cause a variation in the scoring of LET. Since LETD is used for the calculation of
RBE\textsuperscript{1–3}, it will be the main focus in this work and the analytical equation is calculated using

\begin{equation}
\text{LET}_D \left( r^2 \right) = \frac{\int D \left( E, r^2 \right) \text{LET} \left( E \right) dE}{\int D \left( E, r^2 \right) dE}
\end{equation}

where \( D \left( E, r^2 \right) \) is the dose deposited by the proton with energy \( E \) at location \( r^2 \). However, in MC simulation, LET\(D \) is generally expressed as

\begin{equation}
\text{LET}_D = \frac{\sum_{i=1}^{n} \frac{\epsilon_i}{\rho_i}}{\sum_{i=1}^{n} \epsilon_i}
\end{equation}

where \( \epsilon_i \) is the energy deposition by the \( i \)th charged particle, \( \rho_i \) is the step length and \( n \) is the total number of steps in the voxel\textsuperscript{4,13}. As defined in ICRU Report No. 85\textsuperscript{14}, LET is the average energy transfer by the charged particle per unit length due to electronic interactions at a spatial point. This definition of LET is limited to one specified type of charged particles (proton, electron and other heavy ion) at any one point of time. However, LET\(D \) is used in this work as it accounts for an ensemble of charged particles in a particular voxel instead of considering only one type of particle and this has higher correlation to biological damage. Since primary protons and secondary electrons both contribute to the biological damage in real-life situation, they should be included in LET\(D \) calculation. Therefore, the LET\(D \) is simplified to the total energy deposited by the charged particles in MC simulation\textsuperscript{7} as described by Eq. (2).

There were several works done on using MC simulation to sample LET\(D \). A large range cut for secondary electrons is often used in a typical MC simulation for proton therapy application\textsuperscript{15,16} because of the increased computation time for explicit electron tracking. This poses a problem in a real-life situation of a lung patient where the electrons do travel over a higher range due to the low density of lung and secondary electrons need to be factored in for greater dose accuracy. As demonstrated by Guan et al\textsuperscript{17}, they used GEANT4 MC toolkit\textsuperscript{17–19} to simulate a proton beam with a high range cut (no explicit secondary electron production) and consider only electronic inelastic interactions (nuclear interactions are neglected) to compare LET\(D \) and LET\(p \) values. In the work by Cortes-Giraldo et al\textsuperscript{20}, they showed that there is a difference in the calculated LET\(D \) based on the different LET\(D \) scoring methods, range cut and voxel dimensions used. However, their work was done using MC simulation with a cylindrical volume rather than a voxelized geometry which is used clinically.

In addition to the variation of parameters in MC simulation, the scoring methods for LET\(D \) differ with different studies. Both Guan et al\textsuperscript{17} and Granville et al\textsuperscript{21} compared the LET\(D \) scoring methods using the BJR LET\(D \) calculation. They had recommended a scoring method which provided a stable unrestricted LET\(D \) with different voxel sizes and production cuts. However, this method simplifies the LET\(D \) scoring method to unrestricted LET\(D \) and is similar to the Unrestricted method in Sec. (2). Thus, their method is excluded in our comparison. This shows that LET\(D \) scoring method is not clearly defined in MC and there is no strong physical basis on which scoring methods should be used in scoring LET\(D \) especially when both primary protons and secondary electrons are present in the simulation.

In this work, we are interested in the scoring of both primary protons and secondary electrons due to the aforementioned problem in real-life situation. We examine the best step length (\( \text{stepMax} \)), range cut (\( \text{setCut} \)) value and LET\(D \) scoring methods (Table 1) that should be implemented in MC simulation to achieve a reproducible LET\(D \) value in a clinically relevant voxel geometry. Although LET\(D \) must be insensitive to variations of hyperparameters of the simulation, one should not omit the fact that hyperparameters do affect the LET\(D \) results. Therefore, we aim to propose and standardize a step length, range cut and LET\(D \) scoring method for MC simulation so as to obtain a most reproducible LET\(D \) result.

**METHODS AND MATERIALS**

MC simulation settings

A mono-energetic proton beam of 80 MeV, 150 MeV and 200 MeV were irradiated at central axis of a 30×30×30 cm\(^3\) water

<table>
<thead>
<tr>
<th>Unrestricted</th>
<th>Method 1</th>
<th>Method 2</th>
<th>Method 3</th>
<th>Method 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \sum_{i=1}^{p} \frac{\epsilon_i}{\rho_i} )</td>
<td>( \sum_{i=1}^{p} \frac{\epsilon_i}{\rho_i} )</td>
<td>( \sum_{i=1}^{p} \frac{\epsilon_i}{\rho_i} )</td>
<td>( \sum_{i=1}^{p} \frac{\epsilon_i}{\rho_i} )</td>
<td>( \sum_{i=1}^{p} \frac{\epsilon_i}{\rho_i} )</td>
</tr>
<tr>
<td>( \frac{\epsilon}{\rho} )</td>
<td>( \frac{\epsilon}{\rho} )</td>
<td>( \frac{\epsilon}{\rho} )</td>
<td>( \frac{\epsilon}{\rho} )</td>
<td>( \frac{\epsilon}{\rho} )</td>
</tr>
</tbody>
</table>

Table 1. This table shows the LET\(D \) scoring methods where \( n_p \) (\( n_e \)) refers to the number of protons (electrons), \( \epsilon_p \) (\( \epsilon_e \)) is the energy deposition of protons (electrons) and \( \rho_p \) (\( \rho_e \)) is the step length of protons (electrons). The last row shows the mathematical expectation of each corresponding LET\(D \) scoring methods where \( i \in p, e \).
phantom using GEANT4 MC Toolkit, respectively. The water phantom is voxelized into 1 mm³ cube and the z-coordinate (depth) of the water phantom ranges from 0 to 300 mm. The number of particle histories is set to 100,000 and the dose errors are less than 2% across the central axis of the dose. G4EmStandardPhysics_option 4 is used for physics model as it is the recommended physical model for clinical proton beam below 5 GeV\(^4\).

Energy deposition and step length are scored individually for every particle in the selected voxels at Positions 1, 2, 3 and 4 for each proton beam energy as shown in Figure 1 a, b and c. Positions beyond the Bragg peak were not chosen due to the absence of secondary electrons. There is no difference in the LET\(_D\) calculations beyond the Bragg peak were not chosen due to the absence of secondary electrons. There is no difference in the LET\(_D\) calculations beyond the Bragg peak.

In this work, we used the concept of correlation to understand differences between LET\(_D\) scoring methods. Most of the differences in LET\(_D\) definition arises from the inequality of LET\(_D\) scoring methods. There are different ways to calculate the average LET in an ensemble of \(e_p\) and \(l_p\) (\(e_{\epsilon_p}\) and \(l_{\epsilon_p}\)) pair. Table 1 shows the five different LET\(_D\) scoring method to calculate LET\(_D\) for each voxel and its respective mathematical expectation form. The LET\(_D\) scoring methods are the possible ways to calculate LET\(_D\) in MC simulation and the mathematical expectation form can be calculated from the relation in Eq. (7). The expectation is taken across all steps and events in the simulation and is defined similarly for all five methods. Methods 1 to 4 include secondary electrons in

### Table 2

<table>
<thead>
<tr>
<th>Energy/MeV</th>
<th>stepMax/mm</th>
<th>setCut/mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>150</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>200</td>
<td>0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Unrestricted</td>
<td>10⁶</td>
<td></td>
</tr>
</tbody>
</table>

Correlation between LET\(_D\) scoring methods

In this work, we used the concept of correlation to understand differences between LET\(_D\) scoring methods. Most of the differences in LET\(_D\) definition arises from the inequality of LET\(_D\) scoring methods. There are different ways to calculate the average LET in an ensemble of \(e_p\) and \(l_p\) (\(e_{\epsilon_p}\) and \(l_{\epsilon_p}\)) pair. Table 1 shows the five different LET\(_D\) scoring method to calculate LET\(_D\) for each voxel and its respective mathematical expectation form. The LET\(_D\) scoring methods are the possible ways to calculate LET\(_D\) in MC simulation and the mathematical expectation form can be calculated from the relation in Eq. (7). The expectation is taken across all steps and events in the simulation and is defined similarly for all five methods. Methods 1 to 4 include secondary electrons in
the scoring of LET\(_D\). LET\(_D\) scoring methods suggested by both Cortes-Giraldo et al\(^\text{20}\) and Granville et al\(^6\) are similar to our Unrestricted method.

\[
\frac{E\left(\frac{\epsilon^2}{\epsilon_i}\right)}{E(\epsilon_i)} \approx \sum \frac{\epsilon_i^2}{\sum \epsilon_i} \times \frac{1}{n_i} \tag{7}
\]

Unrestricted and Method 1 are similar scoring methods where Unrestricted uses high range cut value leading to no secondary electrons production, hence the absence of \(n_e, \epsilon_e\) and \(l_e\). Methods 1 and 4 use similar concept to the work by Cortes-Giraldo et al\(^\text{20}\) method except that energy deposition from secondary electrons were excluded in the calculation. In Methods 2, 3 and 4, energy depositions are summed before dividing by the sum of step length, whereas Unrestricted and Method 1 are summed after each step energy deposition divided by its step length.

In addition, by using Eq. (6), we can understand why different scoring methods affect the LET\(_D\) results. Thus, Table 1 shows the numerator of each scoring methods expressed in exact mathematical form. Furthermore, by evaluating the reproducibility of LET\(_D\) values with different scoring methods at Positions 1 to 4 (as defined in Sec. (2.1)), a set of MC simulation parameters could be recommended.

**RESULTS**

The results in the variation of LET\(_D\) values from different energy cut for 80 MeV and 200 MeV are shown in Figure 2. Proton–Unrestricted refers to data from range cut of 1000 mm. Proton–Restricted and Proton/Electron–Restricted refer to data from range cut of 0.01 mm using Method 1. The former LET\(_D\) calculation factors in only primary proton while the latter accounts for both primary protons and secondary electrons. Figure 2 shows how LET\(_D\) values depend on the range cut value set for MC simulation. There is a discrepancy between Unrestricted and Restricted LET\(_D\), especially at the plateau region. This is due to the presence of secondary electrons limited by the range cut. Unrestricted LET\(_D\) is higher than Restricted LET\(_D\) despite not including secondary electrons in the calculation. This further proved that we should be careful in choosing the range cut value during simulation.

**Correlation analysis**

The covariance between energy deposition per step and step length of the proton beam is shown in Figure 3. Individual particle track was scored at selected voxels and the energy deposition per step was plotted for each permutation of energy, step length and range cut. Plots a, b and c represent range cut of 0.01 mm at Position 1; Plots d, e and f represent range cut of 0.05 mm at Position 2; and Plots g, h and i represent range cut of 0.1 mm at Position 3. Plots a, d and g represent step length of 0.01 mm; Plots b, e and h represent step length of 0.05 mm; and Plots c, f and i represent step length of 0.5 mm. Only 200 MeV data was presented as it depicts a similar trend with both 80 MeV and 150 MeV data at Positions 1, 2 and 3. Comparing across all simulation parameters, linear and non-linear correlation for both protons and secondary electrons were observed. The Pearson \(r\)-squared values showed up to 0.99.

Unlike at the plateau region in Figure 3, certain simulation parameters do not show any secondary electrons due to the range cut parameter at the Bragg peak region. Table 3 indicates the presence of secondary electrons in different simulation parameters. Only data from range cut of 0.01 mm at Position 4 is shown in Figure 4 as secondary electrons are present and it follows a similar trend for other range cut and step length parameters. Plots a, b and c represent step length of 0.01 mm; Plots d, e and f represent step length of 0.05 mm; and Plots g, h and i represent step length of 0.5 mm. Plots a, d and g represent proton beam energy of 80 MeV; Plots b, e and h represent proton beam energy of 150 MeV; and Plots c, f and i represent proton beam energy of 200 MeV.

Table 4 shows the calculated values of the individual terms of Eq. (6) at Position 1. Data from Positions 2 and 3 was not shown as it follows similar trend to the data from Position 1. The percentage difference accounting for both primary protons and secondary electrons was calculated with respect to \(\frac{E\left(\frac{\epsilon^2}{\epsilon_i}\right)}{E(\epsilon_i)}\). It shows that as range cut decreases, the differences between \(\frac{E\left(\frac{\epsilon^2}{\epsilon_i}\right)}{E(\epsilon_i)}\) and \(\frac{E\left(\frac{\epsilon^2}{\epsilon_i}\right)}{E(\epsilon_i)}\) increase by up to 43%. Results from step length of 0.05 mm show the smallest percentage difference while step length of 0.5 mm shows the largest percentage difference.
At Position 4, the number of secondary electrons decreases as most of the primary protons’ energy falls below the cut-off energy. The percentage difference at Position 4 is much lower (35%) when compared to Position 1. Unrestricted range cut at all positions gave 0% differences since there is an absence of secondary electrons. We aim to achieve better dose accuracy by accounting for secondary electrons during dose calculation. However, all positions show that as the range cut decreases, the percentage difference between \( E(\epsilon^2) \) and \( \frac{E(\epsilon^2)}{E(0)} \) increases.

**LET\(_D\) scoring method analysis**

In this section, LET\(_D\) values were calculated using five scoring methods at all Positions for all permutations of simulation parameters in Sec. (2.1). Every Position for each Energy has three step length values (x-axis) and each step length value would correspond to range cut of 0.01 mm, 0.05 mm and 0.1 mm as represented by (i), (ii) and (iii), respectively in Figure 5. LET\(_D\) value determined by Unrestricted scoring method is plotted for all step length. For a 200 MeV proton beam, range cut of 1000 m and step length of 0.5 mm, approximately 1100 protons/second are simulated on single core of an Intel Xeon Gold CPU running at 2.10 GHz. Table 5 shows the CPU time needed for all simulation parameters for 200 MeV and particle histories of 100,000.

Percentage difference between scoring methods was calculated with reference to the Unrestricted scoring method LET\(_D\) value within each set of simulation protocols. The largest difference of 200% occurs at Position 3 of 80 MeV, step length of 0.5 mm and range cut of 0.01 mm using Method 3. At the Bragg peak region of 200 MeV proton beam, the largest percentage difference (81%) occurs at step length of 0.5 mm and range cut of 0.01 mm using Method 3. The percentage difference compared across all energies using Method 1 is up to 8% regardless of simulation parameters chosen at the Bragg peak region. Furthermore, the percentage difference at Bragg peak region with step length of 0.05 mm and range cut of 0.01 mm is the lowest (up to 45%) as Table 3 shows.

**Table 3. Simulation parameters at Position 4.** ✔ represents the presence of secondary electrons while ✗ represents the absence of secondary electrons.
compared to step length of 0.5 mm (up to 81%) and 0.01 mm (up to 47%) with range cut or 0.01 mm. Scoring Method 1 has one of the lowest percentage difference compared across all simulation parameters.

**DISCUSSION**

There had not been a standardized simulation protocol despite the extensive use of MC simulation in proton therapy. Most works adopt their own set of simulation protocols and this is a challenge for the community when comparing LET_D results across institutions.

In this work, we explored the effect of simulation parameters and scoring methods on LET_D. Figure 3 shows data at the plateau region (Positions 1, 2 and 3) for 200 MeV proton beam. Upon closer inspection of the covariance between energy deposition per step and step length of the proton beam, the distribution of the data points explained that \( E\left(\frac{\epsilon_i^2}{l}\right) \) could differ slightly with a \( r\)-squared value of 0.96 (Figure 3, f and i) or significantly with a \( r\)-squared of \( 9 \times 10^{-5} \) (Figure 3, a, b, d, e, g and f) from \( E\left(\frac{\epsilon_i^2}{l}\right) \). This suggests that the choice of scoring methods and simulation parameters should be carefully selected for LET_D calculation since high \( r\)-squared values relate to higher covariance.

At the Bragg peak region (Position 4) in Figure 4, it shows low covariance between energy deposition and step length with the same set of simulation parameters as Figure 3. This implies that the scoring methods could be arbitrarily selected as the choice of methods will not significantly influence the exact values of LET_D. Therefore, to achieve a reproducible LET_D value, we had calculated and compared the percentage difference between \( E\left(\frac{\epsilon_i^2}{l}\right) \) and \( \frac{E\left(\epsilon_i^2\right)}{E(l)} \) as shown in Table 4 for each permutation for the simulation parameters. The physical LET_D values were also calculated for each scoring method as shown in Figure 5.

Figure 5 shows that as step length and range cut decrease, the deviation of LET_D values compared among scoring methods increases in all positions. For example, in Position 1 of 80 MeV, LET_D values among the scoring methods have larger variation for range cut of 0.01 mm as compared to range cut of 0.1 mm. This depicts the same trend for all positions and step length. The percentage difference of LET_D, with respect to Unrestricted scoring method, is up to 200% (LET_D values at step length of 0.5 mm and range cut of 0.01 mm at Position 3 of 80 MeV) depending on which simulation parameters and scoring methods were used. This proves that simulation parameters and scoring methods have to be chosen carefully in MC simulation.

In this work, step length of 0.05 mm is chosen as it shows the most consistency for all range cut and scoring methods throughout all positions. The rest of the step length have their own limitations which will be discussed in the rest of the paragraph. Comparing the percentage difference between \( E\left(\frac{\epsilon_i^2}{l}\right) \) and \( \frac{E\left(\epsilon_i^2\right)}{E(l)} \) throughout the Bragg peak curve, step length of 0.5 mm is not recommended.

Figure 4. This figure shows the plots of Energy Deposition Vs Step Length of both protons and secondary electrons of 0.01 mm range cut at Position 4. Plots a, b and c represent step length of 0.01 mm; Plots d, e and f represent step length of 0.05 mm; and Plots g, h and i represent step length of 0.5 mm. Plots a, d and g represent proton beam energy of 80 MeV; Plots b, e and h represent proton beam energy of 150 MeV; and Plots c, f and i represent proton beam energy of 200 MeV. The zoomed in plot shows only secondary electrons (red) while the actual plot shows protons (blue) and secondary electrons (red).
due to its highest percentage difference. In addition, the differences of LETD values compared among different scoring methods could differ up to 200%. With step length of 0.01 mm, Figure 5 shows an initial decrease at the plateau region before increasing towards the Bragg peak and this is physically incorrect due to small step size artefacts. Thus, it is not recommended due to the large variance from different scoring methods. Therefore, 0.05 mm is the recommendation for step length to be used in MC simulation.

Subsequently, a range cut of 0.01 mm is chosen since the priority is to obtain a better dose accuracy by including explicit electron transports in the medium. When a high range cut is chosen, there will be fewer or an absence of secondary electrons at the Bragg peak region. Thus, LETD scoring methods as shown in Table 1 would converge to Table 6. Method 1 would be the same as Unrestricted while Methods 2 and 3 are equal.

We expect the percentage difference arising from different LETD scoring methods to decrease as it approaches the Bragg peak. This is explained by the low covariance (Figure 4) and the convergence of scoring methods (Table 6) at the Bragg peak region. However, at low energy with a range cut of 0.1 mm or 0.05 mm, the percentage difference decreases along the plateau and increases as it approaches the Bragg peak. The percentage difference is up to 65% (plateau region) and 41% (Bragg peak region) for these range cut (0.1 mm and 0.05 mm). Despite having larger percentage difference of up to 72% (plateau region) and 59% (Bragg peak region) with range cut of 0.01 mm at 200 MeV, it shows the greatest consistency throughout all energies. Thus, step length of 0.05 mm and range cut of 0.01 mm is a suitable set of simulation parameters for proton therapy.

Pertaining to LETD scoring methods, we could observe that LETD values calculated from Method 3 deviate from other scoring methods at step length of 0.05 mm and range cut of 0.01 mm along the plateau region (Positions 1, 2 and 3) in Figure 5. It is expected at the Bragg peak region (Position 4) that LETD values calculated using Method 2 will be similar to using Method 3 and this is analogous to Method 1 and Unrestricted due to the decrease of secondary electrons at Position 4. LETD values calculated using Method 4 deviate from other scoring methods at Position 4. Therefore, it is more appropriate to use Method 1 since the LETD values are approximately the average of other scoring methods.

From what we have discussed above, we recommend a set of simulation parameters and scoring method that would result in a most reproducible LETD. We recommend using step length of 0.05 mm and range cut of 0.01 mm for all range of energies and scoring Method 1 for LETD calculation. This method can be generalized for a clinically relevant Spread-Out Bragg Peak (SOBP) by introducing a weighting factor to Table 1. The expectation form of each methods will need to include the weighted sum of the individual expectation for mono-energetic proton beam as shown in Eq. (8). The weight (w_j) corresponds to the relative contribution of each mono-energetic proton (denoted by j) required to make up the SOBP.
Furthermore, this recommendation can be applied for other ions which are used clinically such as Carbon or Helium despite being a challenge when tracking the large number of secondary electrons and the inclusion of huge species of nuclear secondary products. This recommendation would allow us to consider for better dose calculation accuracy and LET_D consistency in future simulation results.

CONCLUSION
Our study shows that the simulation parameters and LET_D scoring methods are important when they come to obtain a reproducible LET_D value MC method. This had prompted us to investigate how the simulation parameters and scoring methods affect our LET_D results. Overall, we recommend step length of 0.05 mm, range cut of 0.01 mm and scoring Method 1 for LET_D calculation to be used in MC simulation so as to obtain a more reproducible LET_D values. By establishing these MC simulation protocols, we hope that this would benefit future work in obtaining a more precise biological dose calculation by including a more standardized LET_D values in the RBE formula.

Table 5. CPU time (in protons/second) used for 200 MeV proton beam with different range cut and step size using 10,000 particles

<table>
<thead>
<tr>
<th>200 MeV</th>
<th>Range Cut</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step length</td>
<td>0.01 mm</td>
</tr>
<tr>
<td>0.01 mm</td>
<td>20</td>
</tr>
<tr>
<td>0.05 mm</td>
<td>83</td>
</tr>
<tr>
<td>0.5 mm</td>
<td>200</td>
</tr>
</tbody>
</table>

Table 6. LET_D Scoring methods when there is an absence of secondary electrons

<table>
<thead>
<tr>
<th>Method</th>
<th>Unrestricted</th>
<th>Method 1</th>
<th>Method 2</th>
<th>Method 3</th>
<th>Method 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>LET_D</td>
<td>( \frac{\sum w_i E(\epsilon_i^2)}{\sum w_i E(\epsilon_i)} )</td>
<td>( \frac{\sum w_i E(\epsilon_i^2)}{\sum w_i E(\epsilon_i)} )</td>
<td>( \frac{\sum w_i E(\epsilon_i^2)}{\sum w_i E(\epsilon_i)} )</td>
<td>( \frac{\sum w_i E(\epsilon_i^2)}{\sum w_i E(\epsilon_i)} )</td>
<td>( \frac{\sum w_i E(\epsilon_i^2)}{\sum w_i E(\epsilon_i)} )</td>
</tr>
</tbody>
</table>

REFERENCES
dose-averaged let and let spectra in proton therapy using the geant4 Monte Carlo code. *Med Phys*. 2015; 42: 6234–47 Available from [Internet]. doi: https://doi.org/10.1118/1.4932217


