Contents lists available at ScienceDirect



Nuclear Inst. and Methods in Physics Research, A

journal homepage: www.elsevier.com/locate/nima



Validation of Geant4 fragmentation for Heavy Ion Therapy

CrossMark

David Bolst^a, Giuseppe A.P. Cirrone^b, Giacomo Cuttone^b, Gunter Folger^c, Sebastien Incerti^{d,e}, Vladimir Ivanchenko^{c,f}, Tatsumi Koi^g, Davide Mancusi^h, Luciano Pandola^b, Francesco Romano^{b,i}, Anatoly B. Rosenfeld^a, Susanna Guatelli^{a,*}

Centre for Medical Radiation Physics, University of Wollongong, Australia

^b INFN, Laboratori Nazionali del Sud, Catania, Italy

^c The European Organisation for Nuclear Research (CERN), Switzerland

^d CNRS/IN2P3, Centre d'Etudes Nucléaires de Bordeaux-Gradignan, France

^e Université Bordeaux, Centre d'Etudes Nucléaires de Bordeaux-Gradignan, France

f Tomsk State University, Tomsk, Russia

8 SLAC National Accelerator Laboratory, 2575 Sand Hill Rd, Menlo Park, CA, 94025, USA

^h French Alternative Energies and Atomic Energy Commission (CEA), Saclay, France

¹ National Physical Laboratory, Acoustic and Ionizing Radiation Division, Teddington TW11 0LW, Middlesex, UK

ARTICLE INFO

Keywords: Geant4 Benchmarking Heavy ion therapy

ABSTRACT

¹²C ion therapy has had growing interest in recent years for its excellent dose conformity. However at therapeutic energies, which can be as high as 400 MeV/u, carbon ions produce secondary fragments. For an incident 400 MeV/u¹²C ion beam, ~70% of the beam will undergo fragmentation before the Bragg Peak. The dosimetric and radiobiological impact of these fragments must be accurately characterised, as it can result in increasing the risk of secondary cancer for the patient as well as altering the relative biological effectiveness. This work investigates the accuracy of three different nuclear fragmentation models available in the Monte Carlo Toolkit Geant4. the Binary Intranuclear Cascade (BIC), the Quantum Molecular Dynamics (QMD) and the Liege Intranuclear Cascade (INCL + +). The models were benchmarked against experimental data for a pristine 400 MeV/u 12 C beam incident upon a water phantom, including fragment yield, angular and energy distribution. For fragment yields the three alternative models agreed between ~5 and ~35% with experimental measurements, the QMD using the "Frag" option gave the best agreement for lighter fragments but had reduced agreement for larger fragments. For angular distributions INCL+ + was seen to provide the best agreement among the models for all elements with the exception of Hydrogen, while BIC and QMD was seen to produce broader distributions compared to experiment. BIC and QMD performed similar to one another for kinetic energy distributions while INCL++ suffered from producing lower energy distributions compared to the other models and experiment.

Crown Copyright © 2017 Published by Elsevier B.V. All rights reserved.

1. Introduction

Since its first clinical trials in 1994 at the National Institute of Radiological Science (NIRS) in Japan [1] carbon therapy has been the object of increasing interest, thanks to its excellent conformity in dose delivery, sparing healthy organs at risk and good performance for oxygen deficient tumours such as head and neck cancers [2].

At the rapeutic energies (up to 400 MeV/u), the 12 C ion beam generates a complex radiation field, with ~70% of the primary beam undergoing fragmentation before the Bragg Peak (BP) [3]. The secondary

Corresponding author. E-mail address: susanna@uow.edu.au (S. Guatelli).

http://dx.doi.org/10.1016/j.nima.2017.06.046

Received 20 February 2017; Received in revised form 26 June 2017; Accepted 27 June 2017 Available online 12 July 2017 0168-9002/Crown Copyright © 2017 Published by Elsevier B.V. All rights reserved.

fragments deliver dose outside of the treatment target, increasing the risk of secondary cancer as well as altering the relative biological effectiveness (RBE). It is therefore vital to accurately determine the secondary fragment production and distribution.

A representation of the nuclear fragmentation process is depicted in Fig. 1. The process involves the overlap of nucleons from the projectile nucleus with nucleons of the target nucleus. Such overlapping nucleons produce an excited pre-fragment product. The excited product de-excites into smaller nuclei, the projectile fragment continues to travel on a path close to the original trajectory with a similar velocity, while the target



Fig. 1. Representation of the fragmentation process of the projectile and target nucleus having an overlap region which results in the creation of an excited product which will de-excite by emitting nucleons and smaller fragments (depicted by the dashed arrows).

fragment remains stationary. Both the projectile and target fragments may also de-excite.

Monte Carlo (MC) codes are extensively used in Heavy Ion Therapy to model the mixed secondary radiation field of 12 C therapy [4,5] and to study associated dosimetry and Quality Assurance technology [6]. This work investigates the accuracy of three different nuclear fragmentation models available in the Monte Carlo Toolkit Geant4 [7–9], the Binary Intranuclear Cascade (BIC), the Quantum Molecular Dynamics (QMD) and the Liege Intranuclear Cascade (INCL + +).

The BIC model describes the interaction between a projectile and a single nucleon of the target nucleus interacting in the overlap region as Gaussian wave functions. The QMD model instead considers all nucleons of the target and projectile, each with their own wave function; this inherently causes QMD to have greater computation times than BIC. Unlike the other two models, INCL + + models the nucleons as a free Fermi gas in a static potential well. The targets and projectiles which can be modelled by the INCL + + model are limited to a mass number of A = 18. For higher A values of both the projectile and target the fragmentation is modelled using BIC. More details on the BIC, QMD and INCL + + physics models can be found in the Geant4 Physics Reference Manual [10].

The models were benchmarked against experimental data for a pristine 400 MeV/u 12 C beam incident upon a water phantom performed at GSI in Germany by Haettner et al. [3]. The experimental data are available as an EXFOR file [11], which provides data for fragment yields per water thickness, fragment angular and kinetic energy distributions.

The experiment was conducted using a variable thickness water phantom, time of flight measurements for fragments were carried out using a start detector before the phantom and a second detector placed on a linear drive after the phantom.

Previous benchmarking studies have been performed by Böhlen et al. [12] who performed similar experimental comparison to [3] using the BIC and QMD models in Geant4 version 9.3. Napoli et al. [13] compared BIC and QMD to thin carbon target data for a 62 MeV/u 12 C beam using version 9.4 of Geant4. More recently Dudouet et al. [14] has compared cross-sections for 95 MeV/u 12 C incident upon PMMA using both: BIC, QMD and INCL+ + using version 9.6 of Geant4.

This work was motivated by the observation that the Geant4 Toolkit evolves in time and therefore it is necessary to develop a testing suite for carbon ion fragmentation, which plays a crucial role in HIT. Results presented here are obtained with Geant4, version 10.2p2, which was the most recent version of Geant4 when developing the project (June 2016).



Fig. 2. Sketch of the simulation set-up, showing the incident mono-energetic 400 MeV/u ¹²C beam incident onto the water slab with variable thickness. The fragments, emerging from the phantom, are scored when reaching the hemisphere depicted in the figure.

2. Materials and methods

2.1. Simulation setup

The simulation setup was defined based on the experimental setup adopted in Haettner et al. [3]. A mono-energetic 400 MeV/u 12 C pencil beam is incident on a water phantom with lateral size of 50 cm. In the simulation the water phantom is positioned in a vacuum. The pencil beam has a FWHM of 5 mm and energy sigma of 0.15% representing a FWHM of ~1.4 MeV/u.

The electromagnetic interactions were modelled using the *G4 Standard EM option 3* Physics List. *G4HadronElasticPhysicsHP* was used to describe the elastic scattering of hadrons which uses the Wentzel model [15]. The neutron High Precision (HP) model was adopted to describe neutron interactions up to 20 MeV. BIC and INCL++ fragmentation models were adopted using their default configuration. The QMD was used with its *Frag* option on and off. The Frag option in QMD changes the interaction criterion of the projectile and target. The results obtained with the Frag option on are only included for fragment yields as angular and energy distributions were seen to be unaffected using this option.

Bragg curve comparisons were made for a 60 cm thick water phantom. A step limit of 0.1 mm was applied within the phantom as well as a production cut size of 0.1 mm. The energy deposited was scored within a 20 \times 20 cm² area at the centre of the beam with a voxel thickness of 0.1 mm along the direction of incidence of the beam. The lateral area corresponds to the physical dimensions of the ionisation chamber (IC) used in the experiment. The thickness of the IC used in the experiments was 3.7 cm [16]. The uncertainty of 1 mm quoted in the experiment refers to the uncertainty in the water equivalent thickness (WET) of materials positioned in front of the IC used. The uncertainty of the BP position quoted in the simulation of 0.1 mm is due to the thickness of the voxels used; because of the relatively large thickness of the experimental IC, this may cause a smearing of the shape of the BP.

The BP position corresponds to a depth in water of 275 mm. The thickness of the water slab, *L*, varied with values: 59, 159, 258, 279, 288, 312 and 347 mm, 10^7 primary ¹²C ions were generated for each water slab thickness. The fragments emerging from the phantom were tallied when traversing a hemisphere with a radius of 2.94 m, placed after the water phantom, as shown in Fig. 2. The radius *R* of 2.94 m corresponds the distance from the mid target to the detector used in the experiment.

The species, energy, time and position of the fragments when reaching the hemisphere were scored. For comparing the total fragment yields to the reference experimental data, the number of fragments within a 10 degree cone given by Eq. (1) were recorded, the 10 degree cone matches the angular range integrated in the experiment. Eq. (1) corresponds to Fig. 2 with angle θ_C being 10 degrees. The yields are normalised to the number of ${}^{12}C$ ions incident upon the water slab.

$$\theta_C = \sin^{-1}\left(\frac{\sqrt{x^2 + z^2}}{R}\right) \tag{1}$$

 θ_1 and θ_2 in Fig. 2 represent the angles made with the left and right edge of the detector. For the angular distribution, fragments were recorded within a 40 mm spherical wedge between angles θ_1 and θ_2 , as shown in Fig. 2, corresponding to the width of the detector used in the experiment. Fig. 2 shows the collection of fragments for an angle of 0° corresponding to $\theta_1 = -\theta_2$. Fragments recorded in the wedge were normalised to the solid angle Ω formed by the wedge, given by Eq. (2), as well as being normalised to the number of incident ¹²C ions.

$$\Omega = 2\pi \left(\cos\theta_1 - \cos\theta_2\right). \tag{2}$$

For kinetic energy distributions, fragments were recorded in the same solid angle used for the angular distribution. The kinetic energy of the fragment, KE_F , as it reached the hemisphere was calculated using the same method as adopted in [3]. This method assumes that all fragments were produced in the middle of the water phantom and by determining how long it would theoretically take for the primary ^{12}C ion with energy of 400 MeV/u to reach the middle of water phantom (depicted in 3), this time being t_P . The time for the fragment to reach the detector, t_F , is determined by subtracting t_P from the total time it takes for the primary particle to be fired and for the fragment to be recorded at the hemisphere. With t_F being known KE_F can be calculated by means of Eq. (3), where *c* is the speed of light and m_0 the rest mass of the fragment.

$$KE_F = \left(\frac{1}{\sqrt{1-\beta^2}} - 1\right) m_0 c^2.$$
 (3)

The underlying assumption when using the rest mass is that the fragments recorded are only due to the most abundant isotope ie ¹ H, ⁴He, ⁷Li, ⁹Be and ¹¹B. The value of β is calculated using Eq. (4), where *R* is the radius of the hemisphere (2.94 m). The timing error associated with the experimental setup of 0.53 ns (FWHM) was incorporated to the simulation's time of flight.

$$\beta = \frac{R}{ct_F}.$$
(4)

For both the angular and kinetic energy distributions they were normalised to obtain the same area under the curve of the corresponding experimental measurements.

Quantitative comparisons of each Geant4 fragmentation model to experimental results for each physical distribution under study were done by adopting the quantity X^2 , shown in Eq. (5), where *n* is the number of bins in the distribution being compared. The quantity X^2 is the same as χ^2 in Pearson's χ^2 test except no *p*-value calculations were performed with the distributions due to the test being over-conservative for the large population sizes being investigated and because the main interest was to rank the performance of each model against one another with lower values of X^2 representing better agreement with experiment.

$$X^{2} = \sum_{i=1}^{n} \frac{\left(\text{Sim}_{i} - \text{Exp}_{i}\right)^{2}}{\text{Exp}_{i}}.$$
(5)

To provide a simple indication of how closely each Geant4 fragmentation model agrees with the experiment the percentage errors (PEs) are also presented. The PEs are derived from taking the mean PE of all points in the distribution being compared, as shown in Eq. (6). *n* represents the size of the distribution being compared.

$$\langle PE \rangle = \frac{100}{n} \left(\sum_{i=1}^{n} \left| \frac{\operatorname{Sim}_{i} - \operatorname{Exp}_{i}}{\operatorname{Exp}_{i}} \right| \right).$$
 (6)



Fig. 3. Diagram depicting the method to calculate the kinetic energy of the fragments recorded in the collection hemisphere based on the time it takes for the fragment to reach the hemisphere (not to scale).

Table 1

 X^2 values resulting from the comparison of the Bragg Curve calculated with Geant4 and from reference experimental data, lower values represent better agreement. These calculated values were obtained by comparing 51 data points of the experiment to the simulation.

	BIC	QMD	QMD-F	INCL
X^2	53.098	54.335	46.720	52.021

3. Results and discussion

3.1. Bragg curve

The comparison between the Bragg curves obtained from the experiment and Geant4 is shown Fig. 4. The experiment and simulation curves were normalised based on the average value of dose between 100 and 150 mm in the phantom. There is no significant difference in the calculation of the position of the BP between the three models, this is to be expected since the position of the BP is mainly dictated by the primary 12 C through its continuous energy losses, governed by the electromagnetic physics.

We observe a good agreement between the experiment and simulation, the X^2 values calculated using Eq. (5) to quantify the agreement between the Geant4 simulation and the experiment are shown in Table 1. It can be observed that all the default fragmentation models provide similar agreement with the reference data when calculating the Bragg curve. However, QMD with the *Frag* option (QMD-F) provides the best agreement with the experiment.

3.2. Fragment yields

Fig. 5 shows the fragment yields *Y* scored at the hemisphere, within the cone with $\theta_1 = 10$ degrees, with respect to the water thickness. *Y* is calculated as the number of the scored fragments *N* divided by the number N_0 of incident ¹²C ions.

Table 2 reports the mean PE averaged over all the water thicknesses under study using Eq. (6). It can be observed that overall BIC, INCL + + and the QMD models provide *Y* values which agree between 5% and 35%, depending on the type of fragment.



Fig. 4. Comparison of the Bragg Curve of the experiment compared to the different models, with the right side showing a zoomed view of the Bragg peak. The statistical error of the simulation is less than 0.2%. The QMD-F entry of the legend refers to QMD with the *Frag* option activated.



Fig. 5. Fragment yields for elements: H, He, Li, Be and B for different thicknesses of water.

Table 2

Mean percentage error PE of the Geant4 ion fragmentation models compared to experiment, when calculating the fragment yields for each element reported on the column in the left.

Z	BIC	QMD	QMD-F	INCL
1	19 ± 2	14 ± 2	5 ± 2	8 ± 2
2	6 ± 1	17 ± 1	5 ± 1	10 ± 1
3	4 ± 7	25 ± 7	31 ± 7	21 ± 7
4	32 ± 10	14 ± 10	22 ± 10	15 ± 10
5	19 ± 8	20 ± 8	26 ± 8	33 ± 8

Table 3 reports the X^2 values calculated by comparing the fragment yields calculated by means of the Geant4 simulation with the reference data.

When comparing the QMD model with *Frag* (labelled as QMD-F) against the default QMD, it can be seen that the QMD-F shows better agreement for H and He yields. For the remaining fragment species, QMD-F produces lower *Y* values which reduce the agreement with the experimental measurements. It can be noted that the error

bars affecting experimental measurements of H and He fragments is ~5%, while for heavier fragments they increase to ~20%, with errors being larger for positions before the BP. Given such larger error bars, it is difficult to provide a conclusive comment on the accuracy of the Geant4 fragmentation models for heavier fragments before and at the Bragg Peak. However, the impact of fragments is most important beyond the BP, where the experimental errors are smaller due to the primary ¹²C beam not masking fragment events. In this region, the experimental error bars decrease by ~10%. After the distal edge the Geant4 fragmentation models have a reasonable agreement with the experimental measurements for Be and B ions. In the case of the Li fragment yield, the BIC model performs better than the other Geant4 fragmentation models.

H represents the majority of produced fragments, with He being the second most dominant, each having ~ 10 times higher production than the remaining fragments. They also leave the treatment region the most due to their larger range and increased scatter compared to other heavier fragments. Based on this observation, the QMD with *Frag* may be indicated as the best fragmentation model of Geant4 to estimate more correctly the fragmentation yields of lighter, more abundant isotopes.

Table 3

 X^2 values of the three fragmentation models compared to experiment in the case of fragment yields calculation, for each element reported in the left column. The best agreement is indicated by a lower X^2 value and it is shown in bold characters. The number of data points used correspond to those shown in Fig. 5, which is six for H and seven for all other elements.

Z	BIC	QMD	QMD-F	INCL
1	1.25×10^{6}	7.97×10^{5}	9.16×10^4	3.09×10^{5}
2	2.00×10^{5}	1.02×10^{6}	9.35×10^4	5.17×10^{5}
3	1.01×10^4	1.90×10^{5}	3.04×10^{5}	1.34×10^{5}
4	1.62×10^{5}	2.77×10^4	6.62×10^{4}	3.31×10^4
5	6.12×10^4	1.45×10^{5}	2.44×10^{5}	2.41×10^{5}

Table 4

PE calculated for the three Geant4 fragmentation models compared to experimental values, in the case of the angular distribution, for each type of fragment under study. The PE is averaged over all water phantom thicknesses considered.

Z	BIC	QMD	INCL
1	14 ± 4	7 ± 4	15 ± 4
2	24 ± 2	16 ± 2	7 ± 2
3	29 ± 8	26 ± 8	16 ± 8
4	47 ± 14	42 ± 14	18 ± 14
5	132 ± 12	135 ± 12	28 ± 13

3.3. Angular distribution

Fig. 6 shows the angular distribution for a selection of fragments and water phantom thicknesses which there are 35 distributions in total. Table 4 presents the PE for the fragmentation models under study. Here, for the case of calculating the mean PE for each fragment element the mean PE is averaged over the total number of distributions for each element, m, as shown in Eq. (7), where n_j is the number of points for the *j*th distribution of m.

$$\langle PE \rangle = \frac{1}{m} \sum_{j=1}^{m} \left(\frac{100}{n_j} \left(\sum_{i=1}^{n_j} \left| \frac{\operatorname{Sim}_{i,i} - \operatorname{Exp}_i}{\operatorname{Exp}_i} \right| \right) \right).$$
(7)

Fig. 7 shows the X^2 values for each thickness of water for each element. The QMD model and BIC to a lesser extent commonly produce noticeably broader angular distributions than INCL + + which agrees with the experimental measurements the most. We observe that the INCL + + model with the exception of H performs the best quite significantly over the other models, particularly for heavier fragments. BIC and QMD both reproduce the angular distributions of the larger elements very poorly, particularly Boron. However Be and B suffer from much higher experimental error than the lighter fragments in general, with Be and B having many angles with an error of more than 40%. Fig. 7 again shows the better performance of the INCL + + model compared to the other models except for H where the INCL + + performs similar to BIC for each distribution.

3.4. Fragment kinetic energy distribution

Fig. 8 shows example energy distributions from the total 151 distributions for different combinations of: thickness, fragment element and angle. It can be observed that in general the models perform reasonably well at reproducing the general experimental energy distributions. The energy distributions predicted by the INCL + + model are systematically shifted to lower energies compared to the other models. Table 5 summarises the mean PE for each element. Fig. 9 shows the distribution of X^2 values for all 151 kinetic energy distributions divided up for each different fragment species, the dashed lines separate the X^2 values for each water thickness, the points represent smaller angles on the left, with a minimum of 0°; points further to the right represent larger angles with a maximum of 8°.

Apart from the large errors in the experimental distributions, with many having values greater than 20%, another factor for the discrepancy between the experimental and simulation results may be partially

Table 5

PE of the three fragmentation models compared to the experiment for energy distributions for each type of fragment, calculated over all water phantom thicknesses.

Z	BIC	QMD	INCL
1	26 ± 6	22 ± 6	46 ± 6
2	30 ± 7	33 ± 7	73 ± 7
3	41 ± 8	42 ± 8	93 ± 8
4	61 ± 9	52 ± 9	116 ±9
5	221 ± 11	194 ± 10	398 ± 10

Table 6

Comparison of the mean PE of the energy distributions for each fragment species. 59 and 288 mm are the depths under investigation in the experimental data set with the expected incident carbon ion energy. 279, 312 and 347 mm are the depths of the experiments with higher than expected carbon ion energy.

	59 and 288 mm		279, 312 and 347 mm			
Z	BIC	QMD	INCL	BIC	QMD	INCL
1	40 ± 6	31 ± 6	55 ± 6	15 ± 5	14 ± 5	33 ± 5
2	47 ± 7	53 ± 9	88 ± 8	16 ± 6	17 ± 5	39 ± 6
3	35 ± 10	35 ± 9	47 ± 10	47 ± 6	50 ± 6	89 ± 6
4	49 ± 10	45 ± 10	78 ± 11	76 ± 7	61 ± 7	120 ± 8
5	129 ± 14	116 ± 12	204 ± 12	387 ± 8	333 ± 7	635 ± 8

attributed to the shift of the energy spectrum of the primary ¹²C beam. The experiment was performed over two separate occasions with the calculated kinetic energy of the incident carbon ion beam shifting from 358 ± 23 MeV/u to 402 ± 26 MeV/u, from 256 ± 13 MeV/u to 261 ± 13 MeV/u and from 85 ± 3 MeV/u to 92 ± 3 MeV/u, for 59 mm, 159 mm and 258 mm water thickness, respectively [16]. The expected energies for these thicknesses of water are 350 MeV/u, 250 MeV/u and 80 MeV/u, respectively, as calculated by the ATIMA code [17]. Based on this, Table 6 shows the mean PEs for the separate sets of experimental measurements. The results show a minor improvement for the INCL++ model when considering only results obtained with the expected incident energy of the carbon ion beam (59 and 288 mm), with results being $\sim 10\%$ closer to BIC and QMD. This happens because INCL + + produces consistently lower peak energies, so the disagreement becomes amplified when comparing to the experimental results obtained with slightly higher incident beam energy.

The kinetic energy distribution peak position was retrieved from the experimental and simulated distributions, the mean PE was calculated using Eq. (7) ($n_j = 1$), Fig. 10 shows the results. It can be observed that overall QMD is the best fragmentation model reproducing the kinetic energy distribution and its associated peak and INCL + + produces consistently lower kinetic energy distributions.

3.5. Computation times

Table 7 shows a summary of the relative computational intensity for each model using different water thicknesses. The first column reports the average computation time of ten simulation runs firing 10⁵ primary ¹²C ions for different water thicknesses using the BIC model, the reported error is the standard deviation. The remaining columns to the right give the ratio of each model with respect to the BIC model. The simulations were run using Intel[®] Xeon[®] E5-2650v3 processors clocked at 2.30 GHz.

As expected the QMD model was much more computationally intensive than BIC since QMD considers wave functions for all nucleons of the target and projectile, as mentioned in Section 1. QMD using the *Frag* option resulted in execution times which were approximately a third faster than the default QMD. This is convenient since QMD-F gave better agreement than the default for smaller fragment's yields as shown in Section 3.2 but not differing for the angular and energy distributions.

Thinner thicknesses of water showed the greatest separation of the models with QMD having more than 10 times the computation time than BIC and INCL + + being 20% faster than BIC. For thicknesses greater than 59 mm BIC and INCL + + showed no significant differences.



Fig. 6. Angular distributions of a selection of fragments types and thicknesses of water.



Fig. 7. X² values of the different angular distributions compared for each model at different thicknesses of water for each element, lower values represent better agreement.

4. Conclusions

Nuclear fragmentation is a vital factor to be considered in hadrontherapy. The BIC, QMD and INCL + + models were benchmarked in Geant4 against experimental data for a pristine 400 MeV/u ¹²C ion beam using version 10.2p2. It was found that for fragment yields the models agreed within ~5%-35% compared to experimental values, with the QMD model using the Frag option giving the best overall agreement. For angular distributions of fragments the INCL + + model was shown to reproduce experimental measurements significantly better than the other two models. For kinetic energy distributions the QMD model was seen to produce the best agreement, however the energy distribution results show noticeably less agreement, which can in part, be attributed to systematic errors in the experiment.

In general, when considering the angular and energy distributions BIC and QMD are seen to perform much similar to one another compared



Fig. 8. Kinetic energy distributions of a selection of fragments types and thicknesses of the water phantom.



Fig. 9. X^2 values of the different kinetic energy distributions compared for each atomic element. The dashed lines separate the X^2 for each water thickness. For each water thickness the left most points represent the smallest angle and the right most being the largest angle for the particular element and water thickness.

to INCL + +. This is not surprising considering that both BIC and QMD models the fragmentation process as Gaussian wave functions while INCL treats the process as a free Fermi gas. Unfortunately, there is no clear superior model overall, with INCL + + performing much better in reproducing angular distributions but noticeably more worse for energy distributions with lower shifted energies. Additionally, all the tested fragmentation models showed that the agreement between simulation and experimental measurements deteriorated with larger fragments.

Larger fragments have a larger RBE and can contribute significantly to the distal edge beyond the Bragg Peak, where organs at risk may be located. Therefore further developments in fragmentation modelling are recommended at clinical energies (up to 400 MeV/u), to obtain a better description of the mixed radiation field and of the RBE associated with HIT.

One key point that emerged from this study is that a detailed knowledge of the experimental measurements is crucial to perform an



Fig. 10. Mean PE of the simulation and experiment maximum energy. Left shows the mean calculated for each depth and Right shows the mean PE calculated for each element.

Table 7

Comparison of the computation times for the different models investigated. The BIC column gives the average computation time of ten simulations each generating 10^5 primary 12 C ions for different water thicknesses using the BIC model. The reported error is the standard deviation. The remaining columns to the right give the ratio of each model with respect to the BIC model.

Thickness	BIC (s)	QMD/BIC	QMD-F/BIC	INCL/BIC
59	97.5 ± 3.3	10.83 ± 0.45	7.73 ± 0.29	0.79 ± 0.05
159	569 ± 18.2	5.40 ± 0.18	3.94 ± 0.14	0.97 ± 0.03
258	1382.9 ± 90.7	3.67 ± 0.25	2.85 ± 0.24	1.04 ± 0.06
279	1643.4 ± 57.9	3.41 ± 0.15	2.46 ± 0.31	1.03 ± 0.12
288	1765 ± 63.6	3.29 ± 0.13	2.11 ± 0.22	1.01 ± 0.10
312	1979.1 ± 73.9	3.16 ± 0.13	2.26 ± 0.13	1.03 ± 0.05
347	2380.3 ± 47.6	2.86 ± 0.06	2.17 ± 0.08	1.00 ± 0.04

accurate validation study of Monte Carlo codes for Heavy Ion Therapy. There is also the need to have more detailed experimental measurements available, made by independent sources, which can be used as reference to comprehensively benchmark Monte Carlo codes, limiting the effect of possible systematics affecting the experimental data.

The simulation application developed in this work will be used for the regression testing of public releases of Geant4 to benchmark the effect of the evolution of the Toolkit on important physical quantities, such as the yield, angular and kinetic energy distributions of fragments, typical of the radiation field of Heavy Ion Therapy.

Acknowledgement

This research is supported by an Australian Government Research Training Program (RTP) Scholarship.

References

 M. Torikoshi, S. Minohara, N. Kanematsu, M. Komori, M. Kanazawa, K. Noda, N. Miyahara, H. Itoh, M. Endo, T. Kanai, Irradiation system for HIMAC, Radiat. Res. 48 (2007) 15–25.

- [2] W. Tinganelli, M. Durante, R. Hirayama, M. Krämer, A. Maier, W. Kraft-Weyrather, Y. Furusawa, T. Friedrich, E. Scifoni, Kill-painting of hypoxic tumours in charged particle therapy, Sci. Rep. 5 (2015).
- [3] E. Haettner, H. Iwase, M. Krmer, G. Kraft, D. Schardt, Experimental study of nuclear fragmentation of 200 and 400 MeV/u¹²C ions in water for applications in particle therapy, Phys. Med. Biol. 58 (23) (2013) 8265.
- [4] D. Johnson, Y. Chen, S. Ahmad, Dose and linear energy transfer distributions of primary and secondary particles in carbon ion radiation therapy: A Monte Carlo simulation study in water, J. Med. Phys. 40 (4) (2015) 214–219.
- [5] D. Bolst, S. Guatelli, L. Tran, L. Chartier, M. Lerch, N. Matsufuji, A. Rosenfeld, Correction factors to convert microdosimetry measurements in silicon to tissue in ¹²C ion therapy, Phys. Med. Biol. 62 (6) (2017) 2055.
- [6] Hiroyuki Nose, Tsukasa Aso, Yuki Kase, Naruhiro Matsufuji, T. Kanai, Verification of biological dose calculation for carbon ion therapy with a monte carlo method, J. Med. Phys. 28 (4) (2009) 131–141.
- [7] J. Allison, et al., Geant4 developments and applications, IEEE Trans. Nucl. Sci. 53 (1) (2006) 270–278.
- [8] S. Agostinelli, et al., Geant4 a simulation toolkit, Nucl. Instrum. Methods Phys. Res. A 506 (3) (2003) 250–303.
- [9] J. Allison, et al., Recent developments in Geant4, Nucl. Instrum. Methods Phys. Res. A 835 (2016) 186–225.
- [10] http://geant4.web.cern.ch/geant4/UserDocumentation/UsersGuides/PhysicsReferenceManual.pdf.
- [11] http://www.jcprg.org/master/exfor/D/d0589.txt.
- [12] T.T. Böhlen, F. Cerutti, M. Dosanjh, A. Ferrari, I. Gudowska, A. Mairani, J.M. Quesada, Benchmarking nuclear models of FLUKA and GEANT4 for carbon ion therapy, Phys. Med. Biol. 55 (19) (2010) 5833.
- [13] M.D. Napoli, C. Agodi, G. Battistoni, A.A. Blancato, G.A.P. Cirrone, G. Cuttone, F. Giacoppo, M.C. Morone, D. Nicolosi, L. Pandola, et al., Carbon fragmentation measurements and validation of the Geant4 nuclear reaction models for hadrontherapy, Phys. Med. Biol. 57 (22) (2012) 7651–7671.
- [14] J. Dudouet, D. Cussol, D. Durand, M. Labalme, Benchmarking Geant4 nuclear models for hadron therapy with 95 MeV/nucleon carbon ions, Phys. Rev. C 89 (2014) 054616.
- [15] V.N. Ivanchenko, O. Kadri, M. Maire, L. Urban, Geant4 models for simulation of multiple scattering, J. Phys. Conf. Ser. 219 (3) (2010) 032045.
- [16] E. Haettner, Experimental Study on Carbon Ion Fragmentation in Water Using GSI therapy beams (Master's thesis), KTH Engineering Sciences, 2006.
- [17] H. Geissel, H. Weick, C. Scheidenberger, R. Bimbot, D. Gardés, Experimental studies of heavy-ion slowing down in matter, Nucl. Instrum. Methods Phys. Res. B 195 (1–2) (2002) 3–54.