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Calculation by GAMOS/Geant4 simulation of cellular energy distributions from alpha and lithium-7 particles created by BNCT

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HIGHLIGHTS

- GAMOS codes with different Geant4 physics models are studied for the range calculations of alpha particles.
- Alpha and lithium-7 particles produced by BNCT are studied.
- The distributions of deposited energy in cellular medium originated by $^{10}B(n,\alpha)^{7}Li$ are proposed.

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ABSTRACT

Monte Carlo (MC) has demonstrated to be a suitable technique to evaluate the microdosimetric parameters at the cellular level for Boron Neutron Capture Therapy (BNCT).

The objectives of the current study are first to validate GAMOS MC codes with different Geant4 physics models for the range calculations of alpha particles. Once the proper physics is selected, the second objective is to determine the distributions of deposited energy in cellular medium originated by alpha and lithium-7 particles induced by $^{10}B(n,\alpha)^{7}Li$.

1. Introduction

Recently, significant research studies have been in progress in the field of the neutron capture therapy, especially boron neutron capture therapy (BNCT) (Barth et al., 2012). BNCT is a kind of external radiotherapy based on the nuclear capture and fission reactions that happen when ^{10}B, which is a nonradioactive component of natural elemental boron, is bombarded with thermal neutrons (Barth et al., 2012). The reaction produces the high linear energy transferred (LET) alpha particles and recoiling lithium-7 nuclei, which have a high relative biological effectiveness (RBE). An average of 2.79 MeV per neutron capture is released per boron neutron capture reaction (Ghassoun et al., 2009). The alpha particle and lithium-7 nucleus transport an average of 2.34 MeV as shown in the following reactions:

$$^{1}n_{th}(0{\cdot}025\ eV) + {}^{10}B \rightarrow {}^{11}B^{*} \rightarrow {}^{7}Li(0{\cdot}84\ MeV) + \alpha(1{\cdot}47\ MeV) + \gamma(0{\cdot}48\ MeV)\ (93{\cdot}7\%)$$

$$^{1}n_{th}(0{\cdot}025\ eV) + {}^{10}B \rightarrow {}^{11}B^{*} \rightarrow {}^{7}Li(1{\cdot}01\ MeV) + \alpha(1{\cdot}78\ MeV)\ (6{\cdot}3\%)$$

These heavy particles deposit their energy in the range of 4–10 μm, which is the same order of the cell diameter, and thus, they transfer most of their kinetic energy to the tumor cell where ^{10}B is located. To produce lethal damage to the cells, an adequate amount of ^{10}B must be selectively delivered to the cell, at least 10^{9} atoms/cell or 20 μg/g, and sufficient thermal neutrons must be absorbed to result in double strand DNA breaks caused by the alpha and lithium-7 particles produced by $^{10}B(n, \alpha)^{7}Li$ capture reaction (Barth et al., 2012, 2005), which has a cross section of ^{10}B (σ = 3837barn) for thermal neutrons of energy 0.025 eV.

An important element to reach good Tumor Control Probability (TCP) is the delivery agent. The agents most frequently used in clinical trials are sodium borocaptate (BSH) and p-boronophenylalanine (BPA). BPA naturally deposits in malignant melanoma because the chemical structure of BPA is parallel to tyrosine and dihydroxy-phenylalanine,

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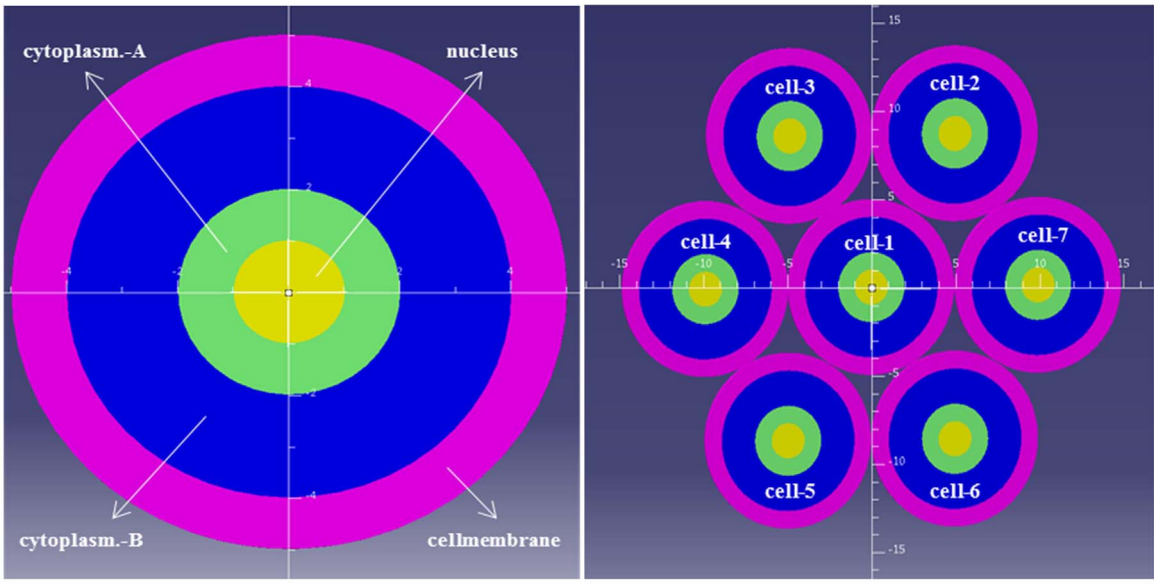

Fig. 1. a) Cell regions (μm), b) Cell regions and locations in multi cell model (μm).

which is the pioneer of the melanin metabolism. Besides, BPA is an amino acid analogue, therefore it is caught by the cells, in which amino acid metabolism is efficient and can pass through the Blood Brain Barrier (BBB). Moreover, BPA specially accumulates around the cell nucleus (Amemiya et al., 2002). BSH cannot undertake into normal brain cells because of the BBB effect. However, the BBB of tumor cells is damaged, so that BSH can accumulate in tumor cells, especially around the cell membrane (Mukawa et al., 2011). With these agents ^{10}B concentration ratios of the tumor: normal tissue or tumor: blood is approximately 3 (Barth et al., 2012). Nevertheless, an important effect to take into account is the deposition of energy in the neighboring cells by the alpha or lithium particles created in one cell.

To understand how much of the energy escapes from the cell where the neutron capture happens, it is necessary to simulate the stochastic nature of energy depositions from alpha particles at a cellular level (ICRU, 1983), for what microdosimetry has proved to be a suitable technique. Rossi (1968) invented the theory and formulations of microdosimetry and Roesch (1977) extended it to alpha emitters. Nikjoo et al. (2016) reviewed on Monte Carlo (MC)-based microdosimetric calculations and how they could be linked to radiobiological models of cell-kill and DNA-damage.

During the recent years, MC simulation methods, which utilize random number generators to simulate the stochastic nature of ionizing radiation interactions with matter, has been used to search for biological effects caused by ionizing radiation (Geng et al., 2014). Among the many MC codes, we have chosen GAMOS (Arce et al., 2014) version 5.1.0, based on Geant4 version 10.02, because of its flexibility and easiness of use. By using GAMOS we avoid the need of writing several hundreds of lines of C++ code to define the Geant4 input and output, and instead we define them with a few command lines. The use of this tool not only makes it much easier the simulation with Geant4, but also let us profit from the robustness of the GAMOS code, supported by its more than 2500 registered users.

The objectives of the present study are to evaluate the accuracy of the different Geant4 (Agostinelli et al., 2003; Allison et al., 2006) physics models in the simulation of alpha particles ranges at different energies, and then to use the most appropriate physics model to calculate the fraction of energy that escapes to neighboring cells when alpha and lithium-7 particles are created in a cell by BNCT.

2. Materials and methods

2.1. Evaluation of Geant4 physics models for alpha particles Continuous-slowing-down approximation (CSDA) ranges in water

There are several physics lists available in GAMOS to simulate the interactions of alpha particles:

- *GmEMStandardPhyiscs:* This physics use the so-called Geant4 standard electromagnetic physics package. This package is based on a class II algorithm (Berger, 1963) and theory-driven cross sections. For more details on each of the models, see Geant4Collaboration (2015).
- *GmEMStandardPhyiscs_option1:* uses G4hMultipleScattering model for multiple scattering and G4ionIonisation for ionization (see Geant4Collaboration, 2015 for a detailed explanation of the physics options).
- *GmEMStandardPhyiscs_option3:* adds to option1 the G4NuclearStopping for nuclear stopping due to multiple scattering, and changes the Rover Range to 0.1 and the Final Range to 0.01 mm (see Geant4Collaboration, 2015 for a detailed explanation of the meaning of the physical parameters).
- *G4QGSP_BIC:* adds to G4hMultipleScattering and G4ionIonisation the physics to simulate hadronic interactions through the Quark Gluon String Precompound (QGSP) and the Binary cascade (BIC) models.
- *G4QGSP_BIC_AllHP:* uses to simulate the hadronic interactions of alpha particles the cross sections read from a database built with experimental data plus TALYS interpolations where the data are not available (Koning et al., 2007).
- *Geant4-DNA (*Incerti et al., 2016): is an alternative physics package designed for microdosimetry, which simulates step-by-step interactions instead of using an algorithm of class II (Berger, 1963). For alpha particles, it includes the processes of nuclear scattering, electronic excitation, ionization and charge decrease and increase (Bernal et al., 2015). It is important to remark that the cross sections are only available for liquid water.

We have calculated the alpha particle CSDA range in water at energies from 2 keV to 40 MeV, and we have compared them with ICRU report 49 values (ICRU, 1993). The CSDA range can be defined by the