Analysis of inter-track effect in chemical stage for FLASH irradiation using Geant4-DNA

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1. Introduction

Ultra-high dose rate (UHDR) radiotherapy, also known as FLASH RT, is an emerging technique that has the potential to spare healthy tissues while maintaining tumor control. Various studies have been conducted to investigate the mechanism of UHDR radiotherapy. Compared to conventional radiotherapy, UHDR requires the consideration of additional factors, such as the inter-track effect, when studying its mechanism. The inter-track molecular reactions can impact the chemical yield for UHDR irradiation. In this study, we used the Geant4-DNA Monte Carlo track structure (MCTS) code to preliminarily calculate the effect of inter-track molecular reactions on chemical yield for UHDR irradiation [1].

2. Methods and Results

2.1 Monte Carlo track structure code

The Monte Carlo (MC) simulation has been considered as golden standard computational method for evaluating physical quantities in radiotherapy. The general-purpose MC codes uses the condensed history approach so that it can enable the radiation transport in sub-millimeter scale in reasonable time without simulating all interactions that can occur in sub-micrometers.

However, for mechanistic research, a simulation based on spatial resolution of a sub-cellular level such as DNA is required, and a technique called a track-structure approach is applied for this purpose. The condensed history approach simulates numerous interactions occurring in the electron transport process by grouping them into one, whereas the track-structure approach simulates all interactions at the nanoscale of individual electrons. Therefore, there is a demand for codes to which physical models specialized for low-energy electron transport are applied, rather than physical models applied to general-purpose MC codes, and codes developed for this purpose are called MCTS codes.

2.2 Geant4-DNA Monte Carlo simulation

This study utilized Geant4-DNA, an MCTS code based on Geant4. Geant4-DNA can simulate transport for electrons, protons, alpha particles, and some ions for liquid water and DNA targets.

Geant4-DNA follows the classical approach for simulating radiolysis and evaluating DNA damage, as depicted in Figure 1 [2]. The scope of this study is limited to radiolysis and subsequent yield calculations, which are divided into three stages: physical, pre-chemical, and chemical. Each stage simulates radiation transport and interaction, resulting initial radical generation, diffusion and reaction of molecules including radicals. Meanwhile, we evaluated the chemical yield generated through simulation using G-value, which is defined as the number of molecules generated per unit energy stored in the medium.

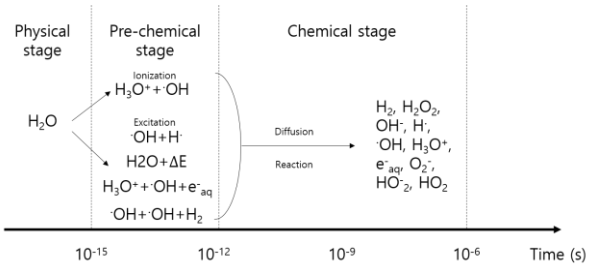


Fig. 1. Scheme of water radiolysis simulation in Geant4 DNA

2.3 Algorithm for simulating UHDR irradiation

In a typical MCTS simulation, a primary particle is transported in one event. In this study, in order to mimic the UHDR condition, an algorithm was developed to start the chemical stage after the dose delivered to the volume of interest reached the threshold value through irradiation of several particles in one event.

2.4 Configuration

In common, a cubic water phantom with a side of 3.2 μm was irradiated with 100 MeV protons, and G4emDNAPhysics_option2 and G4emDNAChemistry_chemistry option3 were used as physics and chemistry constructors, respectively. In order to confirm the maximum effect of the inter-track effect, the G-values of hydroxyl radical in overlapped

beam irradiation and planar irradiation were compared. In addition, the change in G-value was observed by changing the dose threshold to 0.1, 1, 2, 5 and 10 Gy.

2.5 G-value comparison

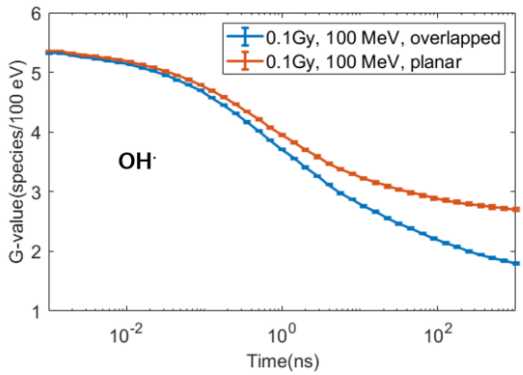
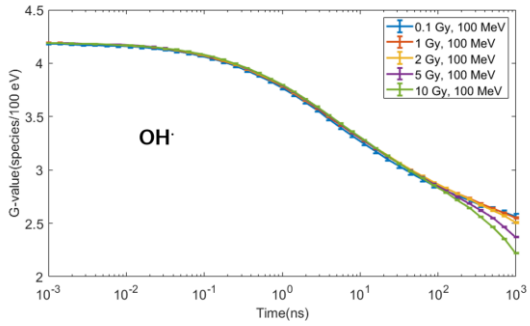


Fig. 2. Comparison of G-values for hydroxyl radical in overlapped beam and planar beam irradiation

When overlapping beams, the inter-track effect is maximized, resulting in a decrease in the G-value of the hydroxyl radical over all time periods. A decrease of 22% was observed at 1 μs.



When irradiated with a planar source and varying the dose threshold, there was almost no change in the G-value of the hydroxyl radical up to 0.1 μs, but a maximum of 13% difference in G-value of hydroxyl radical was observed near 1 μs. Considering the changing aspect of the G-value, extension of simulation time would be required.

3. Conclusions

In this study, as the starting point of the UHDR irradiation mechanism study, chemical yield changes according to simulation configuration were observed by MCTS simulation. This study is limited to preliminary results due to the absence of a beam time structure and the absence of long-term simulations for comparison with measurement results.

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