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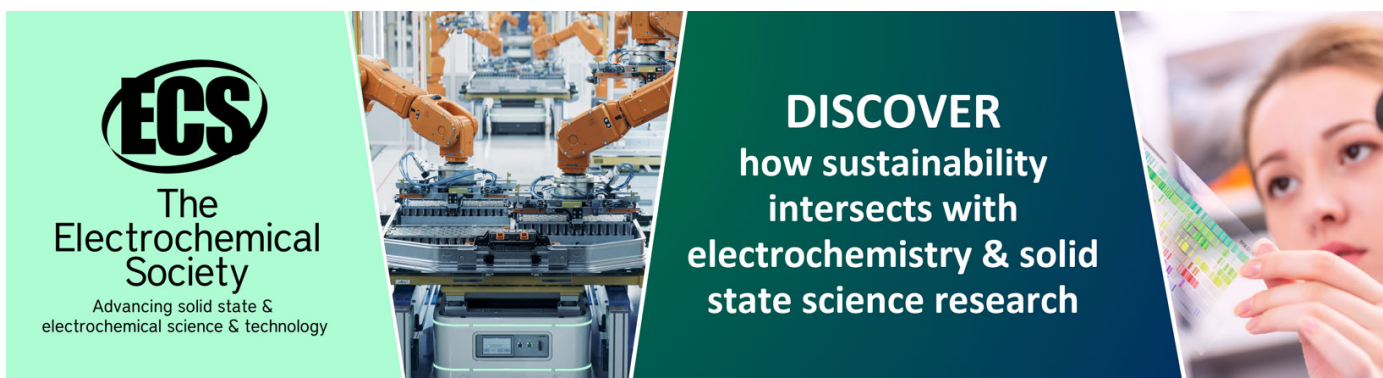
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Evaluation of RBE-weighted doses for various radiotherapy beams based on a microdosimetric function implemented in PHITS*

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Abstract. University of Tsukuba is developing a new TPS for boron neutron capture therapy (BNCT) equipped with Monte Carlo dose-calculation engine based on Particle and Heavy Ion Transport code System PHITS. It is currently in the process of extending its adaptation to other radiotherapy beams. For this extension, not only physical doses but also their relative biological effectiveness (RBE) must be evaluated for various radiotherapy in the same framework. Frequent and dose probability densities of lineal energy, y , are the key quantities in the RBE estimation, and they must be precisely evaluated for various locations in a patient. In this study, the probability densities of y for a site diameter of 0.564 μm were calculated for X-ray, proton, carbon-ion, and BNCT beams with appropriate geometry settings using the microdosimetric function implemented in PHITS, and they were converted to the corresponding RBE-weighted doses using the microdosimetric kinetic model. The accuracy of the calculated data were well verified by several experimental data, indicating the adequacy of the use of PHITS and microdosimetric kinetic model in the dose-calculation engine for TPS applicable to various radiotherapy.

1. Introduction

Microdosimetric quantities, such as lineal energy, y , [1] can express small-sized stochastic energy depositions, and are useful as an index to characterize beam quality. Evaluating microdosimetric quantities is extremely important because the beam quality in radiotherapy directly affects the therapeutic effect (i.e., the relative biological effectiveness (RBE)). Microdosimetric approaches can be classified into experimental and computational methods. A popular microdosimetric experimental approach often utilizes a tissue-equivalent proportional counter (TEPC) for various types of radiotherapy beams [2].

As regards the microdosimetric computational approach, several biophysical models were developed. The microdosimetric kinetic model (MKM) [3] is one of the most popular biophysical models. The MKM has been used to estimate RBE in various radiotherapies [4, 5], and is already beginning to be utilized for treatment planning of carbon ion therapy [6]. The microdosimetric computational approach can easily obtain the probability density of the microscopic quantities in a

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patient at various locations; hence, it is particularly useful while considering its possible applications in treatment planning systems (TPSs). University of Tsukuba has developed a TPS (tentative name: Tsukuba-Plan) for boron neutron capture therapy (BNCT) [7], and is currently extending its adaptation to radiotherapy beams other than BNCT. With Tsukuba-Plan, we aim to evaluate not only the physical dose but also the biological dose (i.e., RBE-weighted dose). To perform RBE-weighted dose evaluation, we examined a method to combine the MKM and the microdosimetric function [8] implemented in Particle and Heavy Ion Transport Code System (PHITS) code, and validated this method for a 155 MeV proton beam [9].

In this study, the probability density of lineal energy (y): $f(y)$ for various external radiation beams were calculated using a microdosimetric function in PHITS. Dose probability densities of y : $d(y)$ were also calculated from $f(y)$, and dose spectra $yd(y)$ for all beams were also compared. In addition, we attempted to calculate the RBE-weighted dose from the calculated $yd(y)$ spectrum for charged particle beams.

2. Materials and Methods

2.1. Microdosimetric function in PHITS

PHITS can calculate deposit energy, flux, etc. in a macroscopic region for various types of radiation. However, PHITS transports charged particles using the condensed history method, except for electrons below 1 keV. Hence, directly calculating the y distribution in the microscopic region, where the event-by-event simulation of ionization and excitation is necessary, is impossible. Sato *et al.* incorporated the results of a track structure simulation into PHITS via a mathematical model and made it possible to calculate the $f(y)$ and $d(y)$ for the nm scales [8]. PHITS also contains a function that can be used to estimate the RBE for cell survival by applying the MKM from the calculated $yd(y)$ spectrum as a function for evaluating the RBE-weighted dose. The dose estimation determined using a combination of PHITS and the MKM is already evaluated for a carbon-ion beam [10], a reactor-based BNCT beam [11], and a 155 MeV proton beam [9].

2.2. Calculation of the $yd(y)$ spectrum and the RBE-weighted dose in a water phantom

In this study, $yd(y)$ spectra of various types of radiation beams, such as X-ray beams (10 MV of clinical linear accelerator: LINAC, 200 keV from X-ray irradiator for cells), a proton beam (200 MeV), a carbon-ion beam (290 MeV/u), and an accelerator-based BNCT beam, were evaluated for the site diameter of 0.564 μm , which was a domain size used in MKM as discussed later.

For the calculation geometry of LINAC, equipment including a metal target, a flattening filter (copper), jaws (tungsten), and a multi leaf collimator (tungsten-alloy) were placed upstream of a water phantom. The incident beam was set to the energy distribution of the X-rays adopted from published data [12]. The $yd(y)$ spectrum of the 10 MV X-rays was calculated at 100 mm deeper from the beam's entrance of the water phantom. Meanwhile, a continuous energy of X-rays generated from a tungsten target were assumed for the 200 keV X-rays. The inherent filtration was set to 0.8 mm of beryllium.

With regard to the proton beam, Takada *et al.* evaluated a 155 MeV proton beam at the Proton Medical Research Center (PMRC) at University of Tsukuba hospital [9]. Hence, we evaluated herein a different incident energy (i.e., 200 MeV). The structure of some devices in the beam delivery system was different because the incident energy was different. Assuming that the double scattering method was used for the proton beam irradiation, a 60 mm width of spread-out Bragg peak (SOBP) was created by a ridge filter (aluminum alloy). Patient-specific beam-shaping assemblies, such as a range compensator or bolus, were not considered.

As regards the carbon-ion beam, a wobblers-scatterer irradiation with 60 mm in width of an SOBP beam was assumed. The incident carbon-ion beam was modulated by the scatterer (tantalum) and the ridge filter (aluminum alloy). The irradiation field was limited by a four-leaf collimator (aluminum alloy). The calculated point of the $yd(y)$ spectrum for these charged particle beams was placed at the center of the SOBP in the water phantom.

For the BNCT beam, a LINAC-based BNCT beam that was generated at University of Tsukuba, which combined an 8 MeV proton beam and a beryllium target, was assumed [7]. The calculated points of the $yd(y)$ spectrum for the BNCT beam were set at a 0 mm and 20 mm depths from the beam's entrance into the phantom. The composition of the phantom was set as a soft tissue composed of hydrogen, carbon, nitrogen and oxygen [13]. Boron was not considered as a component constituting the phantom.

For the RBE-weighted dose estimation of the charged particle beams, the biological endpoint of RBE was set for the 10% surviving fractions (RBE_{10}) of human salivary gland (HSG) cells. Note that the RBE was calculated as RBE_{10} , in other words, the RBE dependency of the dose or dose rate was not considered in this study. The RBE_{10} was determined by the MKM parameters evaluated from biological experimental data, that is, surviving fractions of the HSG cells irradiated with various heavy-ions [14] and the saturation-corrected dose-mean specific energy calculated from the $yd(y)$ spectrum in this study. The MKM parameters of α_0 , β , and the saturation parameter (y_0) were selected as 0.155 Gy^{-1} , 0.0615 Gy^{-2} , and $93.4 \text{ keV}/\mu\text{m}$, respectively [9, 15]. The 200 kVp X-rays (α : 0.19 Gy^{-1} , β : 0.05 Gy^{-2} in the linear quadratic model) were set as the reference radiation used to calculate the RBE [14]. The details of the calculation procedure for the RBE-weighted doses are presented in [10].

The calculated RBE-weighted dose for the carbon-ion beam herein was compared with the microdosimetric measurement data collected in similar experiments [16].

3. Results and discussions

3.1. Calculation results of the $yd(y)$ spectrum

Figure 1 shows the calculated $yd(y)$ spectra for the X-ray beams, charged particle, and BNCT beams.

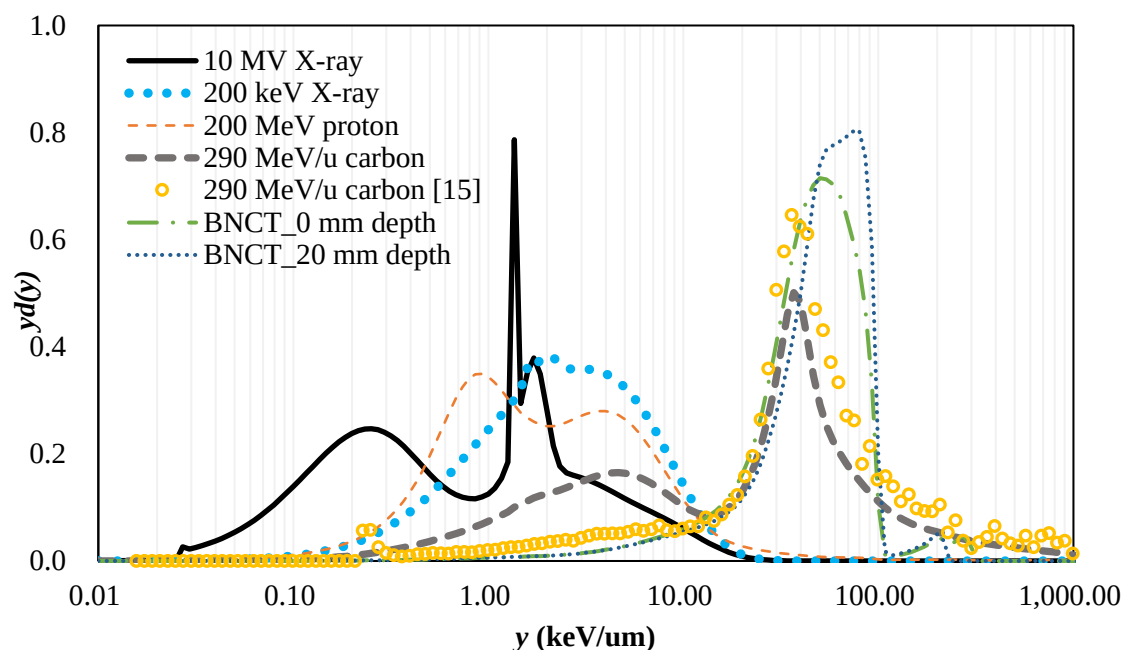


Figure 1. Comparison of the $yd(y)$ spectra for various radiation beams. The lines represent the calculation results, while the symbol represents the measured data for the 290 MeV/u carbon-ion beam [16].

The difference of the $yd(y)$ spectrum caused by the difference in the X-ray energy can be clearly observed in Fig. 1. The tendency of the $yd(y)$ spectrum of the low-energy X-rays obtained by PHITS calculation to shift to a higher y value is similar to the result shown by Okamoto *et al.* [5]. In the calculated $yd(y)$ spectrum of 10 MV X-ray beam, sharp peaks were observed approximately at a y -value of 1 ($\text{keV}/\mu\text{m}$). This peak was attributed to the production of Auger electrons from an oxygen atom.

High-energy electrons can produce Auger electrons by knocking out an electron at the 1s state of oxygen with a binding energy of 533 eV. The deposition energy caused by this event was 533 eV, which corresponded to 1 keV/ μm if no other ionization event occurred in the site. Meanwhile, ionization chambers, such as the TEPC, can only measure the number of ionization events that occur in the target volume irrespective of the actual deposition energy per event. Thus, the peak was observed only in the simulation.

A slight difference in the $yd(y)$ spectrum of the carbon-ion beam was observed between PHITS calculation in this study and the measured data obtained by the TEPC [16]. Two peaks were observed at approximately 5 keV/ μm and 40 keV/ μm of the y value in the $yd(y)$ spectrum calculated by PHITS. However, only one peak was observed in the measurement by the TEPC. Two peaks were generated by irradiation with a carbon-ion beam because of the contribution by the primary component of the carbon-ion and δ rays. This result was clarified by the $yd(y)$ spectrum measurement for the carbon-ion beam irradiation using a wall-less TEPC [17]. In contrast, in the case of the commercially available TEPC, the surroundings of the detecting part were covered with a plastic wall, which was thought to be caused by the delta-rays that cannot be correctly measured by the wall effect in the measurement using the commercially available TEPC.

In the calculated $yd(y)$ spectrum of the BNCT beam, two peaks were observed at approximately 40–50 keV/ μm and 200 keV/ μm of the y value. The contribution of boron, which was the main energy deposition component of the BNCT, was not considered in the calculation. Nevertheless, the distribution range of the y value showed considerably high values. The energy deposition from protons produced by the elastic scattering and generated from the nuclear reaction of thermal neutrons to nitrogen atoms (e.g., $^{14}\text{N}(n,p)^{14}\text{C}$) was generated in the irradiation of the BNCT beam to the soft tissue. The elastic scattering of atoms constituting the soft tissue (e.g., nitrogen, carbon, and oxygen) also occurred. These components can be thought of as the reason for the high y values. In an actual BNCT treatment, the patient is administered with boron compound to enhance the therapeutic effect. Therefore, the y value is predicted to become even higher because of the capture reaction of boron and neutrons. The shift of the y value to a higher- y region by boron addition was confirmed in a previous study [18].

3.2. Calculation results of the RBE-weighted dose for the charged particle beams

Figures 2 and 3 depict the RBE-weighted doses evaluated by combining the $yd(y)$ spectra of the charged particle beams and the MKM.

The calculated physical depth dose of the proton beam was compared with the measurement data from this study obtained at the PMRC. The calculated physical dose was normalized with the measurement data at the center of the SOBP. However, no measurement data for the RBE-weighted dose for a 200 MeV proton beam were collected at the PMRC. Thus, the RBE-weighted dose calculated using the PHITS code was normalized using the same method as that used for the 155 MeV proton beam [9].

The calculated physical dose and RBE-weighted doses were normalized with the published measurement data [16] at the entrance of the water phantom and the center of the SOBP, respectively. The calculated physical depth dose of the carbon-ion beam nearly agreed with the measured data published by Kase *et al.* [16]. The RBE-weighted dose of the carbon-ion beam was also in good agreement with the measured data obtained by the commercially available TEPC.

We successfully calculated the RBE-weighted dose for the therapeutic particle beams with SOBP beam of 60 mm width. As regards the practical use of the function, we will evaluate every SOBP width for particle beams. Moreover, we plan to evaluate not only the depth dose distributions shown in this study but also the lateral dose distribution at various depths of beam penetration.

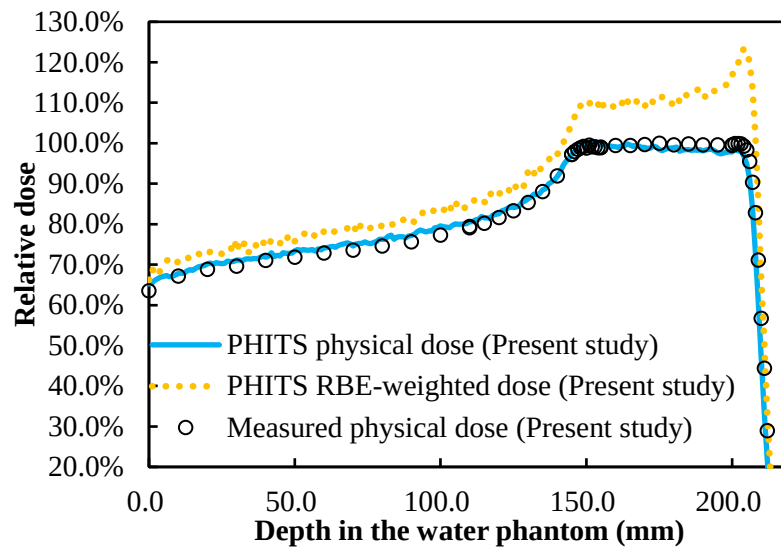


Figure 2. Comparison of the calculated physical and RBE-weighted doses for the 200 MeV proton beam with the measured physical dose.

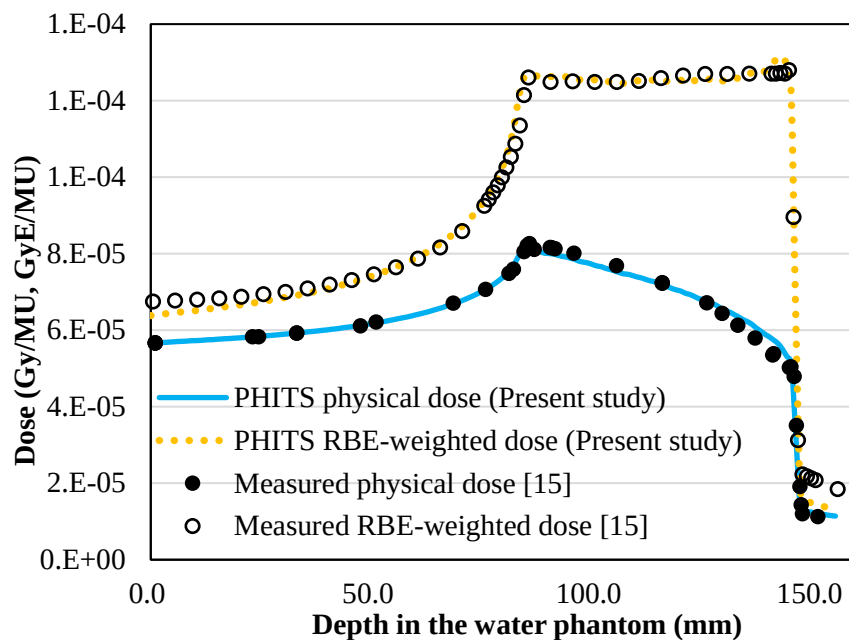


Figure 3. Comparison of the calculated physical and RBE-weighted doses for a 290 MeV/u carbon-ion beam with the measured data.

4. Conclusion

This research provides a microdosimetric calculation of the $yd(y)$ spectrum and the RBE-weighted dose using a microdosimetric function implemented in PHITS code for various external radiation beams. By incorporating the results obtained in this study into the Tsukuba-Plan, the Tsukuba-Plan could simultaneously calculate the RBE-weighted and physical doses for various external radiotherapy beams.

The next goal for the RBE-weighted dose calculations is their application to treatment planning for human bodies, which have a complicated shape. In PHITS, the physical and RBE-weighted doses can be calculated at the same time, which is a very useful function when combining multiple radiation types. However, problems remain. For example, a computational time of several hours is necessary

when calculating the RBE-weighted dose using the PHITS. Such an issue is a disadvantage compared to commercial-based TPSs when considering the use of these PHITS calculations in a TPS. Reducing the computational time is always a matter of concern for Monte Carlo calculations. We aim for improvements in both hardware (e.g., use of parallel computing techniques) and software (e.g., introduction of effective variance reductions) in the future.

We also plan to incorporate the stochastic microdosimetric kinetic model, SMKM [19], into our TPS to consider the dose and dose-rate dependence of the RBE.

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The numerical calculations for $yd(y)$ spectrum and the RBE-weighted dose were performed using the Cluster of Many-core Architecture processor (COMA) at the Center for Computational Sciences, University of Tsukuba.

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