



CHALMERS

Chalmers Publication Library

PHITS - Applications to radiation biology and radiotherapy

This document has been downloaded from Chalmers Publication Library (CPL). It is the author's version of a work that was accepted for publication in:

13th International Varenna Conference on Nuclear Reaction Mechanisms, NRM 2012 (ISSN: 20788835)

Citation for the published paper:

Sihver, L. ; Sato, T. ; Niita, K. (2013) "PHITS - Applications to radiation biology and radiotherapy". 13th International Varenna Conference on Nuclear Reaction Mechanisms, NRM 2012 pp. 497-502.

Downloaded from: <http://publications.lib.chalmers.se/publication/196881>

Notice: Changes introduced as a result of publishing processes such as copy-editing and formatting may not be reflected in this document. For a definitive version of this work, please refer to the published source. Please note that access to the published version might require a subscription.

Chalmers Publication Library (CPL) offers the possibility of retrieving research publications produced at Chalmers University of Technology. It covers all types of publications: articles, dissertations, licentiate theses, masters theses, conference papers, reports etc. Since 2006 it is the official tool for Chalmers official publication statistics. To ensure that Chalmers research results are disseminated as widely as possible, an Open Access Policy has been adopted. The CPL service is administrated and maintained by Chalmers Library.

PHITS - Applications to Radiation Biology and Radiotherapy

L. Sihver^{1}, T. Sato², K. Niita³, N. Matsuda², Y. Iwamoto², S. Hashimoto², H. Iwase⁴,
H. Nakashima², and S. Chiba^{2,5}*

¹Chalmers University of Technology, Sweden

²Japan Atomic Energy Agency, JAEA, Japan

³Research Organization for Information Science and Technology, RIST, Japan

⁴High Energy Accelerator Research Organization, KEK, Japan

⁵Tokyo Institute of Technology, Japan

* E-mail: sihver@chalmers.se, Phone: +46-31-772 2921

Abstract

PHITS is a 3-dimensional general-purpose Monte Carlo code, which can transport of all varieties of hadrons and heavy ions with energies up to around 100 GeV/nucleon. To be able to estimate the biological damage from neutrons with PHITS, a feature has been included to treat low energy neutron collisions as "events" which means that the energy and momentum is conserved in each event and makes it possible to extract the kinetic energy distributions of all the residual nuclei without using any local approximation. To estimate the direct biological effects of radiation, mathematical functions, for calculating the microdosimetric probability densities in macroscopic material, have been incorporated in PHITS. This makes it possible to instantaneously calculate the probability densities of lineal and specific energies around the trajectories of high energetic charged particle tracks. A method for estimating the biological dose has also been established by using the improved PHITS coupled to a microdosimetric kinetic model.

1 Introduction

The health risks associated with exposure to various components of radiation are of great concern in many different situations, e.g. when planning manned long-term interplanetary missions, such as future missions to Mars, during and after radiotherapy, and after nuclear accidents. Since it is not possible to measure the radiation environment inside of human organs, simulations based on radiation transport/interaction codes are used. When dealing with radiation risks, it is important to be able to predict deterministic as well as stochastic radiation effects. Deterministic effects are observed only at doses above a threshold and their severity increases with dose, while stochastic effects do not seem to have a threshold and their severity is not directly dependent on the dose. The estimation of biological effects is very complicated and has large uncertainties. Although knowledge of the dose is not sufficient for estimating the biological effects of radiation, it is still a basic important component when estimating the risks associated with exposure to ionizing radiation. Using quality factors based on LET spectra, absorbed doses are then converted into dose equivalents, which in turn are converted into risk using appropriate risk coefficients. However, when estimating the direct biological effects of radiation lineal and specific energies are better indexes in comparisons to LET, since LET does not take the energy dispersion due to the created delta electrons into consideration. This paper describes the 3-

dimensional general purpose particle and heavy-ion MC transport code PHITS (Particle and Heavy-Ion Transport code System), and some of its features related to radiation biology and radiotherapy.

2 PHITS (Particle and Heavy Ion Transport code System)

PHITS (Particle and Heavy-Ion Transport code System) [1] is a 3-dimensional general purpose particle and heavy-ion MC transport code, developed and maintained by RIST, JAEA and KEK in Japan together with Chalmers in Sweden, which can transport neutrons from thermal energies up to 200 GeV, and the same method as in the MCNP4C code [2] is employed for neutrons with energies between 1 meV and 20 MeV based on the Evaluated Nuclear Data such as the ENDF-B/VI [3], JENDL-3.3 [4,5]; and for p and n up to 3 GeV for the JENDL-HE [6,7] file. Above 20 MeV, the Bertini model with free p-p and n-n cross sections parameterized according to Niita et al. [8] is used up to 3 GeV, while the simulation model JAM (Jet AA Microscopic Transport Model) developed by Nara et al. [6] is used above 3 GeV for nucleons, above 2.5 GeV for pions, and for all energies for all other baryons. JAM is a hadronic cascade model, which explicitly treats all established hadronic states including resonances with explicit spin and isospin as well as their anti-particles. For protons and other hadrons, JAM is used above 1 MeV, but for charged particles below 1 MeV only the ionization process is considered until the particles are stopped. PHITS also uses Evaluated Nuclear Data for photon and electron transport below 1 GeV in the same manner as in the MCNP4C code based on the ITS code, version 3.0 [9]. The energy range of electrons and photons is restricted to the energy region 1 keV - 1 GeV at the present, but the extension of the maximum energy of these particles is in progress. PHITS can also transport nuclei in any solid, gas or liquid material. Below 10 MeV/n, only the ionization process for the nucleus transport is taken into account, but above 10 MeV/n the nucleus-nucleus collisions up to 100 GeV/n is described by the simulation model JQMD (JAERI Quantum Molecular Dynamics) developed by Niita et al. [10]. In the QMD model, the nucleus is described as a self-binding system of nucleons, which are interacting with each other through the effective interactions in the framework of molecular dynamics. One can estimate the yields of emitted light particles, fragments and excited residual nuclei resulting from the heavy ion collision. The QMD simulation, as well as the JAM simulation, describes the dynamical stage of the reactions. At the end of the dynamical stage, excited nuclei are created and must be forced to decay in a statistical way to get the final observed state. In PHITS the GEM model [11] (Generalized Evaporation Model) is default employed for light particle evaporation and fission process of the excited residual nucleus.

When simulating the transport of charged particles and heavy ions, the knowledge of the magnetic field is sometimes necessary to estimate beam loss, heat deposition in the magnet, and beam spread. This is also of importance when simulating the beam transport in accelerators, e.g. for proton and heavy ion therapy. PHITS can provide arbitrary magnetic fields in any region of the setup geometry. PHITS can simulate not only the trajectory of the charged particles in the field, but also the collisions and the ionization process at the same time. For the ionization process of the charged particles and nuclei, the SPAR code [12] is default used for the average stopping power dE/dx , the first order of Molière model for the angle straggling, and the Gaussian, Landau and Vavilov theories for the energy straggling around the average energy loss according to the charge density and velocity. In addition to the SPAR code, the ATIMA package, developed at GSI [13, 14], has been implemented as an alternative code for the ionization process.

The total reaction cross section, or the lifetime of the particle for decay, is an essential quantity in the determination of the mean free path of the transported particle. According to the mean free path, PHITS chooses the next collision point using the MC method. To generate the secondary particles of the collision, we need the information of the final states of the collision. It is therefore very important that reliable data of total non-elastic and elastic cross sections is used for the particle and heavy ion transport. In PHITS, the Evaluated Nuclear Data is used for neutron-induced reactions below 20 MeV. For neutron-induced reactions above 20 MeV a parameterization is used. As for the elastic cross

sections, the Evaluated Nuclear Data is also used for neutron-induced reactions below 20 MeV, and a parameterization is used above 20 MeV [8]. Parameterizations are also used for proton induced reactions for all energies, and for the double differential cross sections of elastic nucleon-nucleus reactions [8]. We have adopted the NASA systematics developed by Tripathi et al., [15-17] for the total nucleus-nucleus reaction cross section, as an alternative to the Shen formula [18], and a careful benchmarking of the major total reaction cross section models used in particle and heavy ion transport codes has been made [19-21]. PHITS has also been extensively used and benchmarked for many different applications, including different space applications e.g. [22-32].

2.1 Simulations of biological effects

When estimating the local biological effects of high energetic photons and charged particles, the contribution from the neutrons created both outside and inside the human must be considered. It is therefore important to be able to calculate the kinetic energy distributions of the created secondary charged particles from photonuclear and neutron induced reactions. For low energetic neutrons, nuclear data is normally used. However, based on the one-body Boltzman equation, energy and momentum is not conserved in an event during the transport calculations. They are only conserved as an average over many randomly calculated events since the Boltzman equation only include mean values of the one-body observables in the phase space and cannot give two-body and higher correlations. A feature has therefore been included in PHITS to treat low energy neutron collisions as "events" which means that the energy and momentum is conserved in each interaction and makes it possible to extract the kinetic energy distributions of the residual nuclei, two particle correlations, etc. In PHITS, the transport algorithm has been changed for the low-energy neutrons from that on solving Boltzmann equation to an algorithm based on an event generator. By using this event generator mode, energy and LET distributions for all charged particles, created by all charged particles and neutrons, can be calculated.

When estimating the direct biological effects of radiation, microdosimetric quantities, such as the lineal and specific energies, are better indexes for expressing the RBE of the primary and secondary particles in comparisons to the conventionally often used LET, since LET does not take the energy dispersion due to the created delta electrons into consideration. Though, the use of microdosimetric quantities in macroscopic transport codes is limited because of the difficulty in calculating the provability distributions on macroscopic matter. Therefore mathematical functions, for calculating the microdosmetric probability densities in macroscopic material, have been incorporated in PHITS. This makes it possible to instantaneously calculate the probability densities of lineal and specific energies around the trajectories of high energetic primary and secondary charged particle tracks. A method for estimating the biological dose, the product of physical dose and RBE of cell survival, for charged particles has also been established by using the improved PHITS coupled to a microdosimetric kinetic (MK) model [33, 34]. Fig 1. shows an example of calculated RBE_{10} for HSG cells in a slab phantom irradiated by several different heavy ion beams, together with experimental values from [35]. Since the energy distributions of the secondary charged particles from neutron induced reactions can be estimated by using the "event generator" in PHITS, an estimation of the RBE of the neutrons can also be made. The accuracy of this will be evaluated in the near future.

In addition to the direct effects, indirect effects due to radicals or reactive oxygen species (ROS), which are formed along the particle tracks, can further damage the DNA, and induce oxidative stress to the cells and therefore compromise the cellular functions. We have therefore developed a method to use experimentally deduced G-values to estimate the G-values as a function particle and energy in PHITS [36]. This model enables calculation of the radical distribution in an extended volume, e.g. inside an organ, taking into account nuclear interactions calculated with PHITS.

3 Summary and conclusions

When estimating the local biological damage of high energetic photons and charged particles, the contribution from the neutrons created both outside and inside the human must be included. This is also the case when estimating single and multiple event upsets of semi-conductor devices exposed to neutron radiation. In PHITS, an approach has therefore been developed to calculate the deposited energy distributions for the thermal neutron transport and the averaged quality factor for neutrons. This feature treat low energy neutron collisions as "events" which means that the energy and momentum is conserved in each event and makes it possible to extract the kinetic energy distributions of all the residual nuclei, two particle correlations, as well as calculate the dose equivalent based on Q(L) relationship, DNA damage, cell survival, etc. without using the local Kerma factor. In treatment planning of charged particle therapy, it is necessary to estimate not only the physical dose, but also the biological dose defined as the product of the physical dose and the RBE of cell killing, inside the patients. In PHITS, the former quantity can be calculated by macroscopic particle transport simulation, while the latter can be estimated by calculating the α and β parameters using PHITS coupled with a microdosimetric kinetic (MK) model. By doing so, the biological dose can be calculated both in the tumor cells and in the healthy tissue inside the patients. This makes PHITS a great tool for treatment planning of charged-particle therapy.

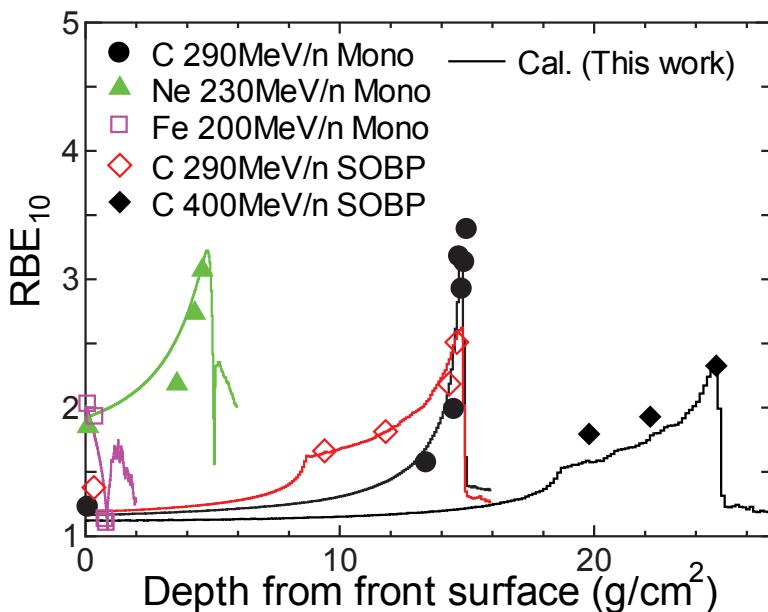


Fig 1. Shows an example of calculated RBE_{10} for HSG cells in a slab phantom irradiated by several different heavy ion beams together with experimental values are from [35].

References

- [1] K. Niita, et al., PHITS: Particle and Heavy Ion Transport code System, Version 2.23, JAEA-Data/Code 2010-022 (2010).
- [2] J. F. Briesmeister, et al., MCNP General Monte Carlo N-Particle Transport Code, Los Alamos National Laboratory report; LA-12625-M (1997).
- [3] V. McLane, et al., ENDF/B-VI Summary Documentation, BNL-NCS-17541 (1996).
- [4] K. Shibata, et al., Japanese Evaluated Nuclear Data Library Version 3 Revision-3: JENDL-3.3, J. Nucl. Sci. Technol. 39, 1125 (2002).
- [5] Watanabe, Y. et al. Nuclear data evaluations for JENDL high-energy file. Proceedings of International Conference on Nuclear Data for Science and Technology, Santa Fe, USA, Sep.26-Oct.1, 2004; AIP CP769, p326-331, 2005.
- [6] Nara, Y. et al. Relativistic nuclear collisions at 10A GeV energies from p+Be to Au+Au with the hadronic cascade model. Phys. Rev. C61:024901, 1999.
- [7] T. Fukahori, et al., JENDL High Energy File. J. Nucl. Sci. Technol., Suppl. 2, 25-30 (2002).
- [8] K. Niita, H. Takada, S. Meigo, Y. Ikeda, High-energy particle transport code NMTC/JAM, Nucl. Instrum. Methods, B184, 406 (2001).
- [9] J. A. Halbleib, et al., ITS Version 3.0: The Integrated TIGER Series of Coupled Electron/Photon Monte Carlo Transport Codes, SAND91-1634 (1992).
- [10] K. Niita, et al., Analysis of the (N,xN) reactions by quantum molecular dynamics plus statistical decay model, Phys. Rev. C52, 2620 (1995).
- [11] S. Furihata, Statistical analysis of light fragment production from medium energy proton-induced reactions, Nucl. Instr. and Meth. B171, 251 (2000).
- [12] T. W. Armstrong, and K. C. Chandler, A Fortran program for computing stopping powers and ranges for muons, charged pions, protons, and heavy ions, ORNL-4869, Oak Ridge National Laboratory, (1973).
- [13] H. Geissel, C. Scheidenberger, Slowing down of relativistic heavy ions and new applications, Nucl. Instr. Meth. B136-138, 114-124 (1998).
- [14] C. Scheidenberger, H. Geissel, Penetration of relativistic heavy ions through matter, Nucl. Instr. Meth. B136-138, 114-124 (1998).
- [15] R. K. Tripathi, F. A. Cucinotta, J. W. Wilson, Accurate universal parameterization of absorption cross sections, Nucl. Instr. and Meth. B117, 347 (1996).
- [16] R. K. Tripathi, J. W. Wilson F. A. Cucinotta, Accurate universal parameterization of absorption cross sections II – neutron absorption cross sections, Nucl. Instr. and Meth. B129, 11 (1997).
- [17] R. K. Tripathi, F. A. Cucinotta, J. W. Wilson, Accurate universal parameterization of absorption cross sections III – light systems, Nucl. Instr. and Meth. B155, 349 (1999).
- [18] W. Shen, et al., Total reaction cross section for heavy-ion collisions and its relation to the neutron excess degree of freedom, Nucl. Phys. A 491 (1) 130-146 (1989).
- [19] L. Sihver, et al., A Comparison of Total Reaction Cross Section Models Used in Particle and Heavy Ion Transport Codes, IEEEAC paper 1476, ISBN/ISSN: 978-142443888-4 (2010).

- [20] L. Sihver, et al., A comparison of total reaction cross section models used in particle and heavy ion transport codes, *Adv. Space Res.* 49, 812-819 (2011), doi:10.1016/j.asr.2011.11.029.
- [21] L. Sihver, et al., A comparison of total reaction cross section models used in FLUKA and PHITS, IEEEAC paper. (in press).
- [22] T. Sato, et al., Applicability of particle and heavy ion transport code PHITS to the shielding design of space crafts, *Rad. Meas.* 41, 1142-1146 (2006).
- [23] L. Sihver, et al., Benchmarking of calculated projectile fragmentation cross sections using the 3-D, MC codes PHITS, FLUKA, HETC-HEDS, and MCNPX”, *Acta Astronautica* 63, 865-877 (2008).
- [24] T. Sato, L. Sihver, K. Gustafsson, D. Mancusi and K. Niita, Shielding Design of Spacecrafts Using PHITS, *American Nuclear Society Transactions*, 99, 592 (2008).
- [25] L. Sihver, T. Sato, K. Gustafsson, V.A. Shurshakov, and G. Reitz, Simulations of the MTR-R and MTR Experiments at ISS, and Shielding Properties Using PHITS, IEEEAC paper 1015 (2009).
- [26] L. Sihver, et al., An update about recent developments of the PHITS code, *Adv. Space Res.* 45, 892-899 (2010).
- [27] L. Sihver, T. Sato, M. Puchalska, and G. Reitz, Simulations of the MATROSHKA experiment at the International Space Station using PHITS, *Radiat. Environ. Biophys.* 49:351-357 (2010).
- [28] K. Gustafsson, L. Sihver, D. Mancusi, T. Sato, PHITS simulations of the Matroska experiment”, *Adv. Space Res.* 46, 1266–1272 (2010).
- [29] L. Sihver, et al., Monte Carlo simulations of MATROSHKA experiment outside ISS, IEEEAC paper 1585, ISSN: 978-142447350-2 (2011).
- [30] T. Sato, et al., “Evaluation of Dose Rate Reduction in a Spacecraft Compartment due to Additional Water Shield”, ISSN 0010_9525, *Cosmic Research*, Vol. 49, No. 4, pp. 319–324. © Pleiades Publishing Ltd. (2011).
- [31] L. Sihver et al., Simulations of absorbed dose on the phantom surface of MATROSHKA-R experiment at the ISS, *Adv. Space Res.* 49, 230-236 (2011).
- [32] M. Puchalska, L. Sihver, T. Sato, T. Berger, and G. Reitz, Simulations of MATROSHKA experiments at ISS using PHITS, *Adv. Space Res.* (accepted).
- [33] T. Sato, et al., Biological Dose Estimation for Charged-Particle Therapy Using an Improved PHITS Code Coupled with a Microdosimetric Kinetic Model”, *Rad. Res.* 171, 107-117 (2009).
- [34] T. Sato et al., Analysis of Cell-Survival Fractions for Heavy-Ion Irradiations Based on Microdosimetric kinetic Model Implemented in the Particle and Heavy Ion Transport code System, *Rad. Prot. Dos.*, 1-6, 2010.
- [35] Y. Kase et al., Microdosimetric measurements and estimation of human cell survival for heavy-ion beams. *Radiat. Res.* 166, 629-638 (2006).
- [36] T. Maeyama et al., Production of a Fluorescence Probe in Ion-beam Radiolysis of Aqueous Coumarin-3-carboxylic Acid Solution 2: Effects of nuclear fragmentation and its simulation with PHITS, *Rad. Phys. Chem.* 80, 1352-1357 (2011).