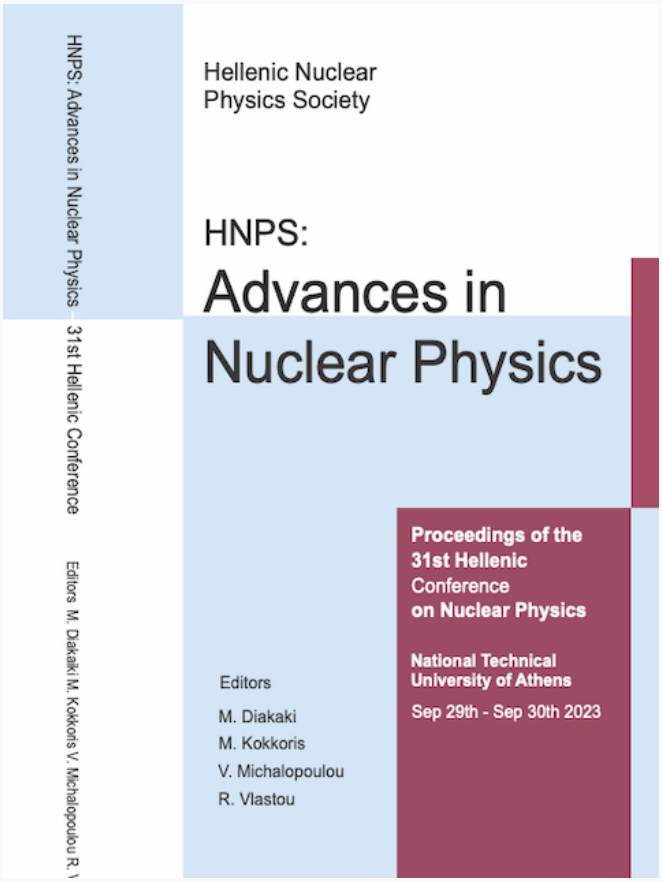
HNPS Advances in Nuclear Physics

Vol 30 (2024)

HNPS2023



Microdosimetric Modelling of Neutron Capture Therapy Effectiveness

Sofia Georgiou, John Kalef-Ezra, Antigoni Kalamara, Efstratios Karavasilis, Ion Evangelos Stamatelatos

doi: 10.12681/hnpsanp.6282

To cite this article:

Georgiou, S., Kalef-Ezra, J., Kalamara, A., Karavasilis, E., & Stamatelatos, I. E. (2024). Microdosimetric Modelling of Neutron Capture Therapy Effectiveness. *HNPS Advances in Nuclear Physics*, *30*, 189–194. https://doi.org/10.12681/hnpsanp.6282

Microdosimetric Modelling of Neutron Capture Therapy Effectiveness

S. Georgiou[1,2], J.A. Kalef-Ezra[3], A. Kalamara[1], E. Karavasilis[2], I.E. Stamatelatos[1,*]

[1] *INRASTES, NCSR "Demokritos", 15310, Aghia Paraskevi, Greece*
[2] *School of Medicine, Democritus University of Thrace, 68100, Alexandroupoli, Greece*
[3] *Medical Physics Laboratory, Medical Department, University of Ioannina, 45110, Ioannina, Greece*

Abstract Monte Carlo simulations were carried out using the MCNP6.1 code to predict the energy deposition at microscopic level in *in vitro* Neutron Capture Therapy studies. Irradiations with neutron beams of energies from 0.025 eV to 14.2 MeV of small spherical targets loaded with either 1000 ppm ^{nat}B (199 ppm ^{10}B) or ^{nat}Gd (156 ppm ^{157}Gd) and located at the center of a small phantom were simulated. ENDF/B-VII.1 and TENDL-2017 nuclear data libraries, as well as INCL4/ABLA and Bertini models were tested using published experimental data as benchmark, i.e. a spherical proportional counter that simulated a 1 μm in diameter tissue equivalent site–irradiated with 13.9 MeV neutrons. The methodology, as developed, was applied to assess the microdistribution spectra to the target in terms of $yd(y)$, $\overline{y_F}$, $\overline{y_D}$ and the kerma to flux ratio for the prediction of the biological response of in vitro cells irradiations.

Keywords neutron capture therapy, Monte Carlo, microdosimetry, dosimetry

INTRODUCTION

Neutron Capture Therapy (NCT) is a binary therapeutic modality for the treatment of malignant tumors. The modality is based on neutron capture in nuclides with a high cross section, such as ^{10}B and ^{158}Gd (~19.9% and 15.6% natural abundance, respectively) that are preferentially loaded to the tumor. The emission of short-range secondary charged particles, such as heavy ions and Auger electrons, leads to high dose non-uniformity at microscopic level. However, the radiobiological response of a specific system, such as cells under *in vitro* conditions, depends on dose, dose rate and the spatial distribution of the imparted energy at both microscopic and macroscopic level. Therefore, the relative biological effectiveness of a dose to a tumor in NCT is a complex function of the numerous energy deposition events. Due to stochasticity, the quantity absorbed dose is inadequate for the prediction of the biological response [1]. Therefore, stochastic microdosimetric quantities and their distribution have to be used, such as the lineal energy, i.e. the quotient of the energy imparted to the matter in a volume by the mean chord length in the that volume [2].

The present study is divided in two parts. The first is devoted to the comparison of an experimentally obtained lineal energy spectrum with the spectra obtained theoretically by Antoni and Bourgois [3] and by Monte Carlo simulations carried out in the present study using the INCL4/ABLA and Bertini models and the ENDF/B-VII.1 and TENDL-2017 nuclear data libraries. The second part discusses simulations of in vitro irradiations of cell cultures aiming to assess microdosimetric quantities for the prediction of the biological response of the irradiated cells.

BENCHMARK SIMULATIONS

A spherical tissue equivalent proportional counter (TEPC) of 12.7 and 17.8 mm inner and outer diameter was irradiated with a monoenergetic 13.9 MeV neutron beam [3]. Its cavity was surrounded by a wall made of A-150 tissue equivalent plastic and filled with methane-based tissue equivalent gas at 7.4 kPa simulating a tissue equivalent site 1.0 μm in diameter and 1.064 g·cm^{-3} in density [4,5].

* Corresponding author: *ion@ipta.demokritos.gr*

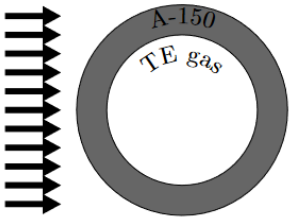
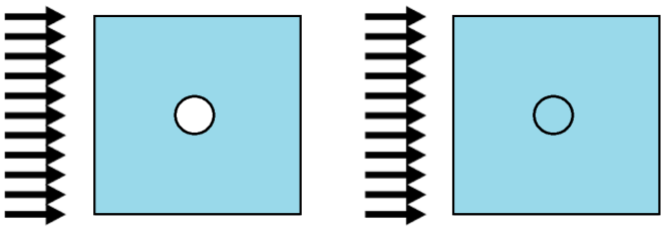


Figure 1. *Geometry in MCNP of the TEPC irradiation (not in scale)*

IN VITRO SIMULATIONS

Monte Carlo simulations were performed on a cubical phantom of 0.25 mm side with a spherical target at its center, 10 μm in diameter, composed of water, and solutions containing either 0.1% natural boron (1‰ ^{nat}B) or 0.1% natural gadolinium (1‰ ^{nat}Gd), simulating a single cell. The phantom was irradiated with three monoenergetic neutron beams, namely 0.025 eV, 1.0 MeV and 14.2 MeV (Fig. 2).



(a) *(b)*

Figure 2. *Geometry in MCNP in case of a 0.25 mm x 0.25 mm x 0.25 mm phantom with a spherical target of 10 μm in diameter at its center (not in scale): (a) heterogeneous and (b) homogeneous distribution*

CALCULATIONS

The quantity lineal energy for each secondary charged particle was estimated by coupling the energy deposition F6 tally with the pulse-height tally F8. The energy spectra card E8, enabled the energy distribution in logarithmic energy bins. The anticoincidence pulse-height card FT8 PHL, was used for counting the events from nuclear reactions in the cavity wall.

The lineal energy of the energy bin *i* in keV/μm is given from the imparted energy divided by the mean cord length in the single cell volume and multiplied by 1000 to convert MeV to keV,

$$y_i = 1000 \frac{\varepsilon_i}{\bar{\ell}} \quad (1)$$

The lineal energy distribution of each secondary particle is given by

$$f(y_i) = \frac{f_i}{\sum_i^n f_i} \quad (2)$$

where f_i is the count in the *i*-th energy bin and n is the number of the energy bins.

The graphical representation of the spectra, *yd(y)* distribution was calculated by,

$$y_i d(y_i) = \frac{y_i f_i}{\sum_i^n y_i f_i} \left(\frac{1}{\log(y_i / y_{i-1})} \right) \quad (3)$$

The non-stochastic quantities frequency-mean lineal energy, dose-mean lineal energy and the quotient of the kerma to the cell volume to fluence ratio, k_f, were calculated using the following equations

$$\overline{y_F} = \int_0^\infty y f(y) dy \equiv \frac{\sum_i^n y_i f_i}{\sum_i^n f_i} \quad (4)$$

$$\overline{y_D} = \frac{1}{\overline{y_F}} \int_0^\infty y^2 f(y) dy \equiv \frac{\sum_i^n y_i^2 f_i}{\sum_i^n y_i f_i} \quad (5)$$

$$k_f = 1.6 \cdot 10^{-13} \left(\frac{\bar{\ell}}{\Phi \rho V} \right) \sum_i^n y_i f_i = \frac{1.6 \cdot 10^{-13}}{\Phi m} \sum_i^n \varepsilon_i f_i \quad (6)$$

where $1.6 \cdot 10^{-13}$ is a unit conversion factor (Gy·g·keV^{-1}), Φ the incident neutron flux (F4 tally), ρ the density and V the volume of the irradiated medium.

RESULTS AND DISCUSSION

TEPC irradiations

Microdosimetric spectra are compared in Fig. 3 and Table 1. The use of INCL4/ABLA model with the TENDL–2017 nuclear data library minimized the deviations between the calculated and the experimental spectra (Table 1 and Fig. 4).

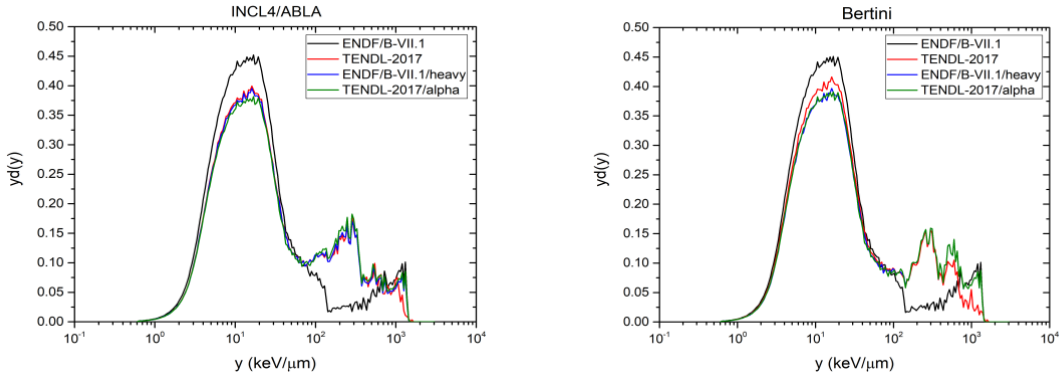


Figure 3. *Comparison of the physics models and cross section libraries under identical irradiation conditions of the TEPC*

Table 1. $\overline{y_F}$, $\overline{y_D}$ *and* k_f *in the TEPC irradiated with a 13.9 MeV neutron beam*

	Antoni-Bourgois [2]	**Present Study**	**Δ**
$\bar{y}_F$ (keV/μm)	11.4 ± 0.1	11.5 ± 0.3	+0.8%
$\bar{y}_D$ (keV/μm)	87.7 ± 1.1	93.7 ± 14.5	+6.8%
k_f (pGy·cm^2)	69.7 ± 0.2	67.2 ± 0.2	-3.5%

Cell irradiations

The comparison of the data obtained by the tested models and libraries showed only minor disparities [6]. Thus, the Bertini model and the ENDF-VII.1 cross section library were used due to the shorter computational time required to obtain adequate statistics. The *yd(y)* spectra to the target irradiated with 0.025 eV, 1.0 MeV and 14.2 MeV neutron beams are shown in Figures 5 and 6 in case of targets composed of water, boron and gadolinium solutions. The presence of ^{nat}B and ^{nat}Gd substantially altered the spectra only in the case of 0.025 eV neutron exposure. As anticipated, their presence in the target had marginal influence when the phantom was exposed to MeV-neutrons.

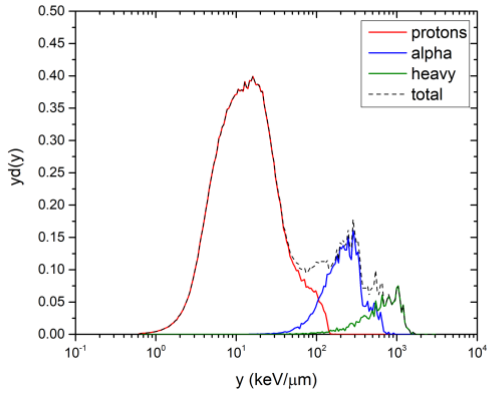


Figure 4. *Microdosimetric spectrum in terms of yd(y) in the gas cavity of the TEPC irradiated with 13.9 MeV neutrons assessed using the INCL4/ABLA model with the TENDL-2017 library*

The frequency-mean lineal energy, the dose-mean lineal energy and the kerma to flux ratio to the small target are shown in Table 2. The estimated 28 pGy · cm^2 kerma to flux ratio when the phantom was exposed to 1.0 MeV of neutrons is marginally higher than the 27.0 pGy · cm^2 kerma-factor given by ICRU in 1989 [5]. On the other hand, the corresponding ratio in case of exposure to 14.2 MeV neutrons, 18.7 pGy · cm^2, is much lower than the one given by ICRU, 70.9 pGy · cm^2 [5], mainly due to the fact that the projected range of most secondary particles (e.g. 0.65 mm in case of 7 MeV protons), is much larger than the dimensions of the phantom itself, leading to energy loss. Note that the estimated quotient refers to the imparted energy to the matter in the specific volume, while the kerma-factor given by ICRU is a point quantity defined under charged particle equilibrium conditions.

Table 2. *Comparison of* $\overline{y_F}$, $\overline{y_D}$ *and* k_f *in a 10 μm spherical target at the center of a small cubical phantom irradiated with 0.025 eV, 1.0 and 14.2 MeV neutron beams using the Bertini model and the ENDF-VII.1 library*

Quantities	0.025 eV	1.0 MeV			14.2 MeV		
	water / 1‰ ^{nat}B	water / 1‰ ^{nat}B	water / 1‰ ^{nat}Gd	water	water / 1‰ ^{nat}B	water / 1‰ ^{nat}Gd	water
$\bar{y}_F$ (keV/μm)	112.0 ± 2.3	28.2 ± 0.9	28.2 ± 0.9	28.2 ± 0.8	16.6 ± 0.9	16.6 ± 1.4	16.5 ± 1.1
$\bar{y}_D$ (keV/μm)	143.0 ± 4.5	43.6 ± 2.0	43.7 ± 1.9	43.6 ± 1.8	98.1 ± 9.7	97.9 ± 15.0	97.5 ± 11.6
k_f (pGy·cm^2)	11.0 ± 0.1	28.0 ± 0.1	28.0 ± 0.1	28.0 ± 0.1	18.9 ± 0.1	18.9 ± 0.1	18.7 ± 0.1

CONCLUSIONS

In the present study, MCNP6.1 code was used for the estimation of microdosimetric quantities in a number of cases. The employed methodology allowed for the estimation of the dose components in neutron fields and the prediction of the radiological response. The presence of either boron or gadolinium as capturing agents in NCT modifies substantially the distribution of the lineal energy at microscopic level only in case of neutrons very low in energy. The use of our methodology initially tested by comparisons with pre-existing experimental data, may facilitate the better understanding of the findings of various *in vitro* NCT studies.

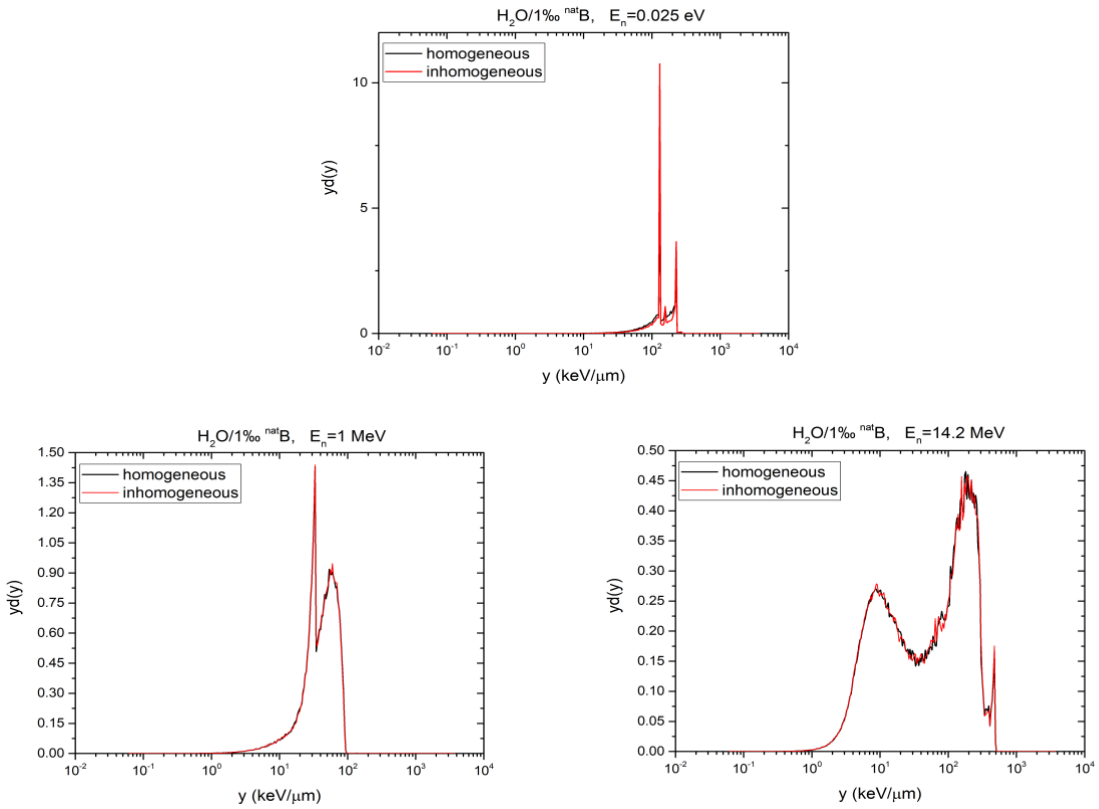


Figure 5. *Microdosimetric spectra in terms of yd(y) for water phantom with the target made of $H_2O/1‰\ ^{nat}B$ (inhomogeneous) and for a phantom with the target, both made of $H_2O/1‰\ ^{nat}B$ (homogeneous)*

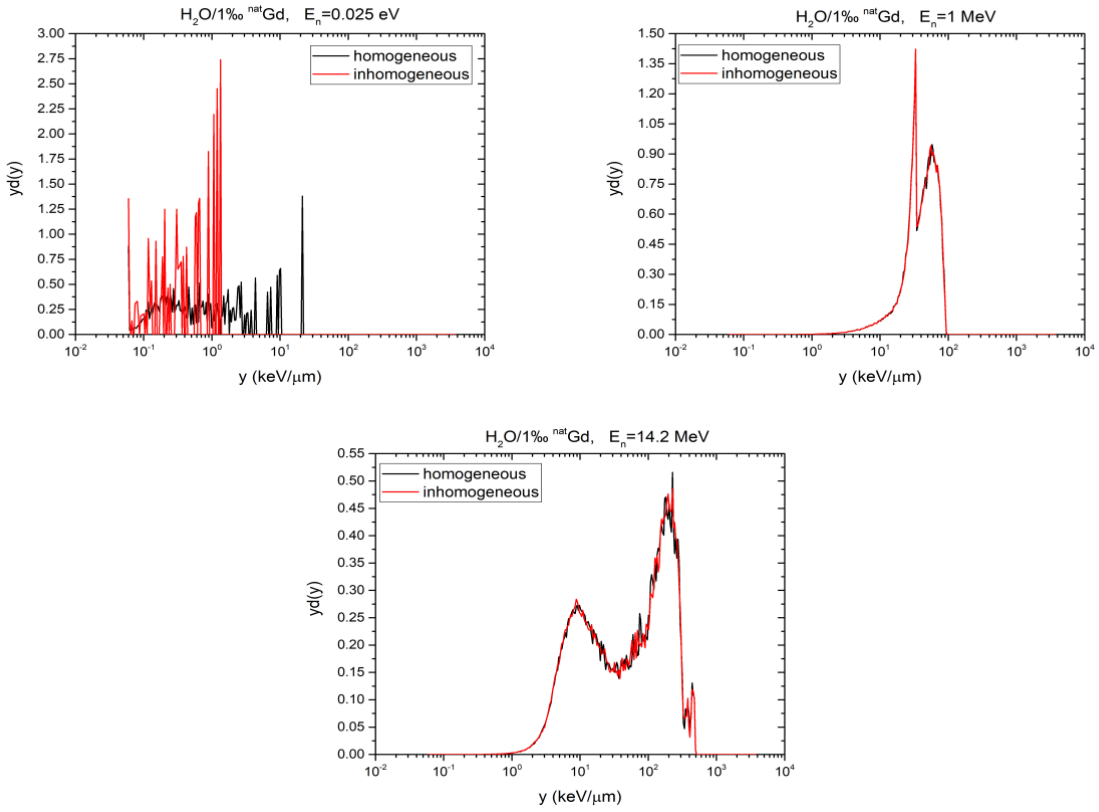


Figure 6. *Microdosimetric spectra in terms of yd(y) for water phantom with the target made of $H_2O/1‰\ ^{nat}Gd$ (inhomogeneous) and for a phantom with the target, both made of $H_2O/1‰\ ^{nat}Gd$ (homogeneous)*

References

[1] D. Gabel et al, In Progress in neutron capture therapy for cancer, 345-348 (1992), Plenum Press, New York
[2] International Commission on Radiation Units and Measurements, 'Microdosimetry', Bethesda, Maryland, Report 36 (1983)
[3] R. Antoni and L. Bourgois, Radiat. Meas. 128, 106189 (2019); doi: 10.1016/j.radmeas.2019.106189
[4] R.J. McConn et al, "Compendium of Material Composition Data for Radiation Transport Modeling", Pacific Northwest Nat. Lab., PIET-43741-TM-963, PNNL-15870, Rev. 1 (2011), Richland, Washington, DC
[5] International Commission on Radiation Units and Measurements, 'Tissue substitutes in radiation dosimetry and measurement', Bethesda, Maryland, Report 44 (1989)
[6] S. Georgiou, "Computational Study in Microdosimetry for Neutron Capture Therapy", M.Sc. thesis, School of Medicine, National and Kapodistrian University of Athens, Greece (2023)