THE RELATIONSHIP BETWEEN INACTIVATION RATE OF V79 CELLS AND PHYSICAL QUALITY PARAMETERS OF DEUTERON AND HELIUM PARTICLES AT LOWER DOSES

Abubaker Ali Yousif, Ismail Bin Bahari, Muhamad Samudi Yasir

Nuclear Science Programme, School of Applied Physics, Faculti Science dan Technology, Universiti Kebangsaan Malaysia, 43600 Bangi, Selangor Darul, Malaysia

e-mail: alghoul75@yahoo.com, Tel: +60172759427

ABSTRACT

To quantify the effectiveness of deuterons and helium particles at low doses, the inactivation rate in vitro for V79 cells has been extracted from radiobiological published data. The Physical parameters characteristics of these charged particles such as the linear energy transfer, the restricted linear energy transfer, the linear primary ionization and the mean free path are determined. The relationship between the inactivation rate and the physical parameters for deuterons and heluim-3 particles has been established in this research. This approach enables in getting the distinctive biological response in terms of varies physical quality parameters. The best statistical regression fittings are formulated for each correlation.

ABSTRAK

Untuk menentukan keberkesanan deuterons dan zarah helium pada dos yang rendah, kadar inactivation dalam vitro untuk sel-sel V79 telah tercabut dari radiobiological data diterbitkan. Ciri-ciri fizikal parameter ini zarah-zarah bercas seperti pemindahan tenaga linear, pemindahan tenaga linear yang terhad, ionisasi utama linear dan laluan percuma min ditentukan. Hubungan antara kadar inactivation dan parameter fizikal untuk deuterons dan zarah-zarah heluim-3 telah dibentuk dalam kajian ini. Pendekatan ini membolehkan mendapatkan yang tersendiri berbeza-beza jawapan biologi segi parameter fizikal kualiti. Kelengkapan statistik regresi yang terbaik akan digubal bagi setiap korelasi.

Keywords: low dose, inactivation rate, physical parameters, deuterons, helium-3

INTRODUCTION

Absorbed dose as a fundamental physical parameter is utilized to quantify the amount of energy deposited by charged particles in a critical volume in the matter. In radiation protection and radiation dosimetry, this parameter is playing an important role as a universal physical quantity. Meanwhile in other fields such as radiation biology, this distinctive quantity is applied to determine biological effects of ionizing radiations. The relationship between the absorbed dose and the biological effect gives a suitable method to indicate the relation between these two different parameters. Linear quadratic model is proposed to explain this relationship in terms of the linear and quadratic coefficients which represent the radiation rates of producing cell killing by primary single and double tracks charged particles. In this model the α component is given as a linear function of absorbed dose, while the β component is given as a quadratic function of the absorbed dose.

At lower doses, the inactivation rate α in this model is usually applied to determine the probability of occurrence of biological damage of ionizing radiation (Booz, & Feinendegen, 1988). Usually, this distinctive component is defined as the inactivation rate of cell irradiated by ionizing radiations. The lethal effect produced by single track per charged particle traversal the cell nucleus is given as the probability of energy deposition events by charged particle in terms of α (Alper, 1979). The average number of single hit leads to inactivation of exposed cell is usually expressed in terms of α.

Usually, alpha parameter depends on cell type and the charged particle that exposed to it, the physical quality parameters which characterize the charged particles are crucial in determining the magnitudes of effectiveness which related to the inactivation rate of irradiated cells. The relationship between the inactivation rate and these radiation physical quality parameters such as energy, linear energy transfer, linear primary ionization, mean free path and effective charge is not completely addressed for all charged particles especially deuterons and heliums particles, which carry more weight in this research.

Identification of distinctive relationships between the inactivation rate α and the physical quality parameters will enable in understanding the underling biophysical mechanism of radiation action of low doses.

The relationship between α and linear energy transfer LET is not well established. The optimum value of LET usually occurs at 100 keV/ m (Hall, 1994) but this typical value is not peculiar for all radiation types. This statement means that the optimum value of LET for any quality of charged particle and for any biological end-point is independent of radiation quality and the type of lethal damage of the exposed cells. As a part of this work, the validity of this assumption will be tested statistically in terms of the best correlation of all characterized physical quality parameters presented graphically against the inactivation rate α. The parameters involve are the particle energy E, the linear energy transfer LET, the linear primary ionization I, the mean free path λ and the effective charge Z_{eff}. Multiple regressions fitting of the best correlations will be drawn out and the best correlations between the inactivation rate α and the physical quality parameters are modelled.

MATERIALS AND METHOD

The dependence of the inactivation rate α of V79 cells irradiated *in vitro* by deuterons and helium particles were characterized based on the physical quality parameters. The analysis was carried using secondary data published by various researchers (Belli et al. 1994; Cherubini et al. 1994; Wouters, 1996). The inactivation rate is mainly extracted from all sigmoid survival curves which are matched the following model (Horowitz, y. 2006):

$$S(D) = e^{-\alpha D - \beta D^2} \qquad (1)$$

where D is absorbed dose given in Gy, α represents the inactivation rate and β represents the quadratic rate of inactivation, S(D) gives the ratio of survival fraction of V79 cells after irradiation.

$$\alpha = \frac{1}{D_0} \qquad (2)$$

D_0 corresponds to the average dose required to score an average one ionization event per cell. The particle energy and LET are taken directly from each original experiment or interpolated utilizing the tabulated values provided by (Watt, D. E. 1993) which determined using the following equations:

The linear primary ionization is given as follows:

$$I(nm^{-1}) = 0.01536 \times \frac{Z}{A} \times \frac{Z_{eff}^2}{\beta^2} \times \left(\frac{1}{IP} - \frac{1}{T_{max}} \right) \tag{3}$$

The radiation mean free path is determined as follows:

$$\lambda(nm) = \frac{1}{I} \tag{4}$$

where the maximum delta-ray energy T_{max}, and the ionization potential IP of water are in eV.

RESULTS AND DISSCUSSION

The relation between α and energy E of deuterons is shown in Figure 1. There is a non-linear relationship between these physical and biological parameters. At the beginning, the inactivation rate α of V79 decreases slightly with increasing deuterons energy reaches the minimum at 10^3 keV of deuterons energy, later the inactivation rate levelled off as the energy increases, thereafter the inactivation rate declines sharply as the energy of deuterons increases.

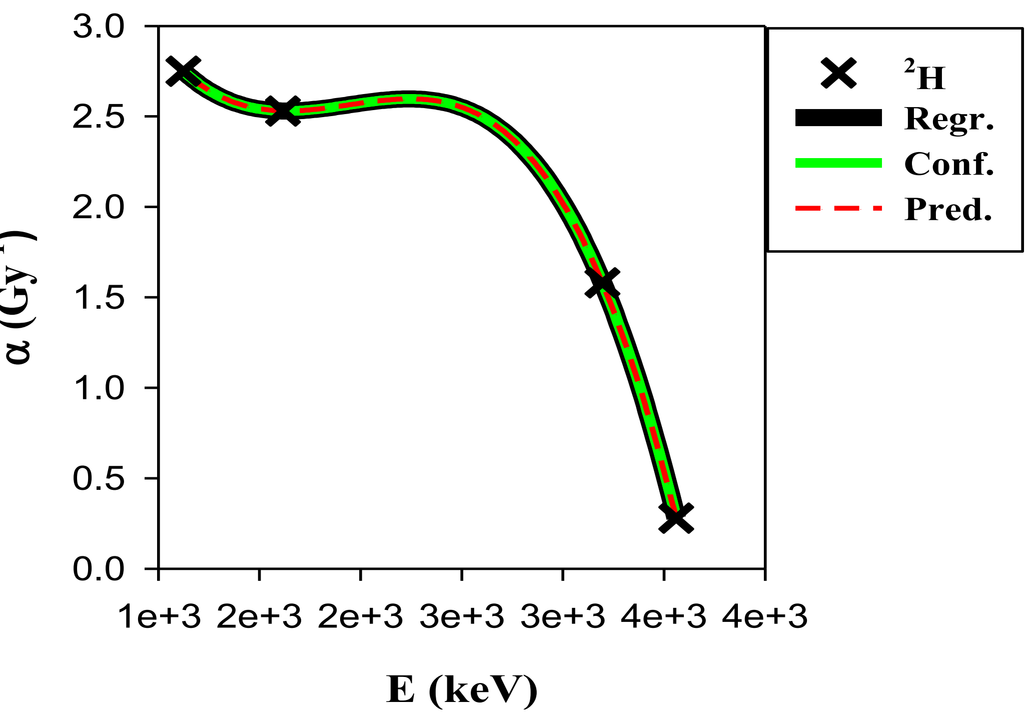

Figure 1. The relationship between inactivation rate α and energy E for deuterons. The legends provided in the small box indicate particle type, regression line, confident interval, and predicted relation.

The best regression model of this relation is given as the following:

$$\alpha(E) = C_1 E + C_2 E^2 + C_3 E^3 + C_4, \quad (5)$$

where $C_1 = -6.55 \times 10^{-3}$, $C_2 = 3.47 \times 10^{-6}$, $C_3 = -5.96 \times 10^{-10}$, $C_4 = 6.58$ and $r^2 = 1$.

Figure 2 indicates the relationship between α and energy E for helium particles. It is noted that there is an inverse non-linear relation between these parameters. The inactivation rate decreased with the energy of helium particles.

This relation can be demonstrated mathematically as follow:

$$\alpha(E) = C_{20} E + C_{21} E^2 + C_{22} E^3 + C_{23}, \quad (6)$$

where $C_{20} = -1.59 \times 10^{-3}$, $C_{21} = 1.68 \times 10^{-7}$, $C_{22} = -5.97 \times 10^{-12}$, $C_{23} = 5.86$ and $r^2 = 1$.

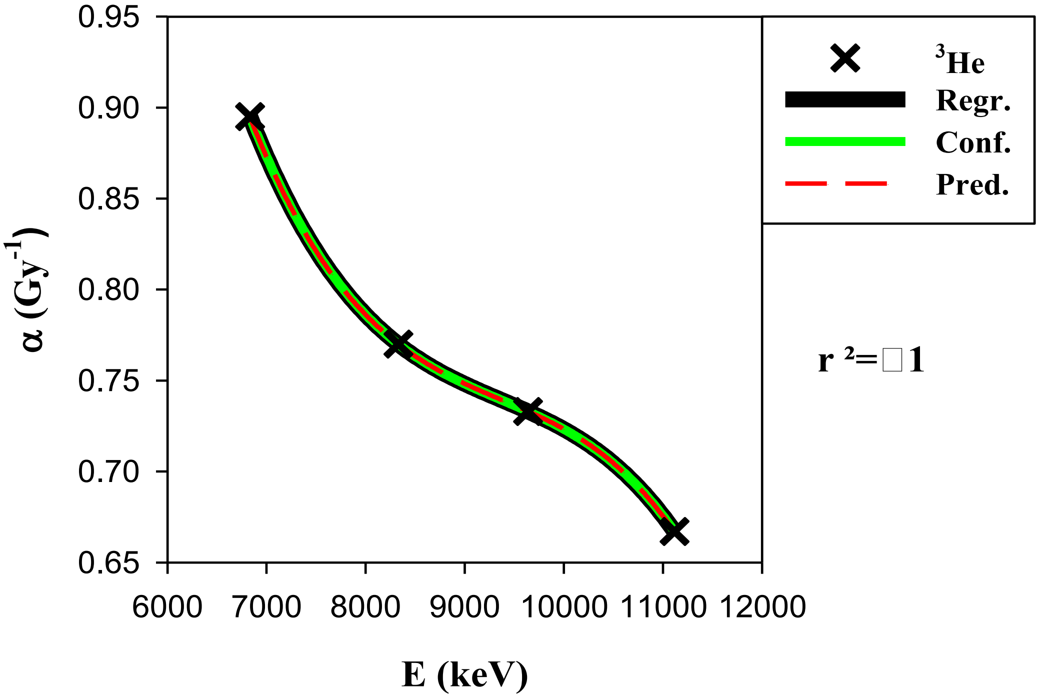

Figure 2. The relationship between inactivation rate α and energy for helium particles. The legends provided in the small box indicate particle type, regression line, confident interval, and predicted relation.

The relationship between Linear Energy Transfer LET for deuterons and inactivation rate is plotted in Figure 3. The inactivation rate increases gradually with LET and reached the maximum value of inactivation rate at 41 keV/ m. The predicted movement of LET against α should be decreased. This well half bell-shape response is not established before for this particle. This distinctive response can be presented mathematically as follow:

$$\alpha(LET) = C_5 LET + C_6 LET^2 + C_7 LET^3 + C_8, \quad (7)$$

where $C_5 = 0.16$, $C_6 = -105 \times 10^{-3}$, $C_7 = -1.55 \times 10^{-5}$, $C_8 = -0.86$ and $r^2 = 1$.

Figure 4 indicates the relationship between the inactivation rate of V79 cells and the Linear Energy Transfer LET of helium particles. As similar of Figure 3, the inactivation rate of V79 cells increases linearly with increasing of energy deposition rate LET up to the maximum at 59 keV/ m. This shape of correlation can be modelled as follows:

$$\alpha(LET) = C_{24}LET + C_{25}LET^2 + C_{26}, \qquad (8)$$

where $C_{24} = 8.41\times10^{-3}$, $C_{25} = 7.52\times10^{-5}$, $C_{26} = 0.14$ and $r^2 = 1$.

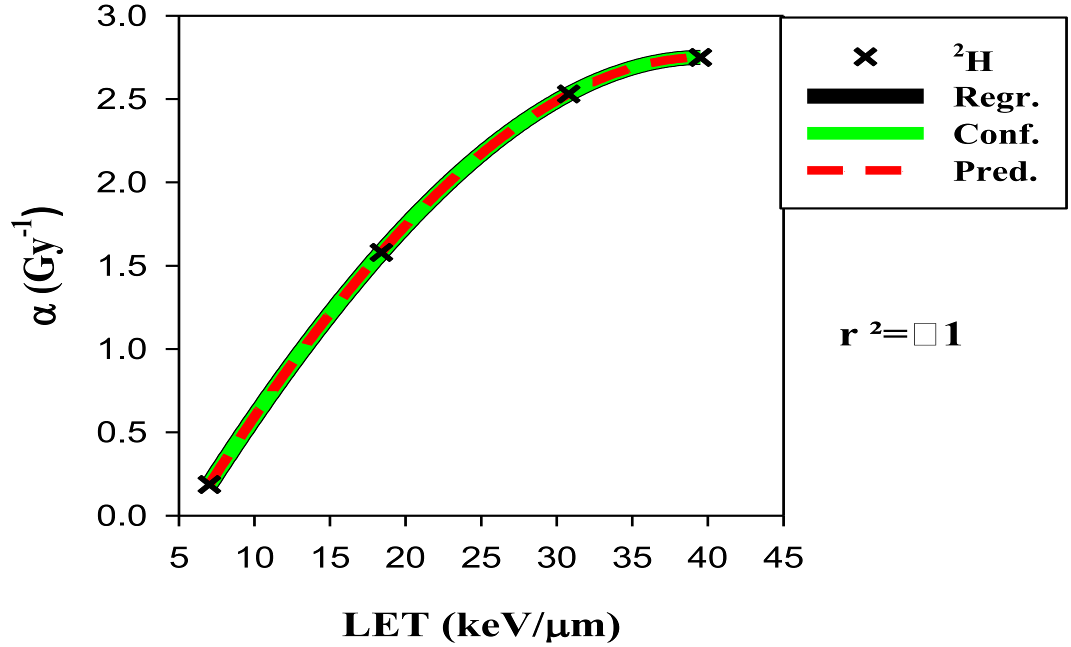

Figure 3. The relationship between inactivation rate α and linear energy transfer for deuterons. The legends provided in the small box indicate particle type, regression line, confident interval, and predicted relation.

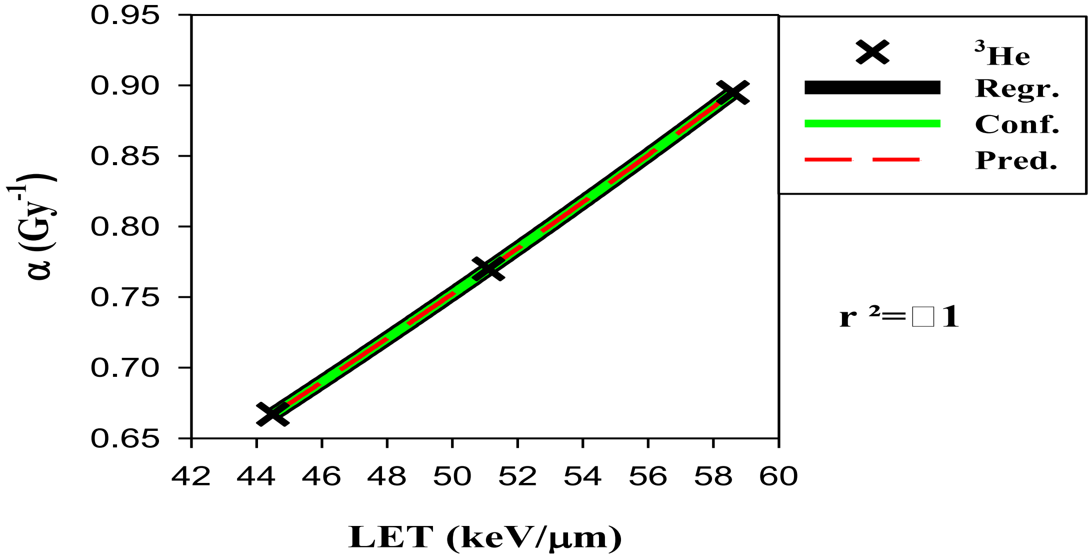

Figure 4. The relationship between inactivation rate α and linear energy transfer for helium particles. The legends provided in the small box indicate particle type, regression line, confident interval, and predicted relation.

The relation between inactivation rate and restricted Linear Energy Transfer for deuterons and helium-3 particles are represented in Figure 5 and Figure 6 respectively.

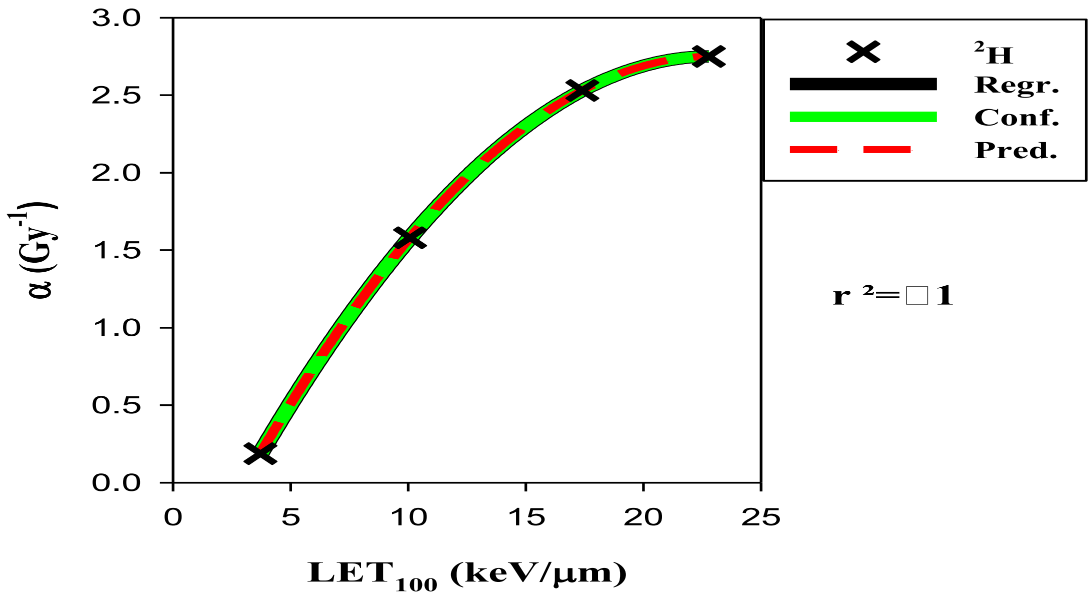

Figure 5. The relationship between inactivation rate α and restricted linear energy transfer for deuterons. The legends provided in the small box indicate particle type, regression line, confident interval, and predicted relation.

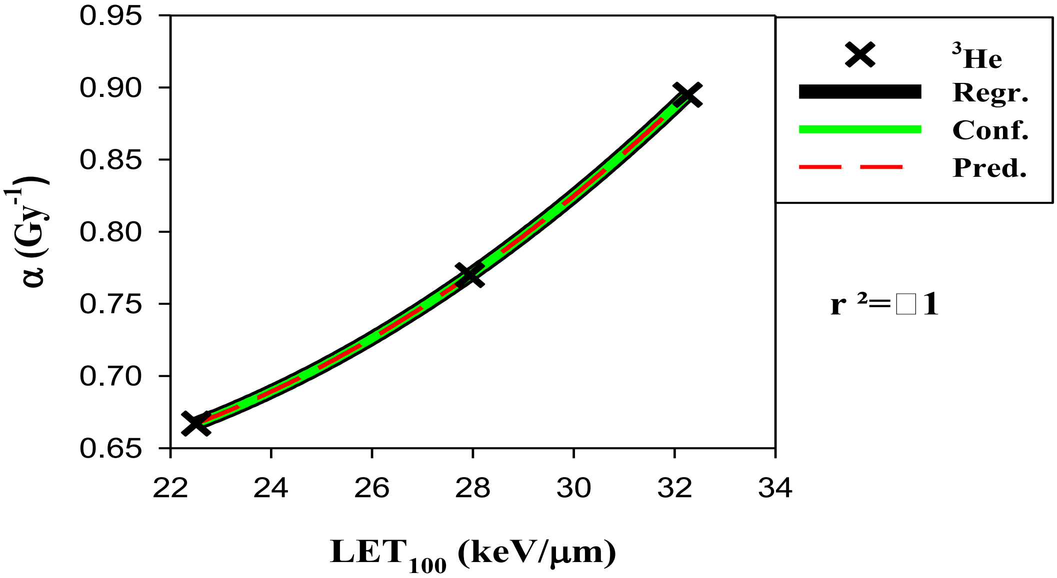

Figure 6. The relationship between inactivation rate α and restricted linear energy transfer for helium particles. The legends provided in the small box indicate particle type, regression line, confident interval, and predicted relation.

For both particles, the inactivation rate increases dramatically as the restricted ionization density increases. The maximum inactivation rates of deuterons and helium-3 particles occur at 23.14 keV/ m and 32.26 keV/ m respectively. These responses are also described mathematically as follow:

For deuterons, the model is given as follows:

$$\alpha(LET_{100}) = C_9 LET_{100} + C_{10} LET_{100}^{\;2} + C_{11} LET_{100}^{\;3} + C_{12}, \qquad (9)$$

where $C_9 = 0.30$, $C_{10} = -5.68\times10^{-3}$, $C_{11} = -2.63\times10^{-5}$, $C_{12} = -0.85$ and $r^2 = 1$.

For helium-3, the model is given as follows:

$$\alpha(LET_{100}) = C_{27}LET_{100} + C_{28}LET_{100}{}^{2} + C_{29}, \tag{10}$$

where $C_{27} = -0.03$, $C_{28} = 1.02\times10^{-3}$, $C_{29} = 0.88$ and $r^2 = 1$.

Figure 7 shows the relation between the inactivation rate α and the linear primary ionization I for deuterons. As the linear ionization increases, the inactivation rate increases as well. The maximum value of linear ionization occurs at 0.24 nm^{-1}.

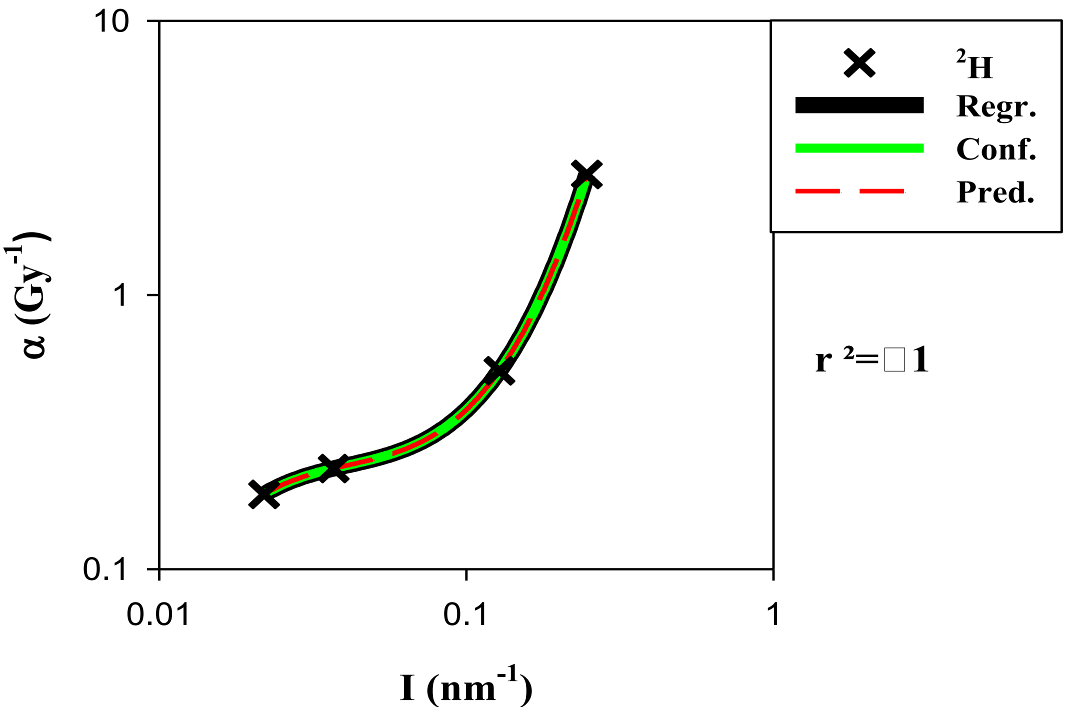

Figure 7. The relationship between inactivation rate α and linear primary ionization for deuterons. The legends provided in the small box indicate particle type, regression line, confident interval, and predicted relation.

This relationship can be described mathematically as follows:

$$\alpha(I) = C_{13}I + C_{14}I^2 + C_{15}I^3 + C_{16}, \tag{11}$$

where $C_{13} = 10.83$, $C_{14} = 7.64$, $C_{15} = 1.84$, $C_{16} = 4.61$ and $r^2 = 1$.

Relationship between inactivation rate α and linear primary ionization I for helium-3 particles is shown in Figure 8. The inactivation rate rises gradually with increasing linear ionization of helium-3 particles. The maximum value of inactivation rate comes out at 0.9 Gy^{-1} when linear ionization is equal to 0.25 nm^{-1}. The mechanism of inactivation of V79 can be interpreted obviously in terms of this distinctive parameter. By comparing the responses in Figure 7 with Figure 8, it can be noted that the deuterons are more capable in producing the inactivation of V79 cells than helium-3 particles. In contrast, the helium-3 particles yield the highest inactivation at lower energy deposition events.

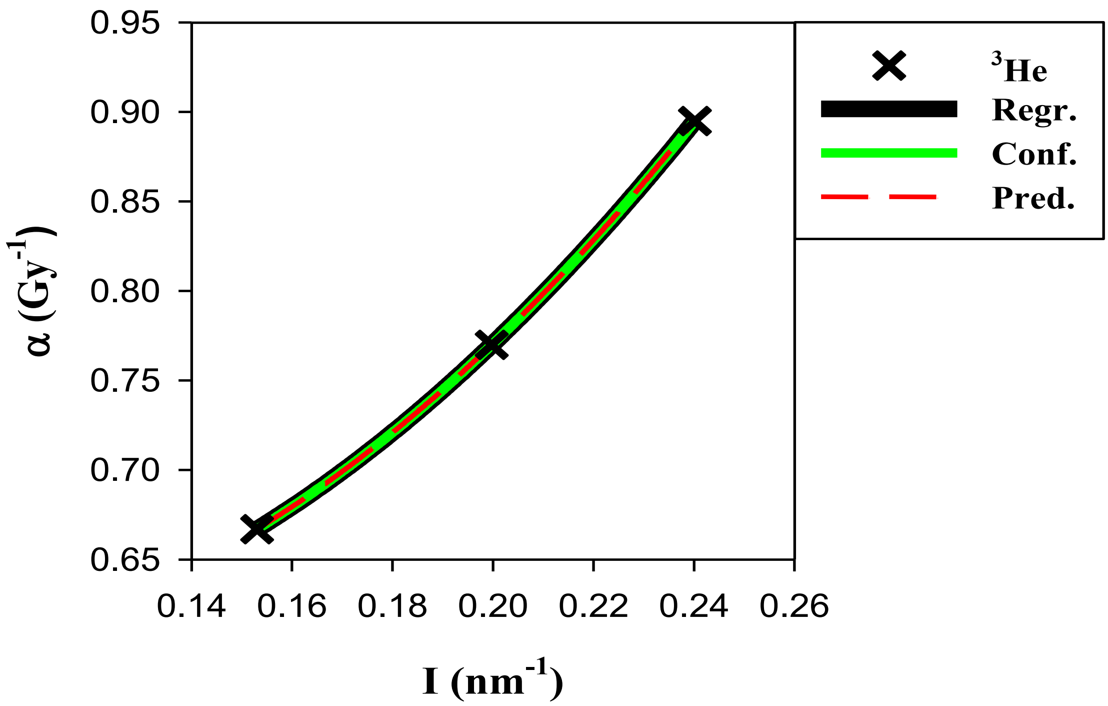

Figure 8. The relationship between inactivation rate α and linear primary ionization for helium particles. The legends provided in the small box indicate particle type, regression line, confident interval, and predicted relation.

The best fitting model which describes this relationship is given as follows:

$$\alpha(I) = C_{30}I + C_{31}I^2 + C_{32}, \tag{12}$$

where $C_{30} = -1.40$, $C_{31} = 10.21$, $C_{32} = 0.64$ and $r^2 = 1$.

Figure 9 illustrates the relationship between the inactivation rate of V79 cells and the mean free path λ for deuterons. The inactivation rate starts decrease sharply as the mean free path increases holding the minimum, later the inactivation rate increases as the mean free path increases. The relation can be fitted accurately applying the following model:

$$\alpha(\lambda) = C_{17}\lambda + C_{18}\lambda^2 + C_{19}, \tag{13}$$

where $C_{17} = -0.19$, $C_{18} = 2.57$, $C_{19} = 3.53$ and $r^2 = 1$.

Finally, the relationship between inactivation rate of V79 cells and the mean free path for heluim-3 particles is represented in Figure 10. At the beginning, the inactivation rate decrease rapidly as the mean free path increases, subsequently the inactivation slightly decreases as the mean free path increases, beyond the inactivation rate decreases dramatically as the mean free path of helium-3 particles rises. Mathematically this relation is modelled according to the following expression:

$$\alpha(\lambda) = C_{30}\lambda + C_{31}\lambda^2 + C_{32}\lambda^3 + C_{33}, \tag{14}$$

where $C_{30} = -3.54$, $C_{31} = 0.63$, $C_{32} = -0.04$, $C_{33} = 7.43$ and $r^2 = 1$.

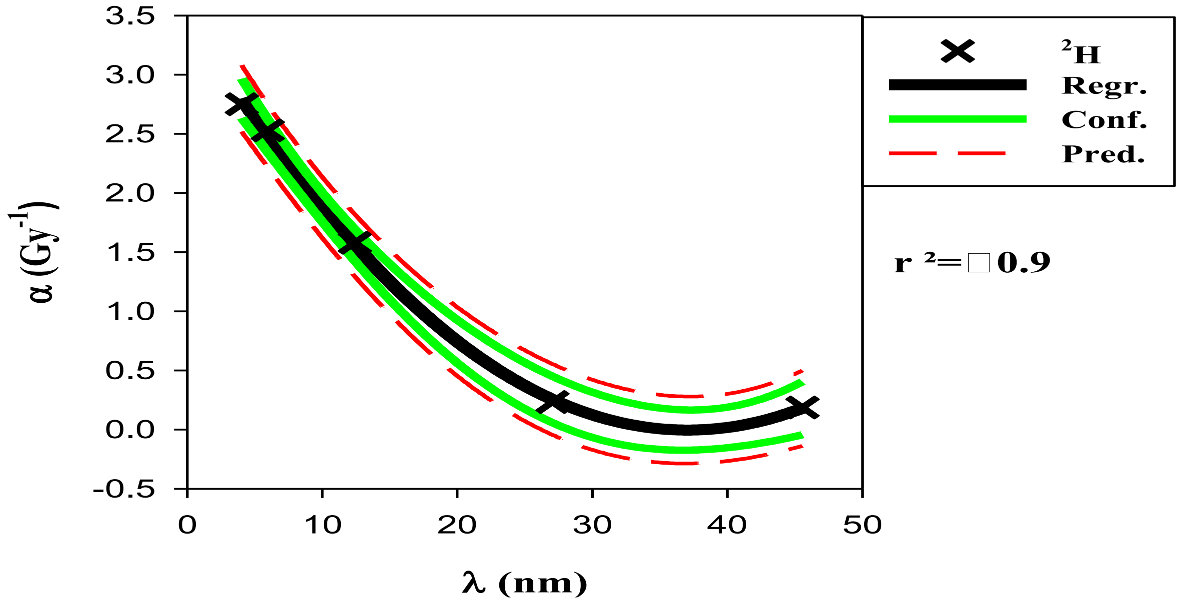

Figure 9. The relationship between inactivation rate α and mean free path for deuterons. The legends provided in the small box indicate particle type, regression line, confident interval, and predicted relation.

Representing inactivation rate of V79 cells in terms of the physical quality parameters which characterize both deuterons and heluim-3 particles allows extensive investigation of the involved mechanism of inactivation effect yielded by these charged particles at low doses where the radiation effects at this region is not absolutely predictable in terms of the convention quantity the absorbed dose, that is often used as a universal physical measure of biological effects of ionizing radiation at higher doses.

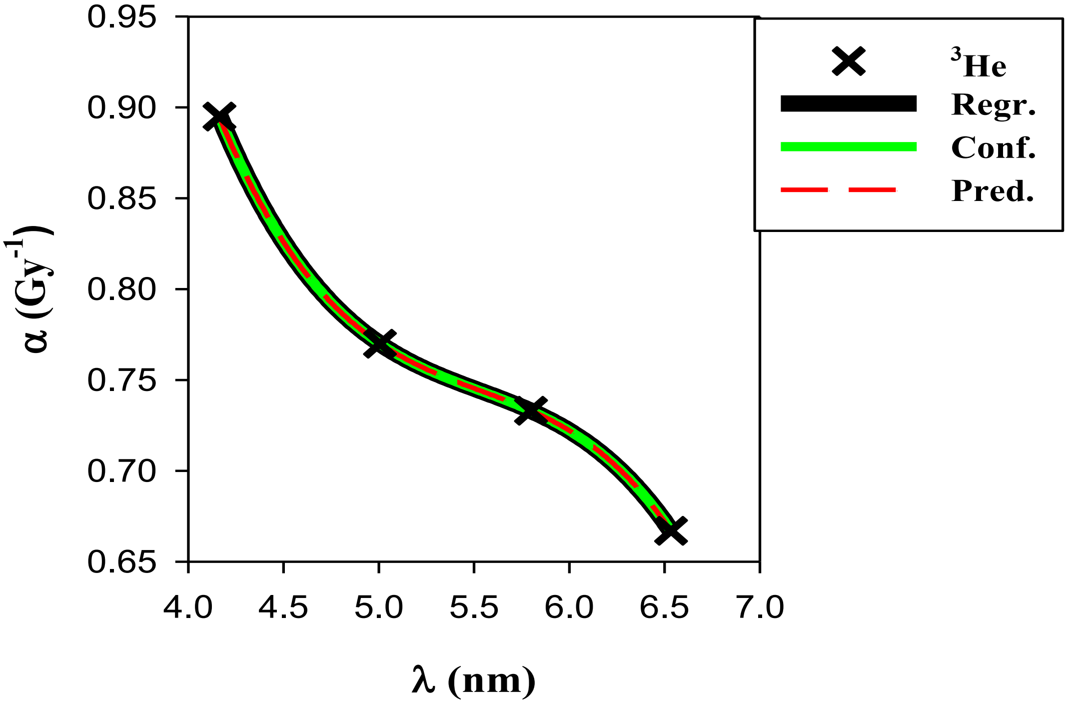

Figure 10. The relationship between inactivation rate α and mean free path for helium particles. The legends provided in the small box indicate particle type, regression line, confident interval, and predicted relation

CONCLUSION

It is very important to identify the physical parameters which are governed in the mechanism of energy deposition events in the medium. The absorbed dose as a universal physical parameter in determining the inactivation of cells is not reliable especially at lower doses. The investigation on the variation of the inactivation rate with the proposed physical quality parameters has the potential to reveal the specific information on the cellular and sub-cellular structural details of radiosensitive sites within the biological targets, the nature of the damage mechanism involved and the suitability of the quality parameters for quantifying the occurred biological effects (end-points).

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