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Physical Parameters that Influence the Effectiveness of Ionizing Radiation at Low Doses

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Abstract: Relative biological effectiveness (RBE) for the inactivation of V79 cells were determined using the initial slopes of survival curves (published in literature), the physical quality parameters are interpolated utilizing the standard values relevant to charged particles such as protons and heliums. The issues of utilizing physical parameters as quantifier of radiation effects that influence the effectiveness have been investigated. The results show that the effectiveness may represent in terms of other physical parameters rather than linear energy transfer (LET). Meanwhile, mean free path for linear primary ionization (I) is expressed the generalized specifier physical quality parameter to quantify ionizing radiation effects at lower doses. Therefore, plot of mean free path as a function of RBE has been made to identify the physical features of this parameter as an alternative physical quality for LET.

Key words: Relative biological effectiveness; physical quality parameters; cell inactivation

INTRODUCTION

In radiation protection, Relative Biological Effectiveness (RBE) is defined as the ratio of absorbed doses of a reference radiation to the absorbed dose of a test radiation, which produces the same biological end-point. RBE is also given as the ratio of initial slope of survival curve of tested radiation to the initial slope of the reference curve of 250 kV x-rays or ^{60}Co gamma rays, at low doses region L. D. Kadri (1999).

The availability of vast information has shown that RBE is also dependent on radiation dose, number of fractionations, dose rates and biological end-points as well as radiation quality. The ability to correlate RBE with the above-mentioned dependent variables has made RBE a biological quality parameter to relatively quantify ionizing radiation effectiveness for any radiation quality.

The relationship between RBE and Linear Energy Transfer (LET) is well documented. The bell-shaped curve for such relationship suggests that there is an optimum RBE for an LET value of around 100keVμm^{-1} Hall (1994). This optimum LET is independent on the surviving fraction of the mammalian cells. However, such bell-shaped response is not universal for all biological end-points. Thus although LET is considered as an essential physical parameter of any radiation type, its application in explaining radiosensitivity (i.e RBE) is limited Watt and L. A. Kadiri (1990).

Besides LET there is other radiation quality or physical parameters that influence RBE, and for charged particles these include the charge of the particles and its velocity. However, not much has been shown or discussed on such relationships, as well as the effectiveness of using these radiation quality parameters to explain cell radiosensitivity.

This paper reviews several published data on the inactivation of V79 mammalian cells by different quality of radiations to better elucidate the relationships between RBE and radiation quality parameters. Five radiation quality parameters, i.e. linear primary ionization (I), radiation mean free path (λ), energy of radiation (E), and Effective charge (Z_{eff}) were studied.

MATERIALS AND METHOD

This study is based on secondary data from published materials (Barendsen and Walter, 1963; Belli, Cherubini and Finotto, 1989; Cherubini and Goodhead, 1994; Folkard, Prise and Vojnovic, 1989). RBE is mathematically defined using equation (1).

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$$RBE = \frac{D_{x-ray}}{D_{ion}} \quad \text{yielding the same end-point} \tag{1}$$

Where $D_{X\text{-}ray}$ and D_{ion} are the absorbed doses of reference and test radiation respectively, yielding the same level of biological end-point.

However, for the purpose of this paper RBE is calculated using equation (2). Equation (2) is based on the initial slopes (a) of V79 radiation induced survival curves. In this case RBE is focused on cell inactivation at low dose (Belli *et al,* 1998; Nikjoo and Lindborg, 2010).

$$RBE = \frac{\alpha_I}{\alpha_X} \tag{2}$$

Where a_I and a_X are the initial slopes of the V79 survival curves produced by test radiation and reference x-ray respectively.

Effective Charge (Z_{eff}) of helium ions is calculated using equation (3) while equation (4) is used to calculate for protons, deuterons, tritiums.

$$Z_{eff} = \left(\frac{E}{84 \times A}\right)^{0.9} \tag{3}$$

$$Z_{eff} = \left(\frac{E}{84 \times A}\right)^{1.2} \tag{4}$$

where E and A are the ion energy and the mass number of charged particles respectively.
I, or linear primary ionization represents the number of ionization events per unit track length of charged particle traversal in the medium.

Radiation mean free path, (λ) represents the spacing between the lethal events of ionizations occurred from traversing of charged particle through the medium, It would be expected that the most effective l would represents the gap between the double strand of a DNA.

The physical parameters for every ion studied in this paper are taken from the same experiments. Linear primary ionization and mean free path are interpolated using the standard values of physical parameters Watt (1993). The bio-physical relationships between RBE and the different physical radiation parameters will be assessed on the types of correlations developed between the selected parameters.

RESULTS AND DISSCUSSION

The relationship between Linear Energy Transfer (LET) and RBE is well documented. Fig. 1 and 2 confirm the bell-shaped response visible for ^{4}He and ^{1}H particles. The maximum RBE value for ^{4}He and ^{1}H particles occur at LET≃ 26 keV mm^{-1} and LET≃ 6.04 keV mm^{-1} respectively. It was interesting to note that the RBE peak for proton is located at a different LET value. Result from ^{1}H particles is in accordance with the conclusion deduced by Belli *et al,* (1998) in their study of the relationship of RBE-LET for cell inactivation and mutation induced by low energy protons in V79 cells Hall (2000). While RBE peak for ^{4}He particles is located at different value which should be at 100 keV/mm this anomalous result is unexpected therefore more investigation is necessity to justify this outcome. The relationship in Fig. 1 is fitted using the following mathematical model

$RBE(L) = C_1L + C_2L^2 + C_3L^3 + C_4L^4 + C_5L^5 + C_6L^6 + C_7$ where $C_1 = 0.77$, $C_2 = -.15$, $C_3 = 0.01$ $C_4 = -5.63\times10^{-4}$, $C_5 = 1.22\times10^{-5}$, $C_6 = -1.03\times10^{-7}$, $C_7 = -0.64$ with R^2= 99%, while Fig. 2 is well fitted by the model

$RBE(L) = C_8L + C_9L^2 + C_{10}L^3 + C_{11}L^4 + C_{12}$ where $C_8 = 0{,}01$, $C_9 = -3.07\times10^{-4}$, $C_{10} = 2.31\times10^{-6}$, $C_{11} = -5.57\times10^{-9}$, $C_{12} = 0.09$ with R^2= 0.95.

An established relationship between RBE-LET is further tested by looking at the influence and or relationships of other physical parameters of radiation on LET. LET is approximately proportional to the Q^2/v, where Q is the charge of the particle and v is its velocity (Hall, 2000). The influence of effective charge (Z_{eff}) of helium and protons on LET is shown in Fig. 3. Regression of all data showed an inverse linear relationship of $Z_{eff}(L) = C_{13}L + C_{14}$ where $C_{13} = -0.64,\ C_{14} = 2.5$ with $R^2 = 1$. The LET of protons decreases with increases in ion effective charge within the range energies between 24.11keV and 23.56´10^2 keV. A clear inverse relationship suggests that as the effective charge of the particle increases its LET value decreases.

Fig. 4 shows an inverse linear relationship between LET and ion energy (E) for helium and proton ions. LET, which represents the ionization density of ionizing radiation (^{4}He and ^{1}H) decreases with increase in energy. For ^{4}He ion, an LET of 100 keV m^{-1} is represented by ion energy of 4.04 ´ 10^3 keV. The responses are represented mathematically as $LET(E) = C_{15}E + C_{16}$ where $C_{15} = -0.77$, $C_{16} = 3.74$ with $R^2 = 0.50$.

This relationship is similar to those shown between LET and effective charge of particles (Fig. 3). As expected, the relationship between the effective charge Z_{eff} of ion and its energy, E, is linear, i.e. the effective charge for (^{1}H) increases with increase in particle energy (Fig. 5). The equation of regression is $Z_{eff}(E) = C_{17}E + C_{18}$ where $C_{17} = 1.2$, $C_{18} = -2.02$ with ($R^2 = 1$). However, only proton shows a clear linear relationship. Plots between RBE and Z_{eff} for ^{1}H and ^{4}He particles showed similar bell-shaped relationships as that shown between RBE and LET. This was expected because an inverse linear relationship existed between LET and Z_{eff}. Due to such relationship two different RBE peaks were observed from ^{1}H and ^{4}He respectively (Fig. 6 and 7). Using RBE peak values shown in Fig. 6 and 7, the Z_{eff} values extrapolated for ^{1}H and ^{4}He particles were 5.66 and 24.48. These values correspond to LET values of 6.04 keV mm^{-1} and 26 keV mm^{-1} (Fig. 4). The response curve in Fig. 6 is corresponded of the mathematical model:

$RBE(Z_{eff}) = C_{19}Z_{eff} + C_{20}Z_{eff}^2 + C_{21}Z_{eff}^3 + C_{22}Z_{eff}^4 + C_{23}Z_{eff}^5 + C_{24}Z_{eff}^6 + C_{25}$ where $C_{19} = 4.14$, $C_{20} = -0.87$, $C_{21} = 0.09$, $C_{22} = -4.91\times10^{-3}$, $C_{23} = 1.36\times10^{-4}$, $C_{24} = -1.50\times10^{-6}$, $C_{25} = -6.76$ with $R^2 = 0.99$, meanwhile the data in Fig. 7 is fitted using the mathematical model:

$RBE(Z_{eff}) = C_{26}Z_{eff} + C_{27}Z_{eff}^2 + C_{28}Z_{eff}^3 + C_{29}Z_{eff}^4 + C_{30}Z_{eff}^5 + C_{31}$ where $C_{26} = 0.08$, $C_{27} = -2.96\times10^{-3}$ $C_{28} = 4.77\times10^{-5}$, $C_{29} = -3.48\times10^{-7}$, $C_{30} = 9.55\times10^{-10}$, $C_{31} = -0.44$, with $R^2 = 0.82$.

Relationships between RBE and particles energy of ^{4}He and ^{1}H are shown in Fig. 8 and 9. The RBE peaks for these two ions are 36.32 ´ 10^3 and 74 ´ 10^2 keV respectively. Applying these values to the regression line in Fig. 4 gave LET values of 2.03 ´ 10^1 keV mm^{-1} and 6.04 keV mm^{-1}. The best model fits the data in Fig. 8 is given as:

$RBE(E) = C_{32}E + C_{33}E^2 + C_{34}E^3 + C_{35}$ where $C_{32} = -1.74\times10^{-4}$, $C_{33} = 8.14\times10^{-8}$, $C_{34} = -6.85\times10^{-12}$ $C_{35} = 0.30$ with $R^2 = 0.94$, while the data in Fig. 9 fitted as:

$RBE(E) = C_{36}E + C_{37}E^2 + C_{38}E^3 + C_{39}E^4 + C_{40}E^5 + C_{41}E^6 + C_{42}E^7 + C_{43}E^8 + C_{44}$ where $C_{36} = -7.84\times10^{-5}$, $C_{37} = 1.40\times10^{-8}$, $C_{38} = -2.37\times10^{-12}$, $C_{39} = 3.63\times10^{-16}$, $C_{40} = -2.90\times10^{-20}$, $C_{41} = 1.15\times10^{-24}$, $C_{42} = -2.18\times10^{-29}$, $C_{43} = -1.58\times10^{-34}$, $C_{44} = 0.29$, with $R^2 = 0.76$.

Fig. 10 and 11 show the relationship between RBE and linear primary ionization (I) for helium and protons used to irradiate V79 cells *in vitro*. The RBE of ions increases linearly with primary ionization (I) to reach the minimum at 0.04 nm^{-1} for protons and 0.14 nm^{-1} for helium ions, after that the effectiveness decreases dramatically with increases in linear primary ionization of both particles. This value represents the number of energy deposition events (ionizations) that is required to break the double strands (DSBs) of DNA (Deoxyribose Nucleic Acid). Above this value, the effectiveness of DSBs is converse. The overall trend is showing parabolic response. Mathematically, the data in Fig. 10 is fitted by the following model:

$RBE(I) = C_{45}I + C_{46}I^2 + C_{47}I^3 + C_{48}I^4 + C_{49}$, $C_{45} = 8.12$, $C_{46} = -209.33$, $C_{47} = 14.64\times10^2$, $C_{48} = -31.14\times10^{-2}$, $C_{49} = 0.30$, with R^2 = 98%. However, the data in Fig. 11 is fitted accurately by the mathematical model which gives as:

$RBE(I) = C_{50}I + C_{51}I^2 + C_{52}I^3 + C_{53}I^4 + C_{54}I^5 + C_{55}I^6 + C_{56}$, $C_{50} = 2.42$, $C_{51} = -15.14$, $C_{52} = 37.70$, $C_{53} = -45.39$, $C_{54} = 26.48$, $C_{55} = -6$, $C_{56} = 0.05$, with R^2 = 0.82.

The relationship between RBE and mean free path l for linear primary ionizations, which represents the relation between the effectiveness of charged particles and the spacing of lethal events of ionizations occurred from traversing of charged particle through the medium, is plotted in Fig. 12 and 13. There is a good correlation between RBE and l in this range of charged particle energies. The maximum effectiveness of inactivation occurs by ^1H and ^4He particles at mean free path 5.1 nm and 23.6 nm respectively. After these values the inactivation of effectiveness dramatically decreases versus increasing in mean free paths for both particles. Fig. 12 has been fitted mathematically using the subsequent model:

$RBE(\lambda) = C_{57}\lambda + C_{58}\lambda^2 + C_{59}\lambda^3 + C_{60}\lambda^4 + C_{61}\lambda^5 + C_{62}$, $C_{57} = 0.15$, $C_{58} = -0.02$, $C_{59} = 1.2\times10^{-3}$ $C_{60} = -2.81\times10^{-5}$, $C_{61} = 2.38\times10^{-7}$, $C_{62} = 0.31$, with R^2 = 0.89. For helium ions, the RBE against mean free path is modeled utilizing the mathematical form:

$RBE(\lambda) = C_{63}\lambda + C_{64}\lambda^2 + C_{65}\lambda^3 + C_{66}\lambda^4 + C_{67}\lambda^5 + C_{68}$ where $C_{63} = -0.02$, $C_{64} = 4.23\times10^{-4}$, $C_{65} = -3.66\times10^{-6}$, $C_{66} = 1.57\times10^{-8}$, $C_{67} = 2.63\times10^{-11}$, $C_{68} = 0.79$, with R^2 = 0.71.

Expressing the biological effectiveness in terms of these parameters provides new approach to understanding the involving mechanism of radiation action in mammal cells at lower doses. In addition, the distinctive correlation between effectiveness and physical parameters for particular effect allows direct interpretation of cell inactivation mechanism.

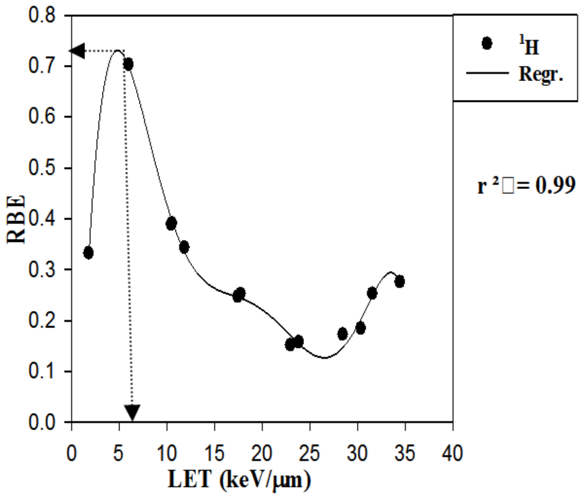

Fig. 1: Relationship between relative biological effectiveness (RBE) and linear energy transfer (LET) for protons used to irradiate V79 cells *in vitro*.

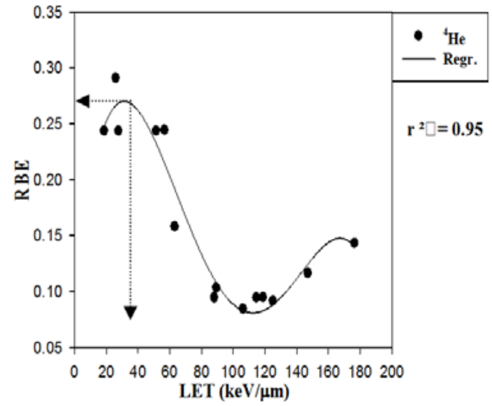

Fig. 2: Relationship between relative biological effectiveness (RBE) and linear energy transfer (LET) for helium used to irradiate V79 cells *in vitro*.

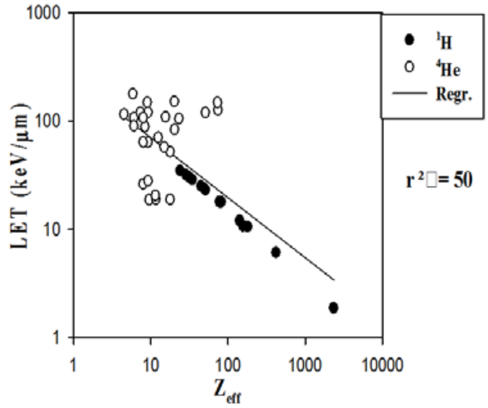

Fig. 3: Relationship between linear energy transfer (LET) and effective charge (Z_{eff}) for heliums and protons used to irradiate V79 cells *in vitro*. The line indicates the linear regression of the data.

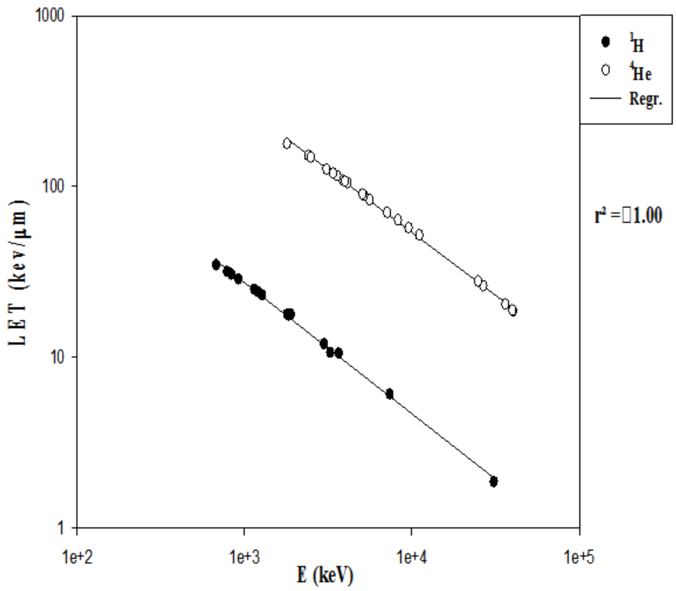

Fig. 4: Relationships between LET and ion energy (E) for helium and protons used to irradiateV79 cells *in vitro.*

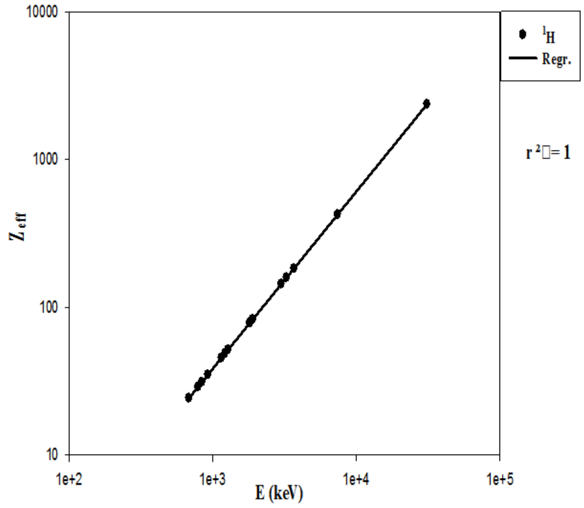

Fig. 5: Relationship between effective charge (Z_{eff}) and energy (E) for protons used to irradiate V79 cells *in vitro*. The lines indicate the linear regression of the data.

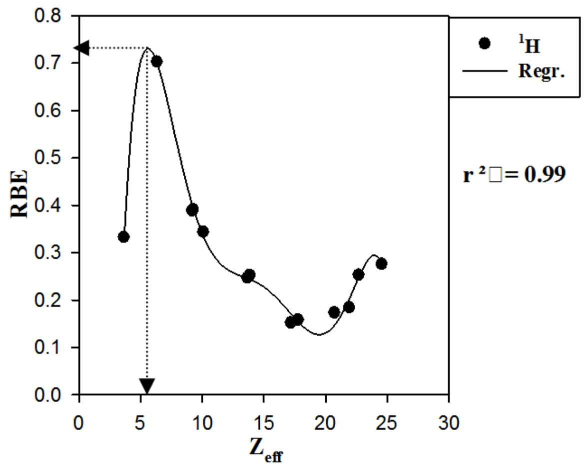

Fig. 6: Relationship between RBE and effective charge (Z_{eff}) for Helium used to irradiate V79 cells *in vitro*.

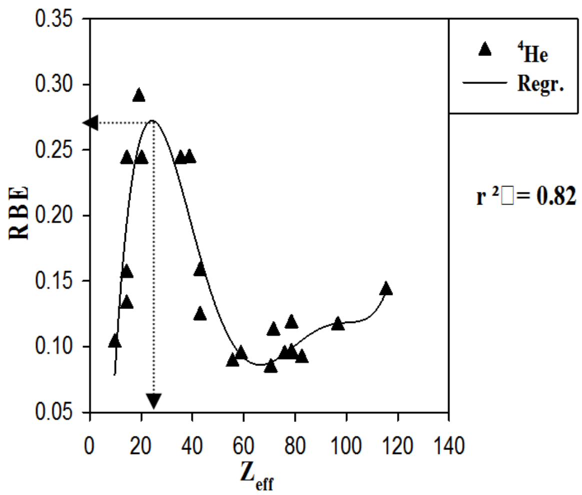

Fig. 7: Relationship between RBE and effective charge (Z_{eff}) for helium used to irradiate V79 cells *in vitro*.

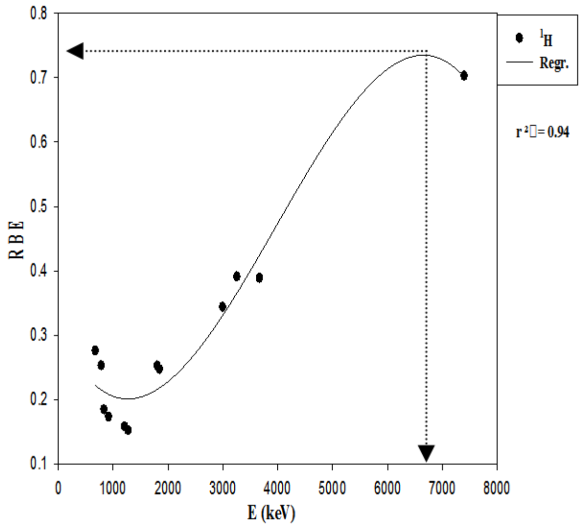

Fig. 8: Relationship between relative biological effectiveness (RBE) and energy (E) for protons used to irradiate V79 cells *in vitro*. The lines indicate the linear regressions of the relevant data.

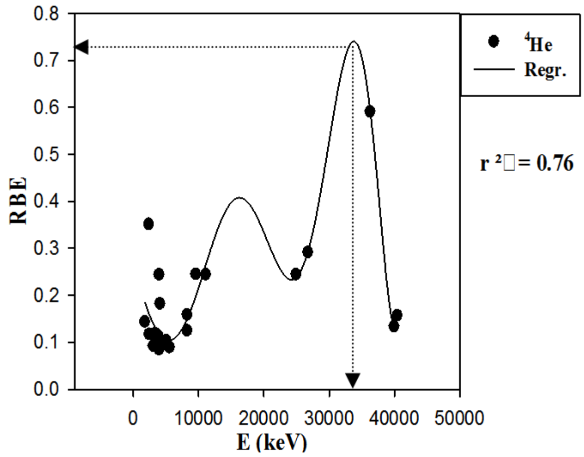

Fig. 9: Relationship between relative biological effectiveness (RBE) and energy (E) for helium used to irradiate V79 cells *in vitro*. The line indicate the linear regressions of the relevant data.

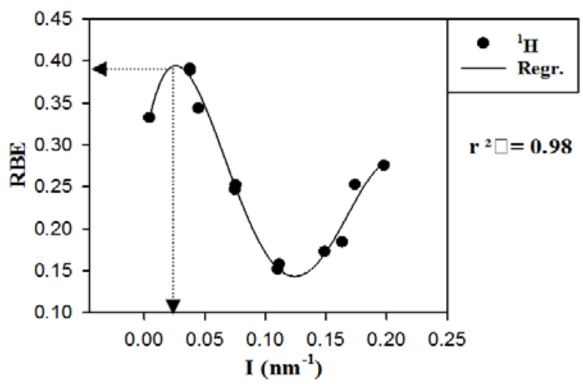

Fig. 10: Relationship between RBE and linear primary ionization (I) for protons used to irradiate V79 cells *in vitro.*

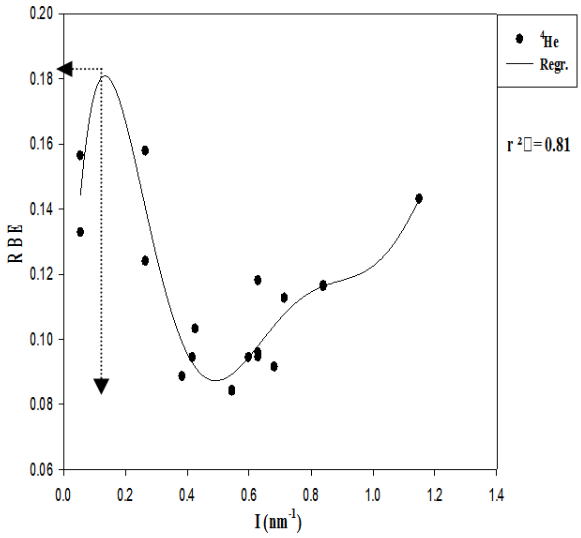

Fig. 11: Relationship between RBE and linear primary ionization (I) for helium used to irradiate V79 cells *in vitro.*

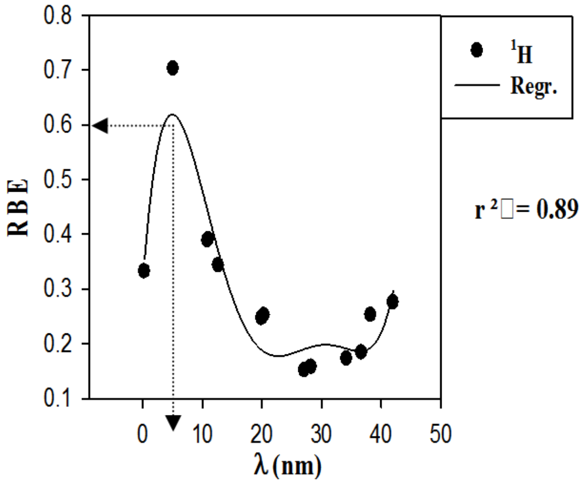

Fig. 12: Relationship between RBE and mean free path (l) for proton used to irradiate V79 cells *in vitro*

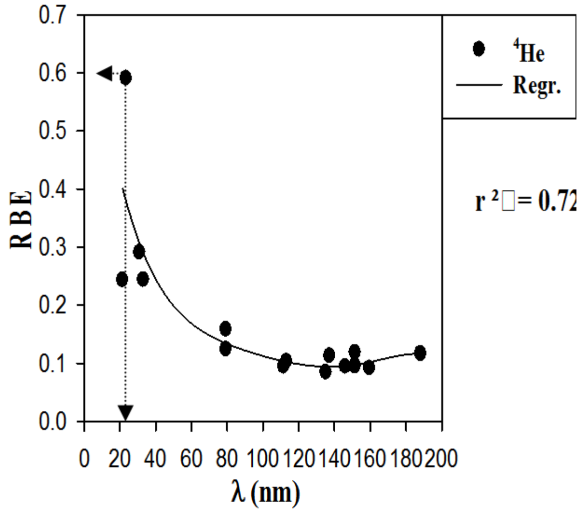

Fig. 13: Relationship between RBE and mean free path (l) for helium ions used to irradiate V79 cells in vitro.

Conclusion:

Various physical parameters that influence RBE other than the LET were investigated for the better application in radiation protection. Energy based physical parameters studied affect the RBE differently. The results revealed that a new system for radiation protection which is represented in the distinguished response RBE-l may need to be established to overcome various issues raised related to the need of RBE-LET response curve alone as a unified system of radiation protection.

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