Microdosimetric investigation of the radiation quality of low-medium energy electrons using Geant4-DNA

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Introduction

It is well known that the biological effects of ionizing radiation depend not only on absorbed dose but also on the type and energy of the radiation; this is the origin of the so-called radiation quality problem [1]. Depending on the context, radiation quality is expressed by the relative biological effectiveness (RBE) or quality factor (Q) or radiation weighting factor (w_R) [2]. In both radiotherapy and radiation protection it is assumed that for electrons and photons $RBE=Q=w_R=1$, irrespective of their energy. However, many studies have shown that for a variety of endpoints, electrons and photons exhibit RBE as high as ~2-4. This has implications in the assessment of risk as well as in the optimization of radiotherapy modalities.

It is recognized that for practical purposes it is important to theoretically determine Q (or w_R) when sufficient RBE data are not available. Microdosimetry offers the physical basis of radiation quality [3]. ICRU Report 40 [4] defined Q as a function of the microdosimetric counterpart of LET, the lineal energy, y. Lineal energy, being a stochastic quantity, makes the absorbed dose to depend upon the spectrum of y. Thus, for any radiation type and energy, the quality factor, Q is given by an average value as

$$< Q(T) >= \int_0^\infty Q(y) d(y;T) dy \qquad (1)$$

with $d(y;T)=(y/y_F)\ f(y;T)$ being the dose probability density distribution of y, $f(y;T)$ the probability density distribution and y_F the frequency-mean lineal energy. The connection between microdosimetry and radiation quality is also reflected in many biophysical models of radiation action , most notable, the TDRA and MKM. Also, the development of Monte Carlo (MC) track-structure codes permits simulations of RBE for various biological endpoints such as DSB (i.e. [5,6]).

The aim of this work is to calculate variation of radiation quality (in terms of Q and RBE) with electron energy in the range 100 eV to 1 MeV using different microdosimetry-based methodologies: **(a) ICRU 40** recommendations [4], **(b)** the **Kellerer-Hahn** approximation, **(c)** the **theory of dual radiation action (TDRA)**, **(d)** the **microdosimetric kinetic model (MKM)** of cell survival, and **(e)** the calculated yield of DNA double strand breaks (DSBs).

The main input in all the above approaches is the lineal energy (y) spectra which, in this work, were obtained for nanometer-sized spherical volumes of liquid water.

Materials and Methods

We have performed track-structure (TS) simulations using the Geant4-DNA low-energy extension of the Geant4 MC code version 10.6 to calculate the microdosimetric spectra using the "microyz" application [7]. The primary and secondary electron spectra were simulated in spherical volumes of liquid water down to the threshold energies of each of the different physics constructors available, namely Option 2, Option 4 and Option 6 [8]. Details of the calculation of lineal energy are given in [7]. Briefly, the lineal energy associated with a particular track is obtained by adding all the energy deposits occurring inside a target volume divided by the mean chord length of this volume. The frequency-mean and the dose-mean lineal energy are calculated by summing up all the lineal energy for each track multiplied each time by its probability or its normalized contribution respectively.

Since the lineal energy, y, depends on the size of the target volume and also volumes of dimensions of a few nanometers (i.e. 10nm) have been recognized as being more closely related to radiobiological effects (i.e. reproduce clinical RBE values), in the present work we have simulated y spectra for nm-sized volumes of 5nm, 10nm and 15nm that correspond to sensitive targets for DSB induction for direct (~10bp or ~3-4nm) and indirect action (radical diffusion distance ~1-10nm).

In the present work, the reference radiation is 100 keV electrons (similar to ICRU 40 which is 100 keV photons), therefore, we have normalized the calculated $<Q(T)>$ values to the value of $<Q(T=100keV)>$.

a. The ICRU40 approach

Within this approach, the average Q for an electron with energy T can be calculated from MC simulations by [4]

$$< Q(T) >_{ICRU\,40} = \frac{\sum_{i=1}^{N} Q_{ICRU\,40}(y_{i,T}) d_{i,T}}{\sum_{i=1}^{N} Q_{ICRU\,40}(y_{i,100keV}) d_{i,100keV}} \qquad (2)$$

N is the total number of primary electron tracks simulated and $d_{i,T}$ is the contribution of y_i for energy T ($y_{i,T}$) to the dose. The functional form of $Q_{ICRU40}(y)$ suggested by ICRU 40 is used in Eq. (2).

b. The Kellerer-Hahn approximation

Same as Eq. (2), but replace $Q_{ICRU40}(y)$ by the functional form $Q_{KH}(y)$ suggested by Kellerer-Hahn [9].

c. The TDRA approach

In the special case known as the "site version" of TDRA, and in the limit of small doses, the average Q can be calculated as

$$< Q(T) >_{TDRA} = \frac{\sum_{i=1}^{N} y_{i,T} d_{i,T}}{\sum_{i=1}^{N} y_{i,100keV} d_{i,100keV}} \qquad (3)$$

d. The MKM approach

The RBE expression for cell-kill is [10]

$$\mathrm{RBE}_{MKM} = \frac{\sqrt{\alpha_{ref}^2 - 4\beta \ln(S)} - \alpha_{ref}}{\sqrt{\alpha_{test}^2 - 4\beta \ln(S)} - \alpha_{test}} \qquad (4)$$

Where $\beta_{ref}=\beta_{test}=\beta$ and $\alpha_{ref\ or\ test}=\alpha_0+(0.204/d^2)\ \beta_{ref\ or\ test}$ with y_D in keV/μm, α_0 in Gy^{-1}, β in G^{-2} and d in μm. The parameters α_0, β, r are tissue-specific and can be found empirically.

e. The DSB approach

The average RBE_{DSB} for an electron energy T can be calculated from MC simulations by the expression:

$$< \mathrm{RBE}(T) >_{DSB} = \frac{\sum_{i=1}^{N} f(\geq E_{DSB})_{i,T}}{\sum_{i=1}^{N} y_{i,T}\, f_{i,T}} \left[\frac{\sum_{i=1}^{N} f(\geq E_{DSB})_{i,100keV}}{\sum_{i=1}^{N} (y_{i,100keV}\, f_{i,100keV})} \right] \qquad (5)$$

where $f(>=DSB)_{i,T}$ is obtained from the frequency of each y_i for a particular energy T ($y_{i,T}$).

Results and Discussion

In the present work, the MC-based calculations of $<Q(T)>$ and $<\mathrm{RBE}(T)>$ vs. T are subject to three main sources of uncertainty: the choice of Geant4-DNA physics model (Opt2, Opt4 or Opt6), the choice of the target size (i.e. sphere diameter), and the choice of the microdosimetric method (ICRU40, Kellerer-Hahn, TDRA, MKM, DSB). In Fig. 1, we present the effect of the different microdosimetric methodologies presented in the previous section for the 10nm diameter sphere and for the mean value of the different physics models of Geant4-DNA (Opt 2,4,6). As it may be observed, the variation of $<Q>$ and $<\mathrm{RBE}>$ over the low-medium energy range is sizeable (up to a factor of ~2-3). All methods agree that above ~50keV and up to 1MeV the approximation $<Q>=<\mathrm{RBE}>=1$ holds. There is almost excellent agreement between ICRU40, Kellerer-Hahn and TDRA over the whole energy range. MKM predicts smaller $<\mathrm{RBE}>$ values at low energies and DSB method the highest $<\mathrm{RBE}>$ values at low energies.

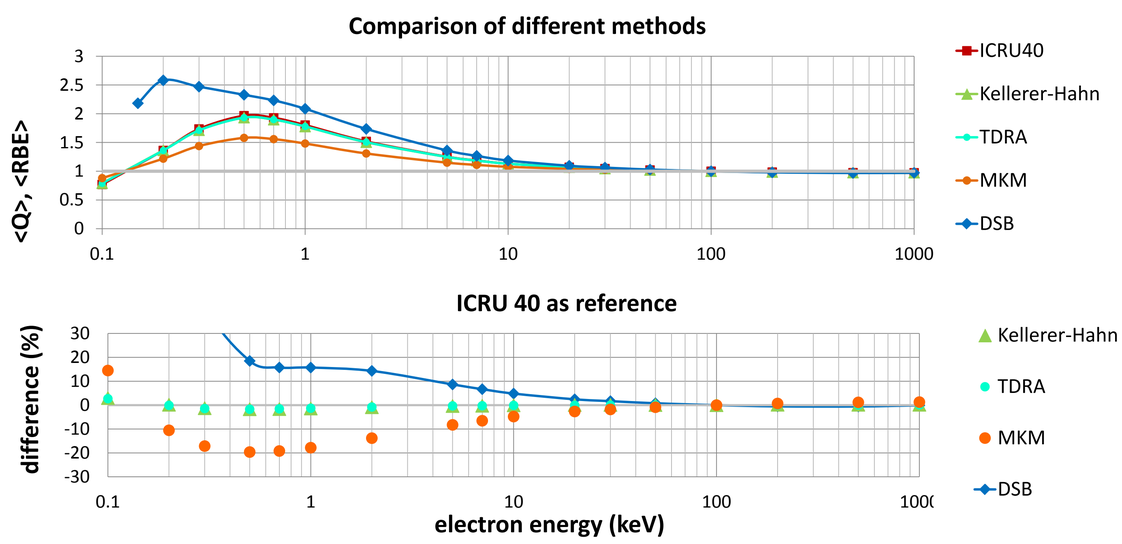

Fig. 1: Top panel: Variation of <Q> and <RBE> with electron energy calculated according to different methodologies based on the 10 nm sphere diameter and averaged over the different physics models of Geant4-DNA (Opt2, opt4/7, Opt6). Bottom panel: percentage difference from ICRU 40.

In Fig. 2 we compare our calculated DSB yield using the different physics models of Geant4-DNA against literature data, some of which include different TS simulations. All studies agree well on the trend of the DSB yield which starting from low energies exhibits an increase followed by a peak at about a few hundred eV and a smooth reduction approaching a plateau around 100keV.

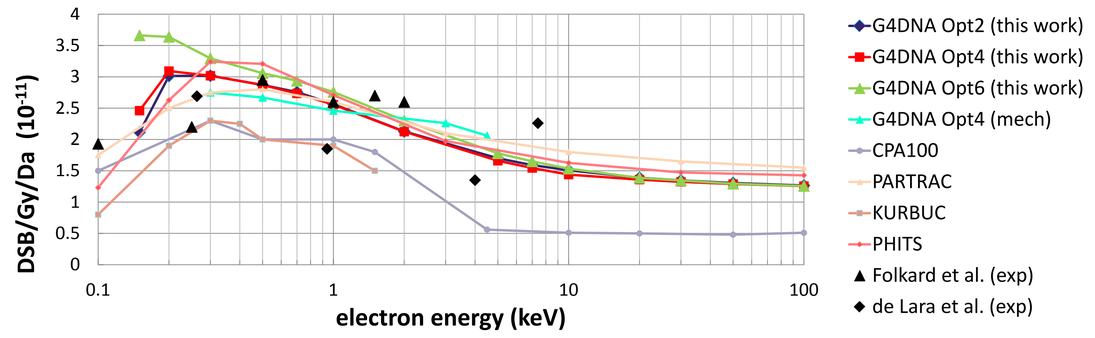

Fig. 2: Total direct and indirect absolute yield of DSB as a function of electron energy. Comparison of present calculations using the different physics models of Geant4-DNA are compared against other MC based studies and experimental data.

In Fig. 3 we present a comparison of different studies and methods on the variation of Q and RBE with electron energy. For reasons of simplicity, we have included only those values determined from the ICRU40 and DSB approaches (both calculated for the 10 nm sphere and averaged over all the different Geant4-DNA models). We observe that although the general trend is similar for all studies, the magnitude of the peak and the exact variation with electron energy are considerably different.

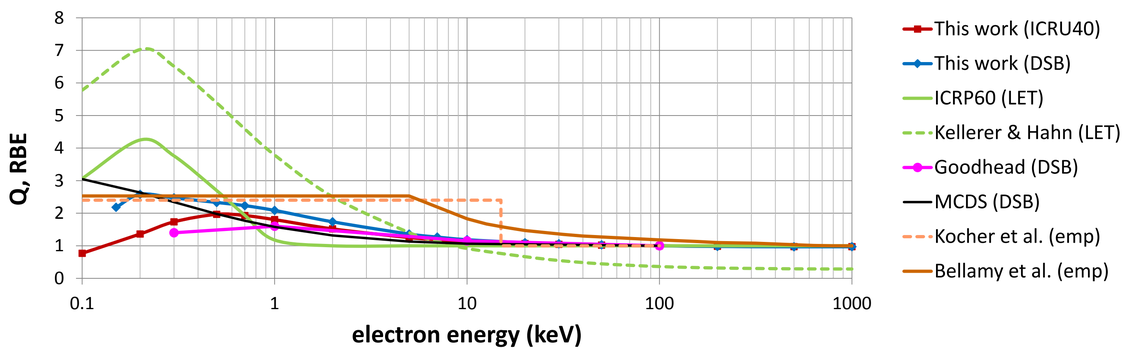

Fig. 3: Comparison of different predictions for the variation of Q and RBE with electron energy.

Conclusions

The results of this work indicate that the widely adopted approximation of $Q=\mathrm{RBE}=1$ is valid only above ~50keV (and up to 1 MeV). At lower electron energies, both Q and RBE exhibit a strong energy-dependence. The effect of different microdosimetric approaches may strongly influence the variation of Q and RBE at lower energies. The results are in-line with other predictions of a gradual increase of the radiobiological effectiveness of low-energy electrons. The present work will contribute towards establishing robust methodologies to determine the energy-dependence of the radiation quality of individual electrons that may be used to complement efforts involving practical electron and photon sources.

References

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