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Average stopping powers for electron and photon sources for radiobiological modeling and microdosimetric applications

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Abstract

This study concerns calculation of the average electronic stopping power for photon and electron sources. It addresses two problems that have not yet been fully resolved. The first is defining the electron spectrum used for averaging in a way that is most suitable for radiobiological modeling. We define it as the spectrum of electrons entering the sensitive to radiation volume (SV) within the cell nucleus, at the moment they enter the SV. For this spectrum we derive a formula that combines linearly the fluence spectrum and the source spectrum. The latter is the distribution of initial energies of electrons produced by a source. Previous studies used either the fluence or source spectra, but not both, thereby neglecting a part of the complete spectrum. Our derived formula reduces to these two prior methods in the case of high and low energy sources, respectively. The second problem is extending electron spectra to low energies. Previous studies used an energy cut-off on the order of 1 keV. However, as we show, even for high energy sources, such as ⁶⁰Co, electrons with energies below 1 keV contribute about 30% to the dose. In this study all the spectra were calculated with Geant4-DNA code and a cut-off energy of only 11 eV.

We present formulas for calculating frequency- and dose-average stopping powers, numerical results for several important electron and photon sources, and tables with all the data needed to use our formulas for arbitrary electron and photon sources producing electrons with initial energies up to ~1 MeV.

Keywords

average stopping power; photon RBE; electron RBE; low-energy x-rays; microdosimetry; nanodosimetry

1. Introduction

The relative biological effectiveness (RBE) of photons and electrons strongly depends on particle energy (Nikjoo and Lindborg, 2010). Understanding and quantifying this dependence is important for many reasons, particularly for estimation of health risks to patients and medical personnel associated with the use of x-rays for diagnostic and treatment purposes. This is becoming increasingly important owing to a rapid increase in the number of computed tomography exams and wide-spread use of mammography screening (Brenner

and Hall, 2007, Mettler *et al*, 2009). In radiotherapy with high-energy photon beams, the RBE is unlikely to deviate substantially from 1, but any variations are important and potentially affect treatment outcomes. This issue is of particular importance in terms of late-effects, the risk of which may be different than expected because scattered photons outside the treatment volume have a lower energy than the primary beam (Kirkby *et al*, 2007, Syme *et al* 2009, Okamoto *et al*, 2011, Scarboro *et al*, 2011, Ezzati, 2016).

Evidence indicates that lower energy particles are more biologically potent than high energy particles. The magnitude of this effect is non-trivial over the range of clinically relevant sources. For example, for low-energy brachytherapy sources such as palladium-103, iodine-125, and electronic sources (miniature x-ray generators), Wu *et al* (1996), Wu and Zaider (1998), Lehnert *et al* (2005), Nath *et al* (2005), and Reniers *et al* (2008) reported RBEs in excess of 1.4. These data underline the sizeable variation of RBE with photon energy. Advances in hadron therapy have emerged as another area that requires accurate estimates of RBE for various sources. The RBE models for hadron beams used in radiotherapy are primarily based on experimental data. These data often lack consistency in choosing the reference radiation for reported RBE. For example, in a review by Paganetti (2014), the list of reference radiations includes x-ray sources from 70 to 300 kVp, megaelectronvolt beams from 1 to 10 MV, cesium-137, and cobalt-60.

Researchers have used two main approaches to analyze the energy dependence of photon and electron RBE. The first approach is based on the Theory of Dual Radiation Action, Kellerer and Rossi (1972). According to this theory, parameter α of the linear quadratic model, and therefore the maximum RBE, is proportional to the dose-mean lineal energy, y_D . The latter quantity depends on the size of the sensitive volume (SV), or "site" in the original terminology, Kellerer and Rossi (1972). The most common SV has been a sphere 1 μm in diameter composed of a tissue-equivalent material. For SVs of this size y_D can be measured directly with a proportional counter. Wu *et al* (1996), and Wu and Zaider (1998) used this size for estimating RBE of brachytherapy sources. A more recent analysis of extensive experimental data by Nikjoo and Lindborg (2010) demonstrated that good correlation of microdosimetric parameters with RBE is achieved with a much smaller SV, of only 10 nm in size. For such a small SV, application of the microdosimetric approach requires advanced computing techniques, such as event-by-event Monte Carlo simulations. Fortunately, Monte Carlo software of this type is becoming increasingly available, as are systematic data on microdosimetric quantities.

The second approach to this RBE analysis is correlating photon and electron RBE with the average linear energy transfer (LET) or, similarly, electronic stopping power of electrons (ICRU 60, 1998). Whereas the definition of LET is unambiguous, how different investigators calculate the average LET has been inconsistent. For example, Kellerer (2002) calculated the average LET using the distribution of the initial energy of primary electrons, in other words, the spectrum of electrons, such as Compton and photo-electrons, at the moment they are ejected from an atom before their first interaction with tissue. We call this spectrum the source spectrum. However, this is not the spectrum of electrons reaching the SV unless the source is localized entirely within it. Usually, most electrons are produced outside the SV. Electrons that reach the SV lose a fraction of their initial energy as they

travel from the point of origin to the SV surface. Furthermore, primary electrons produce an avalanche of low-energy secondary electrons that can also reach the SV. The energies of these electrons are not explicitly included in the source spectrum.

An alternate LET-based approach that has been used calculates the average LET based on the fluence spectrum $\Phi(E)$ of electrons at the point where the SV is located (Kirby *et al*, 2007, and Syme *et al*, 2009). This method is justified by the definition of fluence ICRU 60 (1998), from which it follows that the energy distribution of electrons incident on an SV is given by the fluence spectrum, if we assume that the SV is a sphere. Under the electronic equilibrium conditions that are usually met in radiobiology, the fluence spectrum is referred to as the equilibrium or slowing-down spectrum. The limitation of this method is that for any SV of a finite size, some electrons are produced within it. For modeling the biological effect of these electrons, using the source spectrum is more appropriate than using the fluence spectrum.

Our study resolves these difficulties of the LET-based approach. We derive a formula for the energy distribution of electrons entering the SV. The formula combines linearly both types of electron spectra used in previous studies, the source spectrum and the fluence spectrum. We offer a simple derivation of the formula, but ultimately it is based on the properties of the Boltzmann transport equation and follows from a more general formula presented elsewhere (Vassiliev, 2017). Additionally, we extend previous studies by lowering the electron tracking cut-off energy to 11 eV, the ionization threshold of liquid water. That is, trajectories and all interactions of electrons are simulated explicitly, until their energies fall below 11 eV, without making any additional approximations, such as condensed histories, etc. These calculations were performed using the Geant4-DNA Monte Carlo code (Incerti *et al*, 2010, Bernal *et al*, 2015). This study reports numerical results for several sources and across a range of clinically relevant energies, and includes all the data necessary to apply our approach to arbitrary electron and photon sources emitting electrons with energies of up to about 1 MeV.

2. Methods and materials

2.1. Sensitive volume

Essential to radiobiological modelling is the concept of a sensitive volume (SV). It represents a target within a living cell that is sensitive to radiation. Its size can range from a few nanometers (DNA double helix) to a few micrometers (nucleus). In this study we considered the range of SV diameters from 0 to 1 μm to encompass most of previously proposed SV sizes. The zero-diameter SV was included for completeness, as a theoretical limit, providing a bounding value for calculated quantities at a given source energy.

This study is concerned with the stopping powers of electrons that actually interact with the SV. We group such electrons into two categories: those produced within the SV and those produced outside the SV and entered it through its surface. The electrons in these two categories have different spectra. Both are accounted for in our formalism.

2.2. Frequency distribution of electron energy

Energy spectra of electrons are usually polyenergetic. Choosing an appropriate form of the energy distribution is crucial for calculating the average stopping power. Given that the focus of this study is on radiobiological applications, our main quantity is the frequency distribution of electron energy $N_e(E)$, which is defined as the distribution of electron energy at the moment it appears within the SV, either by entering through the SV surface, or produced by a source within the SV. In this section we derive our main formula for $N_e(E)$.

We consider a spatially uniform source of electrons in a homogeneous medium, producing one particle per unit volume. The energy spectrum of the source is $S_{e,v}(E)$. The subscript emphasizes that this is the spectrum of electrons normalized per unit volume. The units for $S_{e,v}(E)$ are $\text{keV}^{-1} \mu\text{m}^{-3}$. The source spectrum is normalized so that

$$\int_0^\infty S_{e,v}(E) dE = 1 \mu\text{m}^{-3}. \quad (1)$$

The number of electrons with an energy from E to $E + dE$ produced within the SV is then given by

$$N_{e,in}(E) dE = V S_{e,v}(E) dE, \quad (2)$$

where V is the SV volume.

This source produces a fluence of electrons that has an energy distribution $\Phi_{e,v}(E)$. The units for the fluence spectrum $\Phi_{e,v}(E)$ are $\text{keV}^{-1} \mu\text{m}^{-2}$. ICRU 60 (1998) defines it as $d\Phi/dE$, where Φ is the total fluence.

According to the definition of fluence (ICRU 60, 1998) the number of particles produced outside the SV and entered it with an energy from E to $E + dE$ is

$$N_{e,out}(E) dE = A \Phi_{e,v}(E) dE, \quad (3)$$

where A is the cross sectional area of the SV. Then, for the total number of electrons in the SV we have

$$N_e(E) dE = [N_{e,in}(E) + N_{e,out}(E)] dE = [V S_{e,v}(E) + A \Phi_{e,v}(E)] dE. \quad (4)$$

A general form of Eq.(4) was rigorously derived as we described previously using the general properties of the Boltzmann transport equation (Vassiliev, 2017, Section 3.4). This derivation was based on the simple idea that all primary particles, that is, those emitted by the source, can be placed in two categories: those originating within the SV and those originated outside the SV. We can now normalize the energy distribution to the total number of electrons entering from outside and produced inside the SV:

$$\overline{N}_e(E) \equiv \frac{N_e(E)}{\int_0^\infty N_e(E) dE} = \frac{S_{e,v}(E) + (A/V)\Phi_{e,v}(E)}{\int_0^\infty S_{e,v}(E) dE + (A/V)\int_0^\infty \Phi_{e,v}(E) dE}. \quad (5)$$

In this equation it is now convenient to renormalize the source from one particle per unit volume to a source emitting a total of one particle. With such a normalization, the fluence is normalized per one source particle because it is linearly related to the source spectrum. We will use notations $S_e(E)$ and $\Phi_e(E)$ for the renormalized quantities. Also the SV is assumed to be a sphere. Then, V/A is the mean chord length h of the SV. Also, in this new normalization

$$\int_0^\infty \Phi_e(E) dE = R, \quad (6)$$

where R is the total range, that is, the distance traveled by the primary electron until its energy falls below the cut-off energy plus the sum of the distances traveled by all secondary electrons. This relationship between fluence and range is explained, for example, in Vassiliev, 2017. This leads to the final formula

$$\overline{N}_e(E) = \frac{S_e(E) + (R/h)\overline{\Phi}_e(E)}{1 + R/h}, \quad (7)$$

where

$$\overline{\Phi}_e(E) \equiv \frac{1}{R}\Phi_e(E). \quad (8)$$

The fluence spectrum $\overline{\Phi}_e$ has the same normalization as the renormalized source spectrum:

$$\int_0^\infty \overline{\Phi}_e(E) dE = \int_0^\infty S_e(E) dE = 1. \quad (9)$$

Introducing $\overline{\Phi}(E)$ simplifies comparison of the two terms in the numerator in the right side of Eq.(7). For example, the first term, $S_e(E)$, can be neglected for high energy sources, for which $R \gg h$.

2.3. Frequency and dose average stopping powers

Two types of averaging are commonly used in radiobiological modeling: track average and dose average (Paganetti, 2014). In this study we use a terminology similar to that of microdosimetry and instead of track average we will define the frequency average stopping power. The track average and frequency average quantities are very similar, and can be shown to be equivalent under certain conditions. It is beyond the scope of this study to

develop any guidelines on choosing frequency versus dose average quantities in the context of radiobiological modeling.

The frequency average stopping power, β_F , and the frequency average second moment of stopping power, β_2 , can be calculated as

$$\beta_F = \int_0^\infty \overline{N}_e(E) \beta(E) dE = \frac{(S_e, \beta) + (R/h) (\overline{\Phi}_e, \beta)}{1 + R/h}; \quad (10)$$

$$\beta_2 = \int_0^\infty \overline{N}_e(E) \beta^2(E) dE = \frac{(S_e, \beta^2) + (R/h) (\overline{\Phi}_e, \beta^2)}{1 + R/h}; \quad (11)$$

where $\beta(E)$ is the electron stopping power, and we introduced the notation:

$$(f, g) \equiv \int_0^\infty f(E) g(E) dE. \quad (12)$$

The dose average stopping power is the ratio of the second moment and the frequency average stopping power

$$\beta_D = \frac{\beta_2}{\beta_F}. \quad (13)$$

2.4. Calculation of the source and fluence spectra

The source and fluence spectra, $S_e(E)$ and $\overline{\Phi}_e(E)$, as well as the ranges R were calculated using the Geant4-DNA code for monoenergetic electron and photon sources. The low energy physics models used in these calculations have been extensively tested (Incerti *et al*, 2010; Bernal *et al*, 2015; Bordage *et al*, 2016; Incerti *et al*, 2017; Kyriakou *et al*, 2017). The fluence spectra were calculated assuming electronic equilibrium. It is a good approximation for fluence spectra at the location of the SV in radiobiological experiments, because they are normally designed to achieve equilibrium conditions required for accurate dosimetry.

The monoenergetic electron source $S_e(E)$ produced only electrons with energy E , whereas for the monoenergetic photon source, $S_e(E)$ was a polyenergetic spectrum of electrons produced by a monoenergetic photon fluence interacting with a water molecule. The source energies extended from 100 eV to 1 MeV for electron sources and from 250 eV to 1.25 MeV (photon energy) for photon sources.

The fluence spectra and ranges were taken from our earlier work (Vassiliev, 2012), in which all of the details of the algorithm and physical model of electron interactions were described. The cut-off energy for electrons was 11 eV, which is the ionization threshold of liquid water. For the present study we additionally needed to calculate the source spectra, that is the

spectra of electrons $S_e(E)$ produced in the interaction of a photon of given energy with a water molecule. For these calculations, the same physical model we employed previously (Vassiliev, 2012) was used. However, the algorithm was modified so that the history of an electron was terminated immediately after it was produced in a photon interaction and its initial energy was tallied. The spectra included Auger electrons produced after K-shell ionization of an oxygen atom.

In all these calculations each decade of the energy scale was divided into 100 bins of equal size on the logarithmic scale. Calculations were terminated after statistical uncertainties of less than 0.1 % were achieved for the integral over energy of fluence and of fluence times energy. The same method was used for the source function. This resulted in uncertainties on the order of 0.1 % for the integrals in Eqs.(10) and (11).

3. Results and Discussion

3.1. Cobalt-60 source

In this study, we chose unscattered photons from a ^{60}Co source as the reference radiation. For radiotherapy applications, a 6-MV beam from a medical accelerator would be more appropriate. However, this study is based on data generated with the Geant4-DNA code, which does not extend to energies exceeding those of a ^{60}Co source. Furthermore, photon beams from both ^{60}Co and 6-MV sources generally contain scattered photons. The number of scattered photons, their spectrum, and, therefore average stopping power depend on a multitude of factors. It is because of this variability of clinical beams that our reference radiation was selected to be unscattered photons from a ^{60}Co source. In practice, where the reference radiation is likely a more arbitrary radiation source (e.g. a clinical cobalt unit), the spectrum of that reference radiation would need to be determined. Once this spectrum is known, the average stopping power of this reference radiation can be determined using the data in this work, thereby establishing the specific and appropriate reference radiation for an arbitrary experiment.

For the unscattered ^{60}Co photons, the range, as it is defined in Eq.(6), is 2.5 mm. This is much larger than a typical SV size. For this reason the average stopping powers, β_F and β_D , for this source depend only weakly on the SV size. For SV diameters of 0 and 1 μm we determined, respectively, $\beta_F = 0.400$ and 0.401 keV/ μm , $\beta_D = 4.62$ and 4.64 keV/ μm . For comparison, Kellerer (2002), who used only the source spectrum of electrons, found that the dose average LET for a 1 MeV photon source was approximately 0.47 keV/ μm . Our calculated dose average stopping power is much greater than the frequency average because of the large stopping power of low-energy electrons. Figure 1 illustrates the difference between the frequency and the dose weighted quantities. It shows the cumulative dose and frequency distributions of electron energies for the ^{60}Co source, as well as the electron stopping power as a function of electron energy. It can be seen, for example, that only 4.8% of the electrons entering the SV have energies lower than 10 keV, but they deliver 40% of the total dose. Similarly, only 3.9% of the electrons have energies lower than 1 keV, but they deliver 30% of the dose. These results are for ^{60}Co , a high-energy source. Low-energy electrons are even more important for sources such as orthovoltage and low-energy x-rays as shown below. These data emphasize the importance of low-energy electrons in calculations

of average stopping powers. Therefore, performing calculations with cut-off energies much lower than 1 keV is important.

3.2. Monoenergetic electron and photon sources

According to Eqs.(10), (11) and (13), to calculate the frequency and dose average stopping powers, β_F and β_D , the following five quantities are required: R , (S_e, β) , (S_e, β^2) , $(\bar{\Phi}_e, \beta)$ and $(\bar{\Phi}_e, \beta^2)$. All of these quantities are reported in the Appendix, in Tables A.1 and A.2, for monoenergetic electron and photon sources, respectively.

Using these data, we calculated the β_F and β_D for monoenergetic electron and photon sources at several SV diameters ranging from 0 to 1 μm . The results for the electron sources are shown in figures 2 and 3. Because average stopping powers are often used to estimate the RBE, we present these results relative to the respective stopping powers of unscattered ^{60}Co photons (our reference radiation), as the ratios $\beta_F(e^-)/\beta_F(^{60}\text{Co})$ and $\beta_D(e^-)/\beta_D(^{60}\text{Co})$. For the SV sizes examined, the β_F ratio is approximately independent of the SV size for source energies greater than 30 keV. The reason is that at this energy, the range as defined in Eq.(6), is 24 μm . Therefore, the ratio R/h in Eq.(10) is much greater than 1. Below 30 keV, the β_F ratio increases as the SV diameter increases. For the 1 μm SV, the ratio reaches the maximum of 54.4 at 0.12 keV, which is close to the location of the maximum stopping power of monoenergetic electrons shown in figure 1. For the zero-diameter SV (red line), the β_F ratio reaches the maximum of 13.6 at 1.02 keV. For a 1 MeV source, the β_F ratio is 0.896.

The ratios of the dose average stopping powers, figure 3, tend to be much lower than the β_F ratios, and they have a more complex dependence on the SV size. As with the β_F ratio, the maximum β_D ratio is achieved for the 1 μm SV at a source energy of 0.12 keV. However, the maximum ratio is only 4.85. The reason for the relatively low β_D ratio is the rather large β_D for the ^{60}Co source as described in Section 3.1 - the low energy electrons are present and important to the dose averaged stopping power even for high-energy (e.g., ^{60}Co) sources. The minimum β_D ratio is 0.988.

The stopping power ratio for photon sources, $\beta_F(\gamma)/\beta_F(^{60}\text{Co})$, shown in figure 4 has a more complex dependency on source energy. There is a local minimum around 40-50 keV associated with the transition from mostly photoelectric absorption at lower energies to mostly Compton scattering at higher energies. On average, photoelectrons have higher energies than do Compton electrons. Also, there is a discontinuity at 0.539 keV, which is the K-shell ionization potential of an oxygen atom. The data extends down to 0.25 keV. This particular energy was chosen so that our data would include the energy of carbon K-shell x-rays, 0.278 keV, which represents the lowest energy source commonly used in studies with ultrasoft x-rays (Nikjoo and Lindborg, 2010). The minimum β_F ratio is 1, and the maximum is 37.8 for the 1 μm SV, at the source energy of 0.25 keV. For the smallest SV (red line) the maximum β_F ratio of 13.3 is reached at 1.44 keV.

The ratio of dose weighted stopping powers for photon sources, $\beta_D(\gamma)/\beta_D(^{60}\text{Co})$, shown in figure 5, varies less with the source energy and SV size than does the ratio of frequency average stopping powers. The minimum β_D ratio is 1, and the maximum is only 4.32 for the

1 μm SV, at the source energy of 0.25 keV. For the smallest SV (red line) the maximum β_D of 3.68 is reached at 0.331 keV.

Stopping power ratios $\beta_F(\gamma)/\beta_F(^{60}\text{Co})$ and $\beta_D(\gamma)/\beta_D(^{60}\text{Co})$ for several important photon sources are listed in Table 1. The ratios are presented for the minimum and maximum SV diameters considered in this study, 0 and 1 μm . In these calculations the photon spectrum was approximated by a single energy, the average source energy.

3.3. Polyenergetic sources

In the Appendix, in Tables A1 and A2, we list all the quantities needed to calculate the average stopping powers for monoenergetic electron and photon sources. We reiterate that the monoenergetic electron source, $S_e(E)$, emits electrons with energy E , whereas the monoenergetic photon source, $S_e(E)$ is a polyenergetic spectrum of electrons produced by a monoenergetic photon fluence of energy E interacting with water.

To calculate average stopping powers for a polyenergetic source, additionally the energy distribution of the source, $S(E)$, is required. Equations (10) and (11) are linear in terms of the source and fluence spectra, $S_e(E)$ and $\bar{\Phi}_e(E)$. Furthermore, the fluence $\bar{\Phi}_e(E)$ is linearly related to the source because the Boltzmann equation is linear. Therefore, if we have a polyenergetic source $S(E)$, and $\beta_{1,\text{mono}}(E)$ and $\beta_{2,\text{mono}}(E)$ are the first and second moments of stopping power for the monoenergetic source, then the first two moments of the stopping power for a polyenergetic can be calculated as

$$\beta_{i,\text{poly}}[S] = \frac{(S, \beta_{i,\text{mono}})}{(S, 1)}, \quad i=1, 2, \quad (14)$$

where the denominator normalizes the spectrum. The moments of stopping power were defined in Eqs.(10) and (11). By definition, the frequency average is the first moment ($\beta_F \equiv \beta_1$) and the dose average β_D is the ratio β_2/β_1 . Equation (14) can be viewed as a form of the total expectation formula, where $S(E)$ is the distribution of source energy and $\beta_{i,\text{mono}}(E)$ is the conditional expectation, the condition being the source energy.

When we calculated the $\beta_{i,\text{mono}}(E)$ for monoenergetic photon sources, to sample the electron energy, we simulated an inelastic collision of a photon of energy E with a water molecule. Therefore, if the source of electrons are photons, in Eq.(14) the spectrum $S(E)$ is given by the photon collision density, which is the product of the total inelastic photon cross section $\sigma_\gamma(E)$ and photon fluence $\Phi_\gamma(E)$ (Vassiliev, 2017):

$$S(E) = \sigma_\gamma(E) \Phi_\gamma(E). \quad (15)$$

In Table 2, we list the stopping power ratios $\beta_F(\gamma)/\beta_F(^{60}\text{Co})$ and $\beta_D(\gamma)/\beta_D(^{60}\text{Co})$ for four important polyenergetic sources. We calculated the ratios for the minimum and maximum SV diameters considered in this study, 0 and 1 μm . For these calculations, the beta-decay spectrum of tritium (^3H) was taken from ICRP 107 (2008). The x-ray spectra for 30 and 250

kVp beams were calculated using the Monte Carlo code MCNPX (Pelowitz, 2011). The first beam represents a mammography unit, and the second beam is often used in radiobiological experiments. The photon spectrum for a cobalt teletherapy unit was calculated with Monte Carlo by Han *et al* (1987). The cobalt teletherapy spectrum includes scattered photons as it describes the spectrum in air at 80 cm from the source, for a large, 35×35 cm open field. This is why stopping power ratios for teletherapy units are higher, by at least 10%, than those for unscattered photons from a ^{60}Co source (our reference radiation).

To summarize, our study resolves prior difficulties associated with the choice of an appropriate electron spectrum for radiobiological applications. We propose a new formalism that, in fact, unifies the two main previous methods that used either the source or the fluence spectrum. Our method is based on the general properties of the Boltzmann transport equation, Vassiliev (2017) and therefore it is quite general. We offer a simple exact formula for electron energy distribution, which is the energy distribution of electrons actually interacting within the SV. We present tables for calculating frequency and dose average electronic stopping powers using our formula for arbitrary electron sources producing electrons with initial energies ranging from 100 eV to 1 MeV, and arbitrary photon sources with photon energies ranging from 250 eV to 1.25 MeV. We additionally report the average stopping powers for several important sources.

Furthermore, we fully account for low-energy electrons with energies below 1 keV. These electrons are produced in abundance and have stopping powers of up to 22.6 keV/ μm , Francis *et al* (2011). We show that even for high-energy sources, such as ^{60}Co , these electrons contribute a large fraction (~30%), to the total dose. Previous studies used various approximate techniques to account for low energy electrons. Kirkby *et al* (2007) and Syme *et al* (2009) performed Monte Carlo calculations with the electron cut-off energy of 1 keV and then applied a correction from Nahum (1978) to account for electrons with energies below this cut-off. Reiners *et al* (2008) also used a 1 keV transport cut-off but lowered the production threshold to 0.1 keV. Ezzati (2016) performed simulations with a 2 keV cut-off energy and then extended the calculated spectra to lower energies using previously published very low cut-off spectra assuming spectrum continuity at 2 keV. In the present study we use spectra calculated with the event-by-event Monte Carlo code Geant4-DNA, Incerti *et al* (2010), Bernal *et al* (2015), which simulates electron tracks down to very low energies in full detail. We performed all calculations with a cut-off energy of only 11 eV, the ionization threshold of liquid water.

4. Conclusions

We proposed a new formula for energy distribution of electrons interacting with an SV within a cell nucleus. It combines the source spectrum to account for electrons that originate within the SV with the fluence spectrum for electrons that originate outside the SV and travel from the point of origin to the SV surface. This formula is quite general, as it is based on the general properties of the Boltzmann transport equation. We reported numerical results for photon and electron sources producing electrons with initial energies up to about 1 MeV. In these calculations, using a Monte Carlo code, we fully accounted for low-energy electrons down to the cut-off energy of only 11 eV.

In our formalism the average stopping power depends on the size of the SV, except for high-energy sources, for which this dependence becomes negligible. The size of the SV is a radiobiological parameter that depends on the biological endpoint and other factors. Determining an appropriate value for this parameter is outside the scope of this study, which was primarily focused on the physics. We therefore did not estimate the RBE or its variation with energy.

Our results nevertheless have important practical implications. It is well known from experimental data that RBE of photons and electrons increases substantially with decreasing particle energy. Our study offers a new insight into the underlying physics causing this increase, and provides new systematic numerical data for modelling it. As such, this facilitates development of RBE models. Refining RBE models is particularly important for improving risk estimates for low-energy procedures, such as mammographic screening, or potentially even optimization of brachytherapy treatments where the filtering of photons within the source and by patient tissues affect not only the dose distribution but also the RBE. An accurate photon RBE model that accounts for these factors will help in choosing a source design that is optimal for a particular treatment. In addition to these applications, results of this study can help reduce uncertainties in hadron RBE models. Such models are largely based on experimental data and are therefore affected by common and substantial inconsistencies in the choice of reference photon radiation. For this application, an accurate photon RBE model will help quantify the differences between various reference photon radiations, thereby reducing uncertainties in corresponding hadron RBE models. Finally, average stopping power is one of the most fundamental dosimetric quantities and the data we report in this study may prove to be useful for many application in dosimetry and microdosimetry, from characterisation of a detector response to the design of new instrumentation.

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Appendix

Table A.1

Quantities for calculating average stopping powers for monoenergetic electron sources using Eqs.(10), (11), and (13).

E, keV	(S, β) , keV/ μm	(S, β^2) , keV ² / μm^2	$(\bar{\Phi}, \beta)$, keV/ μm	$(\bar{\Phi}, \beta^2)$, keV ² / μm^2	Range ^I , μm
0.1	21.96	482.4	3.360	41.54	0.02308
0.12	22.57	509.3	3.602	49.63	0.02776
0.14	22.58	509.6	3.806	56.42	0.03243
0.17	22.26	495.3	4.060	64.46	0.03938
0.2	21.62	467.4	4.265	70.34	0.04630
0.24	20.64	425.9	4.485	75.89	0.05553
0.3	19.17	367.6	4.737	81.11	0.06940

E, keV	(S, β) , keV/ μm	(S, β^2) , keV ² / μm^2	$(\bar{\Phi}, \beta)$, keV/ μm	$(\bar{\Phi}, \beta^2)$, keV ² / μm^2	Range ¹⁾ , μm
0.4	17.03	290.0	5.016	84.74	0.09282
0.5	15.30	234.1	5.191	85.25	0.1167
0.6	13.91	193.5	5.302	84.37	0.1411
0.7	12.79	163.6	5.371	82.79	0.1661
0.8	11.87	140.8	5.412	80.91	0.1917
1	10.44	108.9	5.439	76.90	0.2446
1.4	8.525	72.68	5.379	69.36	0.3574
2	6.819	46.50	5.201	60.49	0.5432
3	5.207	27.11	4.858	50.30	0.8943
5	3.640	13.25	4.272	38.54	1.737
7	2.850	8.125	3.831	31.80	2.750
10	2.188	4.786	3.348	25.64	4.558
14	1.698	2.884	2.899	20.72	7.462
20	1.298	1.686	2.452	16.40	12.78
30	0.9593	0.9202	1.993	12.46	23.96
50	0.6595	0.4350	1.508	8.743	53.89
70	0.5215	0.2720	1.247	6.907	92.55
100	0.4127	0.1703	1.018	5.388	164.4
140	0.3372	0.1137	0.8422	4.285	281.9
200	0.2791	0.07788	0.6934	3.396	495.0
300	0.2334	0.05446	0.5637	2.663	922.5
500	0.1979	0.03918	0.4486	2.062	1940
700	0.1845	0.03404	0.3966	1.822	3056
1000	0.1759	0.03094	0.3586	1.683	4765

¹⁾ Defined in Eq.(6).

Table A.2

Quantities for calculating average stopping powers for monoenergetic photon sources using Eqs.(10), (11), and (13).

E, keV	(S, β) , keV/ μm	(S, β^2) , keV ² / μm^2	$(\bar{\Phi}, \beta)$, keV/ μm	$(\bar{\Phi}, \beta^2)$, keV ² / μm^2	Range ⁶⁾ , μm
0.25	15.97	330.9	4.578	77.03	0.05171
0.278 ¹⁾	15.58	313.7	4.711	79.99	0.05793
0.32	14.98	288.4	4.865	82.85	0.06743
0.37	14.29	260.4	5.006	84.95	0.07893
0.43	13.53	231.6	5.123	85.46	0.09312
0.5	12.61	201.9	5.215	85.51	0.1098
0.538	12.37	191.5	5.249	85.06	0.1182
0.56	9.613	127.8	4.913	75.95	0.1230
0.58	11.62	154.3	4.920	76.92	0.1273
0.6	13.11	191.9	4.928	77.93	0.1316

E, keV	(S, β) , keV/ μm	(S, β^2) , keV ² / μm^2	$(\bar{\Phi}, \beta)$, keV/ μm	$(\bar{\Phi}, \beta^2)$, keV ² / μm^2	Range ^{d)} , μm
0.64	14.90	253.7	4.951	79.40	0.1403
0.69	15.56	281.2	4.991	81.07	0.1512
0.73	15.63	283.9	5.027	82.19	0.1600
0.79	15.31	268.5	5.079	83.38	0.1735
0.84	14.92	252.8	5.122	83.99	0.1850
0.9	14.43	235.4	5.169	84.50	0.1991
1	13.85	214.6	5.225	84.83	0.2233
1.2	13.04	189.5	5.277	82.96	0.2739
1.486 ²⁾	12.28	169.2	5.303	78.43	0.3505
2	11.48	153.3	5.226	70.39	0.4999
2.5	11.00	145.9	5.100	63.78	0.6581
3	10.67	141.5	4.960	58.31	0.8280
3.7	10.33	137.7	4.763	52.21	1.085
4.5 ³⁾	10.19	136.4	4.552	46.78	1.405
6	9.794	133.2	4.197	39.38	2.073
8 ⁴⁾	9.687	133.6	3.808	32.80	3.082
10	9.611	134.7	3.496	28.31	4.188
14	9.468	136.0	3.031	22.60	6.498
17	9.534	138.5	2.772	19.79	8.105
20	9.684	140.9	2.567	17.78	9.301
24	9.766	140.6	2.351	15.85	10.08
30	9.816	139.3	2.129	14.09	10.51
35	9.602	133.4	2.002	13.31	10.09
40	9.244	124.9	1.946	13.01	9.415
50	8.397	108.5	1.944	13.42	8.183
60	7.606	95.54	2.023	14.26	7.700
70	6.940	85.52	2.128	14.95	7.918
80	6.387	77.59	2.183	15.24	8.438
90	5.931	71.23	2.180	15.03	9.499
100	5.566	66.35	2.168	14.57	11.12
120	5.022	59.51	2.028	13.04	15.67
140	4.625	54.75	1.814	11.23	22.26
170	4.208	50.07	1.564	9.238	35.18
200	3.926	47.11	1.359	7.744	52.72
250	3.615	44.09	1.121	6.120	91.38
300	3.410	42.26	0.9565	5.055	142.2
400	3.172	40.39	0.7600	3.853	275.7
500	3.033	39.42	0.6455	3.187	451.4
662 ⁵⁾	2.907	38.69	0.5408	2.601	799.1
1000	2.794	38.17	0.4364	2.039	1746
1250	2.747	37.96	0.4001	1.850	2535

¹⁾ Carbon K-shell x-rays;

- 2) Aluminium K-shell x-rays;
- 3) Titanium K-shell x-rays;
- 4) Copper K-shell x-rays;
- 5) Cesium-137;
- 6) Defined in Eq.(6).

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Figure 1. Stopping power versus electron energy, and cumulative dose and frequency distributions of electron energies for the ^{60}Co source.

Figure 2. Frequency average stopping powers of monoenergetic electron sources divided by that of the ^{60}Co source. The curve labels are SV diameters in micrometers.

Figure 3.

Dose average stopping powers of monoenergetic electron sources divided by that of the ^{60}Co source. The curve labels are SV diameters in micrometers.

Figure 4.
Frequency average stopping powers of photon sources divided by that of the ^{60}Co source.
The curve labels are SV diameters in micrometers.

Figure 5.
Dose average stopping powers of photon sources divided by that of the ^{60}Co source. The curve labels are SV diameters in micrometers.

Table 1

The stopping power ratios for several monoenergetic photon sources.

Source	Energy, keV	$\beta_F(\gamma)/\beta_F(^{60}\text{Co})$		$\beta_D(\gamma)/\beta_D(^{60}\text{Co})$	
		diam.=0	diam.=1 μm	diam.=0	diam.=1 μm
C, K-shell	0.278	11.8	36.7	3.67	4.32
Al, K-shell	1.486	13.2	24.6	3.20	3.01
Ti, K-shell	4.5	11.4	15.9	2.22	2.56
Cu, K-shell	8	9.52	12.1	1.86	2.25
^{103}Pd	21	6.27	7.44	1.49	1.83
^{125}I	28	5.49	6.63	1.44	1.80
^{192}Ir	370	2.03	2.05	1.11	1.13
^{137}Cs	662	1.35	1.35	1.04	1.04

Table 2

Stopping power ratio for selected polyenergetic sources.

Source	Notes	$\beta_F(\gamma)/\beta_F(^{60}\text{Co})$		$\beta_D(\gamma)/\beta_D(^{60}\text{Co})$	
		diam.=0	diam.=1 μm	diam.=0	diam.=1 μm
^3H	β^- decay, $E_{\text{max}}=18.6\text{ keV}$	10.8	35.0	2.86	3.58
X-rays, 30 kVp	Mo target, no filter	8.93	11.3	1.83	2.21
X-rays, 250 kVp	Ti target, Cu+Al filter	5.10	5.91	1.48	1.72
^{60}Co	teletherapy unit	1.44	1.46	1.10	1.13