

SUPPLEMENTARY MATERIALS

to

Comparative Evaluation of Two Analytical Functions for the Microdosimetry of Ions from ^1H to ^{238}U

Alessio Parisi ^{1,*}, Keith M. Furutani ¹, Tatsuhiko Sato ^{2,3} and Chris J. Beltran ¹

¹ Department of Radiation Oncology, Mayo Clinic, Jacksonville, FL 32224, USA

² Nuclear Science and Engineering Center, Japan Atomic Energy Agency, Tokai, Ibaraki 319-1195, Japan

³ Research Center for Nuclear Physics, Osaka University, Suita, Osaka 567-0047, Japan

* Correspondence: parisi.alessio@mayo.edu

SM1. MCF MKM equations

In the MCF MKM [1, 2], the linear (α) and quadratic (β) terms of the linear quadratic model (LQM) of cell survival are calculated as

$$\alpha = \alpha_0 \int \left(1 + \frac{\beta_0}{\alpha_0} \frac{y}{\rho \pi r_d^2} \right) c(y) d(y) dy \quad (\text{SM1})$$

$$\beta = \beta_0 \left[\int c(y) d(y) dy \right]^2 \quad (\text{SM2})$$

$$c(y) = \frac{1 - \exp \left[-\alpha_0 \left(1 + \frac{\beta_0}{\alpha_0} \frac{y}{\rho \pi r_d^2} \right) \frac{y}{\rho \pi R_n^2} - \beta_0 \left(\frac{y}{\rho \pi R_n^2} \right)^2 \right]}{\alpha_0 \left(1 + \frac{\beta_0}{\alpha_0} \frac{y}{\rho \pi r_d^2} \right) \frac{y}{\rho \pi R_n^2} + \beta_0 \left(\frac{y}{\rho \pi R_n^2} \right)^2} \quad (\text{SM3})$$

where $c(y)$ is a correction factor accounting for the non-Poisson distribution of lethal lesions, y is the lineal energy and $d(y)$ is the dose probability density of the lineal energy, α_0 and β_0 are the LQM terms in the limit of $y \rightarrow 0$, R_n is the mean radius of the cell nucleus, r_d is the mean radius of the subnuclear domains, and ρ is the density of the cell nucleus (set to 1 g/cm^3).

It can be demonstrated [3] that, since R_n is much larger than r_d ,

$$\alpha_0 \left(1 + \frac{\beta_0}{\alpha_0} \frac{y}{\rho \pi r_d^2} \right) \frac{y}{\rho \pi R_n^2} + \beta_0 \left(\frac{y}{\rho \pi R_n^2} \right)^2 \cong \alpha_0 \left(1 + \frac{\beta_0}{\alpha_0} \frac{y}{\rho \pi r_d^2} \right) \frac{y}{\rho \pi R_n^2} \quad (\text{SM 4})$$

Therefore, Equations SM1 and SM2 become

$$\alpha = \int \frac{1 - \exp\left[-\alpha_0 \left(1 + \frac{\beta_0}{\alpha_0} \frac{y}{\rho \pi r_d^2}\right) \frac{y}{\rho \pi R_n^2}\right]}{\frac{y}{\rho \pi R_n^2}} d(y) dy \quad (\text{SM5})$$

$$\beta = \beta_0 \left[\int \frac{1 - \exp\left[-\alpha_0 \left(1 + \frac{\beta_0}{\alpha_0} \frac{y}{\rho \pi r_d^2}\right) \frac{y}{\rho \pi R_n^2}\right]}{\alpha_0 \left(1 + \frac{\beta_0}{\alpha_0} \frac{y}{\rho \pi r_d^2}\right) \frac{y}{\rho \pi R_n^2}} d(y) dy \right]^2 \quad (\text{SM6})$$

For relatively sparsely ionizing radiation such as photons, $c(y)$ is roughly 1 [1, 2].

Therefore, α_0 and β_0 can be derived from the known response of the cells to the reference photons:

$$\alpha_0 = \alpha_{ref} - \beta_0 \frac{\bar{y}_{D,ref}}{\rho \pi r_d^2} \quad (\text{SM7})$$

$$\beta_0 = \beta_{ref} \quad (\text{SM8})$$

where $\bar{y}_{D,ref}$ is the dose-mean lineal energy for the reference photon exposure.

Finally, Equations 4 and 5 in the main body of the article were obtained by substituting the expressions for α_0 and β_0 (Equations SM7 and SM8) into Equations SM5 and SM6.

References

1. Parisi, A., C.J. Beltran, and K.M. Furutani, *The Mayo Clinic Florida microdosimetric kinetic model of clonogenic survival: formalism and first benchmark against in vitro and in silico data*. Phys Med Biol, 2022. **67**(18).
2. Parisi, A., C.J. Beltran, and K.M. Furutani, *The Mayo Clinic Florida Microdosimetric Kinetic Model of Clonogenic Survival: Application to Various Repair-Competent Rodent and Human Cell Lines*. Int J Mol Sci, 2022. **23**(20).
3. Hawkins, R.B., *A microdosimetric-kinetic model for the effect of non-Poisson distribution of lethal lesions on the variation of RBE with LET*. Radiat Res, 2003. **160**(1): p. 61-9.