

## SUPPLEMENTARY MATERIALS

to

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

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### SM1. MCF MKM equations

In the MCF MKM [1, 2], the linear ( $\alpha$ ) and quadratic ( $\beta$ ) terms of the linear quadratic model (LQM) of cell survival are calculated as

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

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

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

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,  $\alpha_0$  and  $\beta_0$  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  $\rho$  is the density of the cell nucleus (set to 1 g/cm<sup>3</sup>).

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,  $\alpha_0$  and  $\beta_0$  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  $\alpha_0$  and  $\beta_0$  (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.