Supplementary material for Minna Wedenberg et al., A model for the relative biological effectiveness of protons: The tissue specific parameter α/β of photons is a predictor for the sensitivity to LET changes, *Acta Oncologica*, 2013;52:580–588

Appendix

For cells irradiated in vitro, the biological response is often described by the clonogenic cell survival fraction. With the linear-quadratic (LQ) model, the survival fraction as a function of dose, D, can be expressed as

$$S = e^{-\alpha D - \beta D^2}, \tag{A1}$$

where α and β denotes the radiosensitivity parameters of the model. The definition of RBE is the ratio of the dose of a reference radiation and the corresponding particle dose giving the same biological response. Based on the LQ model, the RBE of protons can be obtained by equating the expressions for biological response as

$$\alpha D + \beta D^2 = \alpha_{\text{phot}} D_{\text{phot}} + \beta_{\text{phot}} D_{\text{phot}}^2 \tag{A2}$$

where the quantities with the subscript phot refer to photon radiation while the others refer to proton radiation. By rearranging the expression and solving a second-degree equation for the positive root, one obtains

$$D_{\text{phot}} = -\frac{1}{2}\left(\frac{\alpha}{\beta}\right)_{\text{phot}} + \sqrt{\frac{1}{4}\left(\frac{\alpha}{\beta}\right)_{\text{phot}}^2 + \frac{\alpha}{\beta_{\text{phot}}} D + \frac{\beta}{\beta_{\text{phot}}} D^2}\,. \tag{A3}$$

The RBE at a certain proton dose D can then be expressed as

$$RBE = \frac{D_{\text{phot}}}{D} = -\frac{1}{2D}\left(\frac{\alpha}{\beta}\right)_{\text{phot}} + \frac{1}{D}\sqrt{\frac{1}{4}\left(\frac{\alpha}{\beta}\right)_{\text{phot}}^2 + \frac{\alpha}{\alpha_{\text{phot}}}\left(\frac{\alpha}{\beta}\right)_{\text{phot}} D + \frac{\beta}{\beta_{\text{phot}}} D^2}\,. \tag{A4}$$

In this study, the $\alpha/\alpha_{\text{phot}}$ in Equation A4 is expressed as a linear function of LET, L,

$$\frac{\alpha}{\alpha_{\text{phot}}} = 1 + kL \tag{A5}$$

with a slope k that varies with $(\alpha/\beta)_{\text{phot}}$ as

$$k = \frac{q}{(\alpha/\beta)_{\text{phot}}} \tag{A6}$$

where q is a free parameter. Together Equation A5 and A6 gives

$$\frac{\alpha}{\alpha_{\text{phot}}} = 1 + \frac{qL}{(\alpha/\beta)_{\text{phot}}}. \tag{A7}$$

By inserting the expression for $\alpha/\alpha_{\text{phot}}$ (Equation A7) and the assumption made that $\beta/\beta_{\text{phot}} = 1$ into Equation A4, the resulting expression for the RBE as a function of dose, LET, and $(\alpha/\beta)_{\text{phot}}$, becomes

$$RBE\,(D, L, (\alpha/\beta)_{\text{phot}}) = -\frac{1}{2D}\left(\frac{\alpha}{\beta}\right)_{\text{phot}} + \frac{1}{D}\sqrt{\frac{1}{4}\left(\frac{\alpha}{\beta}\right)_{\text{phot}}^2 + \left(qL + \left(\frac{\alpha}{\beta}\right)_{\text{phot}}\right) D + D^2}\,. \tag{A8}$$