SUPPLEMENTARY MATERIALS

to

Clonogenic survival RBE calculations in carbon ion therapy: the importance of the absolute values of α and β in the photon dose-response curve and a strategy to mitigate their anticorrelation

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SM1. α_{ref}/β_{ref} plotted as a function of α_{ref} for ^{12}C ions only

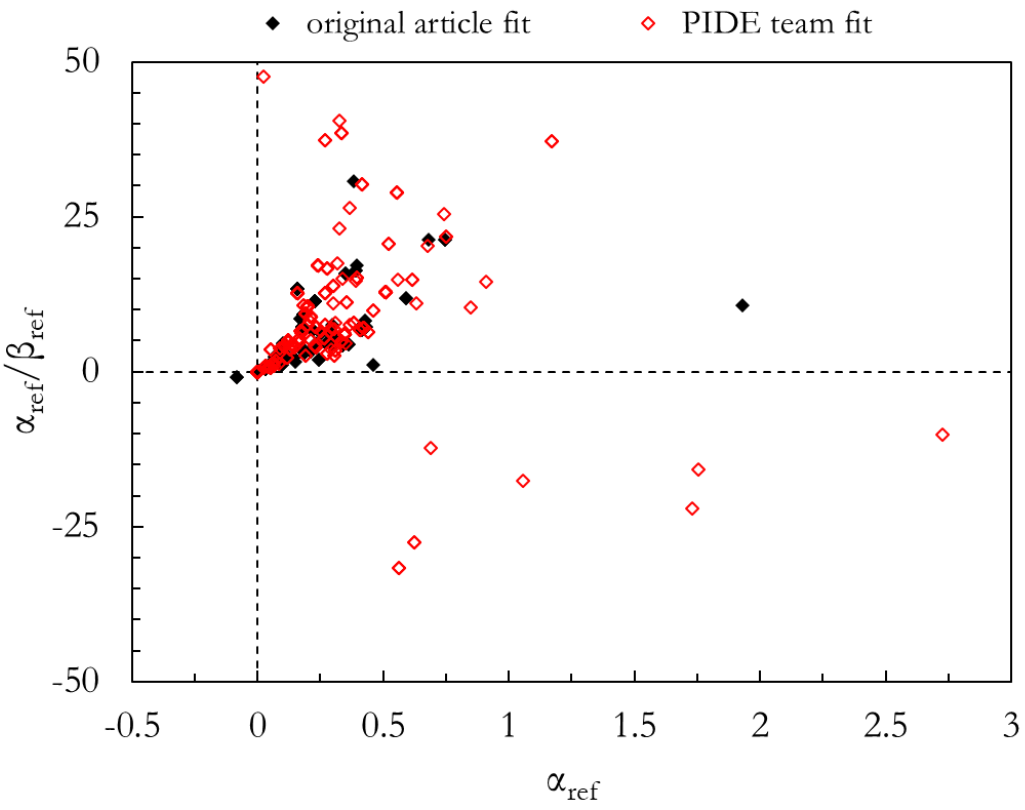

Figure SM1. α_{ref}/β_{ref} plotted as a function of α_{ref} for the asynchronized *in vitro* data from PIDE 3.2 [1] in case of exposures to ^{12}C ions only. The two data series represent the results of the LQM fit performed by the authors of the original publication (full diamonds) and by the PIDE team (open diamonds). To improve the readability of the plot, two in vitro data points were excluded: α_{ref} = 1.73 Gy^{-1}, α_{ref}/β_{ref} = -211 Gy; and α_{ref} = 1.04 Gy^{-1}, α_{ref}/β_{ref} = 3059 Gy.

SM2. Proton-irradiated human glioblastoma cells (U-87 cell line)

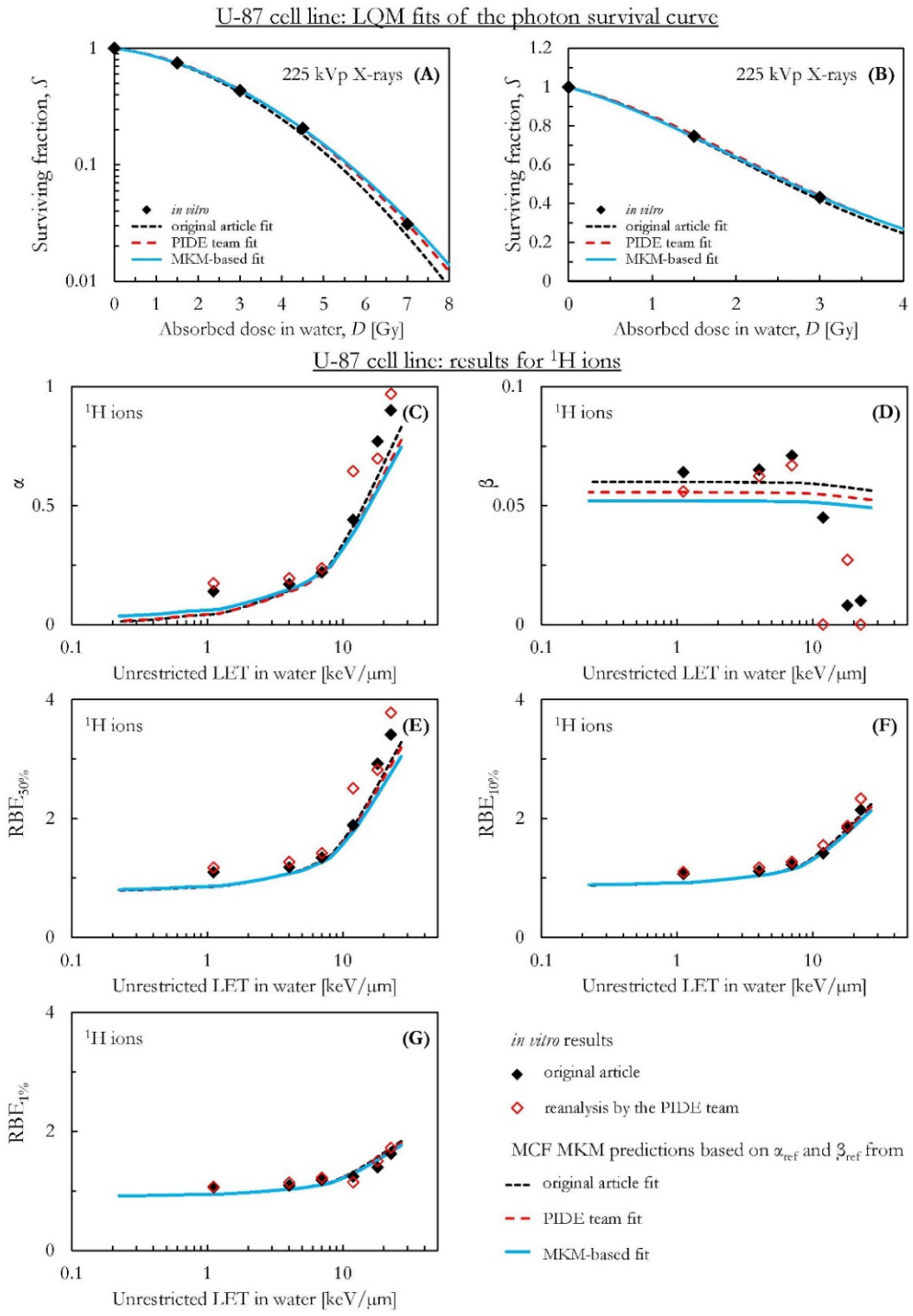

Figure SM2. A) Clonogenic survival of human glioblastoma cells (U-87 cell line) exposed to photons: comparison between the *in vitro* data (black diamonds) and the LQM fits performed by the authors of the original article (black short-dashed line), by the PIDE team (red dashed line), and the novel MKM-based fit (solid blue line). B) Detailed view of the survival data in linear-linear scale. C-G) α, β, $RBE_{50\%}$, $RBE_{10\%}$, and $RBE_{1\%}$ as a function of the LET of protons as experimentally determined by the authors of the original article (black diamonds) and by PIDE team (open red diamonds) in comparison with MCF MKM predictions based on the α_{ref} and β_{ref} obtained by authors of the original article (black short-dashed line), by the PIDE team (red dashed line), and the novel MKM-based fit (solid blue line).

Table SM1. MCF MKM parameters used in the calculations for the U-87 cell line.

Cell line	R_n [μm]	r_d [μm]	LQM fit	α_{ref} [Gy^{-1}]	$\beta_{ref} = \beta_0$ [Gy^{-2}]	α_{ref}/β_{ref} [Gy]	α_0 [Gy^{-1}]
U-87	4.5 [2]	0.3 [2]	original article [3]	0.110	0.060	1.83	-0.029
			PIDE team [1]	0.106	0.056	1.89	-0.024
			MKM-based	0.121	0.052	2.33	0

References

[1] Friedrich, T., T. Pfuhl, and M. Scholz, *Update of the particle irradiation data ensemble (PIDE) for cell survival.* J Radiat Res, 2021. **62**(4): p. 645-655.

[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] Chaudhary, P., et al., *Relative biological effectiveness variation along monoenergetic and modulated Bragg peaks of a 62-MeV therapeutic proton beam: a preclinical assessment.* Int J Radiat Oncol Biol Phys, 2014. **90**(1): p. 27-35.