International Journal of Radiation Biology

ISSN: 0955-3002 (Print) 1362-3095 (Online) Journal homepage: informahealthcare.com/journals/irab20

Comments on the paper "Modelling of cell killing due to sparsely ionizing radiation in normoxic and hypoxic conditions and an extension to high LET radiation" by A. Mairani et al., Int. J. Radiat. Biol. 89(10), 2013, 782–793

Thomas Friedrich, Marco Durante & Michael Scholz

International Journal of Radiation Biology, January 2015; 91(1): 127–128

ISSN 0955-3002 print / ISSN 1362-3095 online
DOI: 10.3109/09553002.2014.952459

informa
healthcare

LETTER TO THE EDITOR

Comments on the paper "Modelling of cell killing due to sparsely ionizing radiation in normoxic and hypoxic conditions and an extension to high LET radiation" by A. Mairani et al., Int. J. Radiat. Biol. 89(10), 2013, 782–793

Thomas Friedrich[1], Marco Durante[1,2] & Michael Scholz[1]

[1]*GSI Helmholtzzentrum für Schwerionenforschung, Darmstadt, and* [2]*Institut für Festkörperphysik, TU Darmstadt, Darmstadt, Germany*

Sir: With interest we have read the article 'Modelling of cell killing due to sparsely ionizing radiation in normoxic and hypoxic conditions and an extension to high LET radiation' by Mairani et al. (2013). In principle we agree with the strategy proposed in the paper, and actually the essential idea of the approach presented by Mairani et al. is conceptually identical to what we have reported in a previous publication as the Giant-Loop Binary-Lesion model (GLOBLE; Friedrich et al. 2012a). We therefore regret that Mairani et al. did not quote our paper, although it was published seven months before they submitted the revised version of their manuscript to the *International Journal of Radiation Biology*.

Concerning photon radiation, the equivalence between the GLOBLE and the method reported by Mairani et al. is clearly evident from the equations and parameters given in the papers. Despite the agreement concerning the general strategy, with regard to the practical application of the GLOBLE approach we noticed several substantial inconsistencies in the paper by Mairani et al, which deserve further careful attention and which will be briefly pointed out in this letter.

Mairani et al. (2103) use experimental data reported by Suzuki et al. (2000) and Combs et al. (2009) for comparison with the model predictions. One would thus expect that the conversion formula (Equation 7) would allow identifying the values given in Table I with the linear-quadratic parameters reported by Suzuki et al. and Combs et al. Intriguingly, Figure 1 suggests such an equivalence, although actually calculating α and β according to Equation (7) leads to substantial deviations from the reported values. The resulting α values are on average 15% smaller, and the β values on average 7% larger than those published by Suzuki et al. and Combs et al. The standard deviation around that mean value is 35% for the α values and 28% for the β values, indicating extremely large fluctuations around the expected values.

We thoroughly tested the GLOBLE model for photon radiation (Friedrich et al. 2012a), and never could observe such huge deviations with respect to the expectations derived from the corresponding LQ-parameters which is also in line with analytical arguments. Consequently, the detected discrepancies in the paper of Mairani et al. (2103) seem not to be due to inherent conceptual problems of the GLOBLE approach, but rather due to differences in the practical application.

We only can speculate here about potential sources for the above mentioned discrepancies. Mairani et al. report that they have re-fit the experimental data and thus might have been using different fitting methods. However, the differences that can be attributed to differences in the fit algorithms are expected to be very small (in the order of typical computing inaccuracies) compared to the actually observed differences, as in the case of simple second order polynomial fits the minimal χ^2 is uniquely defined. Therefore, all minimizers should essentially approach the same parameter values. It would thus be highly desirable if Mairani et al. could explain their methods to derive the model parameters in more detail, since the results cannot be reproduced based on the information given in the paper.

Additional inconsistencies were found in the application to high-LET radiation. These were detected when comparing the results presented by Mairani et al. to our own model predictions, which was straightforward since Mairani et al. refer to the concept of the LEM (Elsässer et al. 2010, Friedrich et al. 2012b) to determine the number of iDSB and cDSB for high-LET radiation. We thus tried to reproduce the calculations shown in Figures 9 and 10 exemplarily for several cell lines. Surprisingly, also here we observed a wide range of deviations from the expected agreement, and neither the parameters given by Mairani et al. nor the parameters derived from the original LQ-parameters allowed to reproduce the results. However, no systematic trend could be observed

Correspondence: Dr Michael Scholz, PhD, GSI Helmholtzzentrum für Schwerionenforschung/Dept. of Biophysics, Planckstrasse 1, D-64291 Darmstadt, Germany. Tel: + 49 6159 71 1340. Fax: + 49 6159 71 2106. E-mail: m.scholz@gsi.de

(Received 8 May 2014; revised 23 July 2014; accepted 4 August 2014)

in these deviations for the different parameter combinations. It is thus unlikely that the deviations can be explained by potential minor differences in the implementation of the approach. Also here, a more detailed description of the modeling procedures would be required in order to decipher the origin of the above-mentioned inconsistencies.

Particularly pronounced discrepancies were found for the results concerning U87-MG and LN229 cells. For both cells lines, the values for K_{cDSB} are significantly lower than those derived from the LQ-parameters reported in the original publications. Here, part of the discrepancy might be due to the fact, that, e.g., for fitting the parameters for LN229 cells the authors seem to exclude the highest dose point from their analysis and also do not display this point in Figure 10, so that the deviation of the predicted curve from the experimental data becomes less obvious. An exclusion of data points, however, is not justified, unless there is a scientific rationale.

In conclusion, we found substantial inconsistencies in the results reported by Mairani et al. (2103) concerning applications to low-LET as well as high-LET radiation. Since the authors aim at the potential application of the approach in the framework of ion beam therapy treatment planning, we feel that a thorough check of the implementation and the resolution of inconsistencies would be urgently required in order to assure the quality and precision needed in this particular field of applications.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

Combs SE, Bohl J, Elsässer T, Weber KJ, Schulz-Ertner D, Debus J, Weyrather WK. 2009. Radiobiological evaluation and correlation with the local effect model (LEM) of carbon ion radiation therapy and temozolomide in glioblastoma cell lines. Int J Radiat Biol 85:126–137.

Elsässer T, Weyrather WK, Friedrich T, Durante M, Iancu G, Krämer M, Kragl G, Brons S, Winter M, Weber KJ, Scholz M. 2010. Quantification of the relative biological effectiveness for ion beam radiotherapy: Direct experimental comparison of proton and carbon ion beams and a novel approach for treatment planning. Int J Radiat Oncol Biol Phys 78:1177–1183.

Friedrich T, Durante M, Scholz M. 2012a. Modeling cell survival after photon irradiation based on double-strand break clustering in megabase pair chromatin loops. Radiat Res 178:385–394.

Friedrich T, Scholz U, Elsässer T, Durante M, Scholz M. 2012b. Calculation of the biological effects of ion beams based on the microscopic spatial damage distribution pattern. Int J Radiat Biol 88:103–107.

Mairani A, Böhlen TT, Dokic I, Cabal G, Brons S, Haberer T. 2013. Modelling of cell killing due to sparsely ionizing radiation in normoxic and hypoxic conditions and an extension to high LET radiation. Int J Radiat Biol 89:782–793.

Suzuki M, Kase Y, Yamaguchi H, Kanai T, Ando K. 2000. Relative biological effectiveness for cell-killing effect on various human cell lines irradiated with heavy-ion medical accelerator in Chiba (HIMAC) carbon-ion beams. Int J Radiat Oncol Biol Phys 48: 241–250.