Oxygen enhancement ratio of heavy ions in partial hypoxic conditions*

M. Durante†[1,2,3], *W. Tinganelli*[1,2], *E. Scifoni*[1], *R. Hirayama*[4], *M. Ozaki*[4], *Y. Kaneko*[4], *A. Maier*[1], *R. Hirayama*[4], *and Y. Furusawa*[2,4]

[1]GSI, Darmstadt, Germany; [2]IOL, NIRS-GSI, Chiba, Japan; [3]TUD, Darmstadt, Germany; [4]NIRS, Chiba, Japan

Hypoxia is a characteristic feature of locally advanced solid tumors resulting from an imbalance between oxygen (O_2) supply and consumption. As a tumor grows, it rapidly outgrows its blood supply, leaving portions of the tumor with regions where the oxygen concentration is significantly lower than in normal tissues. The possibility to scale the dose, but also to exploit in this connection the peculiar features of ion beams, namely the high linear energy transfer (LET) of part of their fields, for targeting specifically the hypoxic regions is highly promising, but requires the most accurate knowledge of the oxygen enhancement ratio (OER) in any voxel of the irradiated tissue, for any configuration of the irradiation parameters [1,2].

The main goal of our study was the verification, with a new set of experimental OER (Oxygen Enhancement Ratio) data points, of a semi-empirical model developed at GSI that is being used for the implementation of adaptive treatment planning in TRiP98 [1], for specifically targeting hypoxic tumors with particle beams. The latter model is based on an extension of the Alper Howard-Flanders formalism, for getting the two-dimensional dependence of the OER on LET of the irradiation mean and the oxygen concentration of the tissue.

Starting from a situation of five experimental points performed at GSI and HIT Heidelberg during the previous years [3] to verify our semi-empirical method other OER measurements were then necessary [4]. In the framework of the IOL, experimental points about the complete anoxic and different partially hypoxic conditions have been measured at NIRS. In the NIRS experiments most irradiations, with X-rays, carbon and silicon ions, were performed with glass petri dishes, seeded with CHO (Chinese Hamster Ovary) cells and gassed together with different mixtures of air, nitrogen and carbon dioxide in order to get the following different concentrations of O_2 (pO_2): 0%, 0.15%, 0.5%, 2%, 21%.

The results of the irradiations performed on the last year confirmed the initial data reported in [4] and are going to be published extensively as the first collection of OER measurements at intermediate range of LET and pO_2 [5]. The full ensemble of data showed a reasonable agreement with the prediction model and with the previous data from GSI, especially in the maximum slope region, where is the largest impact for treatment planning purposes. The higher OER values found for the very high LET are due to the large ions fragmentation, since we used the HIMAC-NIRS passive beam experimental room.

Finally one last experiment has been done to prove our semi-empirical model in an extended target (tumor phantom) irradiation with two opposed fields and for several oxygen concentrations (Fig.1). For the latter experiment the hypoxic chamber developed at GSI were used (left panel). Despite an occurred technical problem of absolute dosimetry, our experimental points, when all the differently oxygenated regions are recomputed with the physical dose scaled to match the oxic control, fit quite well with the calculated prediction data (right panel).

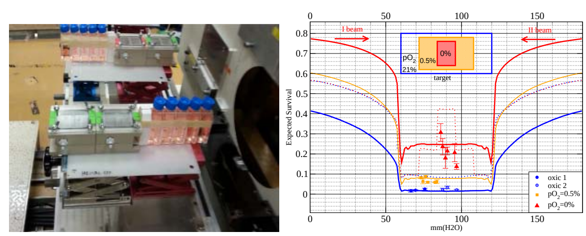

Figure 1: Multiple field irradiation of a complex tumor target with an anoxic core surrounded by hypoxic and then normoxic cells. Left panel: hypoxic chambers used for the irradiation phantom. Right panel: the experimental results are compared with the model prediction.

References

[1] E. Scifoni et al., Phys. Med. Biol. 58 (2013) 3871.

[2] E. Scifoni et al., this Report.

[3] W. Tinganelli et al., J. Radiat. Res. 54 (2013) i23

[4] M. Durante et al., GSI Scientific Report 2012 (2013) 468

[5] W. Tinganelli, M. Durante, R. Hirayama, Y. Furusawa, M. Krämer and E. Scifoni,"Oxygen enhancement ratio for intermediate values of oxygen concentration and LET: first in vitro measurements and impact on treatment planning for hypoxia", *in preparation*.

* Work supported by NIRS International Open Laboratory (IOL) grant to GSI.

† m.durante@gsi.de

doi:10.15120/GR-2014-1-BIOPHYSICS-33