Investigation of substrate- and radiation-dependent cell motility using videomicroscopy

A. Müller, D. Pollet, FH Darmstadt, Germany
M. Scholz, G. Taucher-Scholz, J. Topsch, GSI Darmstadt, Germany

The outcome of tumor therapy like e.g. radiation therapy is closely related to the invasive potential of tumor cells. There are hints, that radiation might increase the motility and the invasive potential of tumor cells, thus counteracting the primary goal of radiotherapy for low-LET-radiation [1], whereas the opposite may be the case for high-LET-radiation [2].

Cell motility and migration can be investigated using e.g. the Boyden chamber assay (see [3]) or by means of video microscopy. For the work presented here, a video microscopy system for long-term observation of individual cells was established and tested. The system consists of a conventional inverted microscope equipped with a mini-incubator allowing to control for temperature, CO_2 and humidity. Aimed at the optimization of the system, the evaporation rate of medium was determined and the growth rate of cells was measured. By using gas permeable, but water impermeable foil lids the evaporation could be minimized, thus assuring optimal cell culture conditions during at least 48 hours.

Analysis of the video image sequences was based on the SIMI BioCell software, and average velocity, the velocity as a function time elapsed since cell birth and the type of movement were measured. The system was used to study in detail the motility of U87 glioblastoma cells with respect to dependence on the substrate and on irradiation with X-rays. The results for X-irradiation presented in this work will serve as reference data for a comparison with experiments using charged particle radiation.

The motility of U87 cells was slightly increased on collagene IV and fibronectin substrates as compared to uncoated culture dishes (see Fig. 1) . Furthermore, cells on fibronectin showed a higher frequency of directional changes during migration as compared to uncoated dishes or dishes coated with collagen IV; this becomes visible in the higher ratio of total to effective velocity. Cells immediately after mitosis showed the highest motility, and velocity steadily decreased with increasing time after mitosis (data not shown).
The proliferation of cells was not influenced by the substrate. However, radiation leads to a reduction of the proliferative capacity in a dose dependent manner.
There was no significant effect of radiation on the motility of cells, independent of the substrate. The variations observed were in the order of below 20% and thus in the range or inter-experimental variations (Fig. 2).

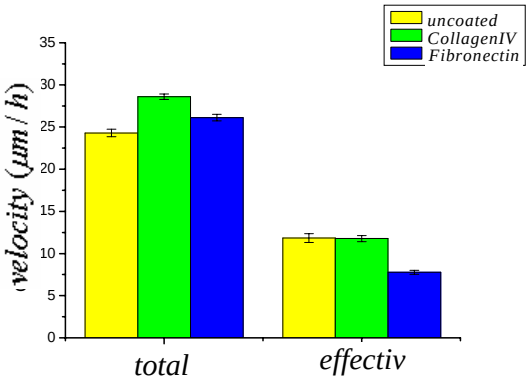

Fig. 1: Substrate dependence of cell motility as measured for U87 glioblastoma cells. Total velocity is defined by the total path length, whereas effective velocity is defined by the shortest distance between the starting and final position of the cell. Measurement interval: 48h

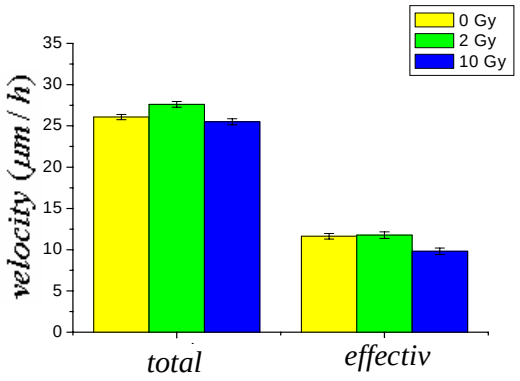

Fig. 2: Impact of X-irradiation on cell motility for U87 glioblastoma cells. Total velocity and effective velocity as defined in Fig. 1. Measurement interval: 48h

[1] Wild-Bode, C., Weller, M., Rimner, A., Dichgans, J., Wick, W., Cancer Res. 61: 2744-2750, 2001
[2] Ogata, T., Teshima, T., Kagawa, K., Hishikawa, Y., Takahashi, Y., Kawaguchi, A., Suzumoto, Y., Nojima, K., Furusawa, Y., Matsuura, N., Cancer Res. 65: 113-118, 2005
[3] Götze, K., Müller-Klieser, W., Taucher-Scholz, G., Scholz, M., this report