

Heavy ion microprobes: a unique tool for bystander research and other radiobiological applications

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New Journal of Physics 10 (2008) 075011 (22pp)

The risk assessment for low doses of high linear energy transfer (LET) radiation has been challenged by a growing body of experimental evidence showing that non-irradiated bystander cells can receive signals from irradiated cells to elicit a variety of cellular responses. These may be significant for radiation protection but also for radiation therapy using heavy ions. Charged particle microbeams for radiobiological application provide a unique means to address these issues by allowing the precise irradiation of single cells with a counted numbers of ions. Here, we focus specifically on heavy ion microbeam facilities currently in use for biological purposes, describing their technical features and biological results. Typically, ion species up to argon are used for targeted biological irradiation at the vertically collimated microbeam at JAEA (Takasaki, Japan). At the SNAKE microprobe in Munich, mostly oxygen ions have been used in a horizontal focused beam line for cell targeting. At GSI (Darmstadt), a horizontal microprobe with a focused beam for defined targeting using ion species up to uranium is operational. The visualization of DNA damage response proteins relocalizing to defined sites of ion traversal has been accomplished at the three heavy ion microbeam facilities described above and is used to study mechanistic aspects of heavy ion effects. However, bystander studies have constituted the main focus of biological applications. While for cell inactivation and effects on cell cycle progression a response of non-targeted cells has been described at JAEA and GSI, respectively, in part controversial results have been obtained for the induction of DNA damage measured by double-strand formation or at the cytogenetic level. The results emphasize the influence of the cellular environment, and standardization of experimental conditions for cellular studies at different facilities as well as the investigation of bystander effects in tissue will be the aims of future research. At present, the most important conclusion of radiobiology studies at heavy ion microbeams is that bystander responses are not accentuated for increasing ionizing density radiation.