New insights into the cellular response to radiation using microbeams

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The Gray Cancer Institute has been involved in the development and application of microbeams of ionizing radiation in a radiobiological context since the early 1990's. The strength of the micro-irradiation technique lies in its ability to deliver precise doses of radiation to selected individual cells (or sub-cellular targets) *in vitro*. Our microbeam uses a 1 μm diameter bore glass capillary to vertically collimate protons, or helium ions accelerated by a 4 MV Van de Graaff. Using $^{3}He^{2+}$ ions, 99% of cells are targeted with an accuracy of $\pm$2 μm, and with a particle counting accuracy >99%. Using automated cell finding and irradiation procedures, up to 10,000 cells per hour can be individually irradiated.

The microbeam technique is a highly effective method for studying a number of unusual and puzzling phenomena that are now known to occur when living cells and tissues are irradiated. One such phenomenon is the so-called 'bystander effect' where unirradiated cells are damaged through signalling pathways initiated by a nearby irradiated cell. This effect predominates at low doses and profoundly challenges our understanding of environmental radiation risk. Furthermore, we now have evidence that simple molecules (such as nitric oxide) are involved in the signalling process, such that it may be possible to chemically influence the bystander response. If so, then this could eventually lead to improvements in the treatment of cancer by radiotherapy. Other studies have shown that the bystander effect is induced with equal effectiveness if either the nucleus or the cytoplasm of a cell is targeted. Also, the bystander effect exhibits an adaptive response, such that a low bathing dose to all the cells prior to targeting one cell will inhibit the bystander response.