Single Particle Irradiation System to Cell (SPICE) at NIRS

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ABSTRACT

Microbeam is a new avenue of radiation research especially in radiation biology and radiation protection. Selective irradiation of an ionizing particle to a targeted cell organelle may disclose such mechanisms as signal transaction among cell organelles and cell-to-cell communication in the processes toward an endpoint observed. Bystander effect, existence of which is clearly evidenced by application of the particle microbeam to biological experiments, suggests potential underestimation in the conventional risk estimation at low particle fluence rates, such as environment of space radiations in ISS (International Space Station). To promote these studies we started the construction of our microbeam facility (named as SPICE) to our HVEE Tandem accelerator (3.4 MeV proton and 5.1 MeV $^4He^{2+}$). For our primary goal, " irradiation of single particle to cell organelle within a position resolution of 2 micrometer in a reasonable irradiation time", special features are considered. Usage of a triplet Q magnet for focussing the beam to submicron of size is an outstanding feature compared to facilities of other institutes. Followings are other features: precise position control of cell dish holder, design of the cell dish, data acquisition of microscopic image of a cell organelle (cell nucleus) and data processing, a reliable particle detection, soft and hard wares to integrate all these related data, to control and irradiate exactly determined number of particles to a targeted spot.

Keywords: ionizing, particle, microbeam, radiation biology, radiation protection

1. INTRODUCTION

Recent evidences of bystander effect gives a strong impact to radiation research at low dose and low dose rate, with respect to mechanisms of radiation actions on one hand, and risk estimation for radiation protection on the other hand. The bystander effect, which has been convincingly evidenced by microbeam irradiation of He ions[1,2,3], appear in biological endpoints including *invitro* cell killing, mutations and oncogenic cell transformation. The microbeam (single particle) irradiation to a cell organelle fastens studies of signal transaction among cell organelle and of cell-to-call communication from the viewpoint of radiation mechanism. It may thus stimulate studies on bystander effect itself, how we quantify it, whether it depends on radiation quality, whether it is modulated by other factors such as varying time interval between successive hits of particles under the condition of microbeam irradiation. The study by microbeam is also relevant to risk estimation at low particle fluence rates, such as in environment of space radiations at ISS (International Space Station). Having these prospects we have started the project to build our microbeam facility named as Single Particle Irradiation System to Cell (SPICE). In this paper we describe our latest version of the plan.

2. MATERIALS AND METHODS

2.1. Accelerator

A tandem and single ended accelerator with a solid state high voltage power supply, Tandetron (HVEE, High Voltage Engineering Europe Ltd.) was installed for PIXE (Proton Induced X-rays Emission) analysis in 1999. The accelerator itself is designed to meet with special features for micro beam applications, achieving terminal voltage ripple 16 Vpp at 1.25 MV, stability ▪ 18 V/3 hr at 1.881 MeV and H^+ beam brightness ▪ 3.9 A・m^{-2}・rad^{-2}・eV^{-1}、using an off-axis Duoplasumatron ion source, an upper stream low energy slit stabilization magnet, a stable high voltage power supply and an upper stream high energy slit stabilization system. The maximum ion energy is 3.4 MeV H^+ and 5.1 MeV He^{2+}.

2.2. Microbeam

A vertical beam port driven up from the horizontal main port by a 90° magnet, as a whole, is installed in a cradle which is hung on a rigid frame structure. In the end of the vertical beam port a focussing triplet Q-magnet, an automated x-y stage of cell dishes and video microscope, are assembled as an a unit solid structure as a whole along the beam port.

This special structure of the beam port will enable the system relatively insensitive against unavoidable environmental vibrations. At height of 4.6m up from floor a workbench is built on the frame structure with a spiral steps to access the workbench. This workbench is workspace for the operator at manipulating the modules such as, the triplet Q-magnet, the beam monitoring, the controller of cell dish stage, the particle detector, the PC operation, electronics, and for users at exchange of sample dishes.

2.3. Acquisition of image data

Light source devices are provided to illuminate a target of a cell. Imaging software works to get coordinates of the target and registers them for successive irradiation. Another software operates precise positioning of x-y stage to the focus point of the microbeam such that a particle irradiates precisely the target registered.

2.4. Control of number of particles

The required number of particle to irradiate is controlled by a combination of two devices, the ion detector embedded in the revolver of the microscope and an electrostatic single ion deflector at a position downstream of the triplet Q-magnet. A thin scintillation counter counts the particles transmitted through the cell and medium. The signals from both the scintillation counter and pre-registered number of particles for irradiation trigger to deflect successive particles off from the beam center axis by the electrostatic shutter within the time around 1 μ s.

2.5. Position resolution required

Position resolution is challenged to achieve that of less than 2 μ m included all relevant factors, such as coordinate acquisition of the target, precise positioning of x-y stage to the beam focussing spot and beam scanning operation.

2.6. Performance of speed of the system

Effort has been made to reduce irradiation time as short as possible from data acquisition to repeated irradiations. At present our estimation as best performance is around 2000 cells / hr.

3. DISCUSSIONS

The processes of design are now finalized to its construction. Experiences in other institutes [4,5,6] suggest that the construction of the facility is only a start for whole processes followed. To achieve actual irradiation of particle to the target of μ m size, tune and adjustment specific in the microbeam require much time and experience. Division of system into modules and independence of software for each module must be important for future revisions. It is the aspects that we consider most at the stage of design. A cell type of cultured mammalian cells that attach down the bottom of cell dish is available for microbeam experiments at present. We are, however, aware of importance of that other type of cells that suspend in medium like blood cell lymphocyte should be irradiated by single particle. More study and some technical innovations for this application are necessary, which is a future subject. The significance of microbeam or single particle experiment resides in new insights, or feedback to conventional broad beam experiments. For instance, the condition of bystander effect being observed in the broad beam is that reaction cross section σ should be estimated at low doses enough to remain fairly large number of cells unirradiated in the dish and at the same time geometrical cross section σg of the target were measured. Then, if the result were $\sigma > \sigma$g , one may suspect bystander effect involved in that broad beam experiment.

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