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Short Communication

Particle induced X-ray emission and ion dose distribution in a biological micro-beam: Geant4 Monte Carlo simulations

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ABSTRACT

The goal of a microbeam is to deliver a highly localized and small dose to the biological medium. This can be achieved by using a set of collimators that confine the charged particle beam to a very small spatial area of the order of microns in diameter. By using a system that combines an appropriate beam detection method that signals to a beam shut-down mechanism, a predetermined and counted number of energetic particles can be delivered to targeted biological cells. Since the shutter and the collimators block a significant proportion of the beam, there is a probability of the production of low energy X-rays and secondary electrons through interactions with the beam. There is little information in the biological microbeam literature on potential X-ray production. We therefore used Monte Carlo simulations to investigate the potential production of particle-induced X-rays and secondary electrons in the collimation system (which is predominantly made of tungsten) and the subsequent possible effects on the total absorbed dose delivered to the biological medium.

We found, through the simulation, no evidence of the escape of X-rays or secondary electrons from the collimation system for proton energies up to 3 MeV as we found that the thickness of the collimators is sufficient to reabsorb all of the generated low energy X-rays and secondary electrons. However, if the proton energy exceeds 3 MeV our simulations suggest that 10 keV X-rays can escape the collimator and expose the overlying layer of cells and medium. If the proton energy is further increased to 4.5 MeV or beyond, the collimator can become a significant source of 10 keV and 59 keV X-rays. These additional radiation fields could have effects on cells and these results should be verified through experimental measurement. We suggest that researchers using biological microbeams at higher energies need to be aware that cells may be exposed to a mixed LET radiation field and be careful in their interpretation of data.

Two other factors can affect the pattern of dose deposition in the biological medium: the phase space distribution of the beam particles and the production of secondary electrons (known as δ-rays). We investigated this by projecting simulated particles oriented at small angles with the beam axis. For lower fluence (2.6×10^4 protons mm^{-2}), we determined that despite only the target cell being assumed to be hit by the particle beam, some significant level of radiation dose was, in fact, delivered to the adjacent cells. This was most probably due to secondary electrons. The simulation showed that two of the cells adjacent to the target cell received 42% and 5% of the dose delivered to the target cell per proton. When the incident fluence on the collimator was increased to 1.3×10^6 protons mm^{-2}, it was observed that a significant number of protons deflected from the collimator spread into an area of 4340 μm^2. This is a significant spread when compared to the target area of 25 μm^2. The maximum number of particles that were delivered off-target was 25% of the particles delivered to the target cell. This equates to a probability of delivering 1 particle anywhere in an area of 4340 μm^2 for every 4 particles delivered to the target cell. This result has significant implications. Results of this work warrant a further investigation because if these results can be re validated, perhaps experimentally or through another simulation code, then they may have significant implications on the interpretation of published data from biological microbeam experiments.

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1. Introduction

The accurate and precise determination of low radiation dose and the subsequent potential effects is a subject of current discussion amongst the scientific community: both beneficial and harmful effects have been observed in cell cultures for low doses of radiation. The beneficial effects (sometimes called radiation hormesis) usually become evident in the form of increased resistance to radiation damage [1], while the harmful effects are manifested as increased mutation and cell death [2]. The available data for making assessments of radiation risk in humans, on a large scale, is very limited and is principally based on studies of the survivors of the atomic bombs that were detonated above Hiroshima and Nagasaki in 1945.

The principle motivation behind this study presented in this paper is to try and better understand the "radiation induced bystander effect". In radiation induced bystander effect studies, cells that were not the primary target of radiation, have been demonstrated to show effects similar to those observed in specifically targeted cells. Radiation induced bystander effect studies usually take one of the two forms either (a) medium is transferred from irradiated cells to non-irradiated cells and subsequent effects in the non-irradiated cells studied or (b) specific targeting of cells is achieved by use of a biological micro-beam. Specific cells are targeted and then nearby cells which are presumed to not have received a radiation dose are studied. Microbeams are presumed to deliver extremely low levels of primary particle fluence, or primary deposited dose, only to the points of interest in radiation biology, such as the cytoplasm or cell nucleus [3,4], in the cell/s of interest, such as HPVG cells and cultured human stem cells [5,6], with presumed little dose being delivered to surrounding cells. Irradiation in this manner is designed to target only specific cells by the initial particle, while sparing others. This Monte Carlo study was a preliminary study to determine if these presumptions in biological microbeam experiments are, in fact, true, and to start discussion at an early stage within the community, via a short communication, as to whether the physics processes in the biological microbeam bystander experiments have been understood completely and correctly.

High LET charged particles generate a significant number of δ-rays (electrons) and photons when they interact with various materials and this includes interactions with cells and cellular media. The extent and biological effects of these δ-rays have been studied and well documented [7,8] although the potential effects are not necessarily always well considered in targeted radiobiology experiments. In addition, the possibility of biological effects that arise as a result of the absorption of photons generated by the primary particle interactions have not been given much attention. Photons can be generated at several points within a microbeam system, for example due to interaction of particles with residual gasses in the beam line, due to interaction of the beam with the cell container material, or due to interaction in the cells. We have performed studies where we irradiated container materials, that could have relevance to radiation biology experiments with protons, and observed the generation of light at UV frequencies [9]. However, in addition to these longer UV wavelengths, we questioned whether short wavelengths (in the X-ray region) could also be produced. These could have obvious effects in biological experiments.

We hypothesized that the X-ray production is especially dependent upon the mechanism of beam collimation employed in a particular microbeam. Collimation can be performed using slits, apertures and/or magnetic focusing. We have been developing a biological microbeam system at McMaster University that uses slits and apertures that is similar to the Columbia University Microbeam [10]. We chose this method because it is robust. However, the particle beam clearly interacts with the collimation system and we questioned the level of production of secondary electrons and X-ray photons. Some of the earliest developed biological microbeam systems used a combination of glass and some suitable scintillating material to confine the beam to the required size and to detect the primary particles [11,12]. Photon generation in the collimation system was integral to such microbeams. The scintillation counters have been replaced by gas-filled particle counters that are placed behind the cell layer in the McMaster University microbeam facility. That is, the beam leaves the collimator, passes through the cell and cell medium layer and is then detected by a gas filled counter. The primary beam therefore requires sufficient energy to pass through the cell layer and be detected. The gas filled counter is of a large surface area and only detects whether a particle has passed through the cell layer. It does not provide spatial information regarding the actual particle track nor does it provide any information if the particle stops within the cellular layer. The experimental assumption is that particles travel along the target path which is determined before turning the beam on. We wanted to test the validity of this experimental assumption.

The McMaster microbeam uses slits and apertures made of tungsten and tantalum to collimate the beam down to a few micrometers in diameter. A lot of the beam is "dumped" and collimation of the beam in this manner means that the system delivers currents of the order of several μA for several minutes to the collimation system with only the required small number of protons reaching the cellular layer. Most of the initial proton beam interacts with the collimator, hence the question of whether these energetic charged particles are capable of producing X-rays of low energies which could change the dose deposition characteristics of the microbeam. We were particularly interested in determining the X-ray dose rates to "non-targetted" cells. There is published evidence of such effects. For example, soft X-rays were intentionally generated using particle induce X-ray emission (PIXE) from titanium to create a soft X-ray microbeam [13].

PIXE is a technique used to determine the elemental composition for various materials and is analogous to our biological microbeam although, of course, our intended fluence is much lower. In fact, the McMaster University microbeam system is built from an accelerator that was used for PIXE work at the University of Guelph. PIXE is a well established technique and the cross section data for the production of X-rays from various materials are available and are incorporated in various Monte-Carlo based simulation codes. We used Geant4 (version 9.5) in order to determine whether X-rays produced in the collimation system are capable of depositing some additional dose to the cells irradiated in the McMaster University microbeam.

2. Microbeam irradiation

In the McMaster University microbeam facility, protons pass through three different stages of collimation. Fig. 1a shows a diagram (drawn to scale) of the actual beam line with the various components used for collimation. The part of beam line shown in Fig. 1a is the (vertical) section after the analyzing magnet (where particles of a specific energy are selectively bent at a 90° angle). At the first collimation stage, the beam is collimated in a rectangular shape with the help of adjustable x–y slits. The second stage is an electronically controlled fast shutter. This shutter has a maximum separation of 60 μm. The shutter is synchronized with the proton detection system, sited beyond the cell irradiation platform, so that after the detection of a pre-determined number of protons, the shutter can be closed. At the third stage, the beam is further collimated using a set of tungsten apertures. Fig. 1b also shows a cross-sectional diagram of the 3rd stage collimator assembly. This