Simulations for X-Ray Synchrotron Beams Using The EGS4 Code System in Medical Applications

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Abstract. X-ray synchrotron beams are commonly used in biological and medical research. The availability of intense, polarized low-energy photons from the synchrotron beams provides a high dose transfer to biological materials. The EGS4 code system, which includes the photoelectron angular distribution, electron motion inside a magnetic field, and the LSCAT package, found to be the appropriate Monte Carlo code for synchrotron-produced x-ray simulations. The LSCAT package was developed in 1995 for the EGS4 code to contain the routines to simulate the linear polarization, the bound Compton, and the incoherent scattering functions. Three medical applications were demonstrated using the EGS4 Monte Carlo code as a proficient simulation code system for the synchrotron low-energy x-ray source.

1 Introduction

X-ray synchrotron beams are widely used in biological and medical researches. The availability of intense polarized low-energy photons produced from the synchrotron beams, offers a high dose transfer to biological objects. During the last decade, several experiments using synchrotron beams had demonstrated a possibility of designing a microbeam using a pinhole with a 30-mm width opening on a few mm length. This way of shaping of a beam is applicable only with a synchrotron beam due to its high intensity. A wiggler magnetic system including a proper filter provided the desired source energy distribution. The energy range for the microbeam study was set to be between 35- to 200-keV (60-keV mean), in order to enable the beam to penetrate through the skull and a few cm of tissue. The microbeam therapy method is based on the assumption that endothelial capillary cells in front of the beam die due to high dose exposure, while the surrounding cells survive and regenerate [1]. In a case of a tumor tissue, the cells will not perform an organized regeneration, and will leave the tissue to starve and to eventually die. A cell culture microbeam experiment was designed to investigate the validity of the microbeam therapy assumption. The change of the absorbed dose profile around a beam was tested for single cell dimensions (10-40 μm) along a 3 mm culture thickness using Monte Carlo simulations. Creating a confined absorbed dose range lead us to a 3-D reconstructed picture of

the damage to the cell culture caused by the radiation. A magnetic field of 6-T magnitude around the cell culture was considered necessary in order to provide the desired absorbed dose confinement along the sample depth.

RNA folding studies have a biological importance due to the diseases that can occur from the aberrant folding of the RNA caused by mutations. Changes in RNA conformation acted as regulatory switches in gene expression and development. X-ray synchrotron beam is used as a technique to resolve early steps in the ribozyme (a catalytic RNA molecule) folding pathway. The X-9A beam-line flux at NSLS (National Synchrotron Light Source) was in the order of 2×10^{11} photons $s^{-1}mm^{-2}$, which was sufficient to cleave 20% of the RNA molecules with duration of 10 ms exposure [2]. "Synchrotron x-ray footprinting" of nucleic acids and proteins, provided us with a unique tool of monitoring the formation of each tertiary contact during the RNA folding reaction

2 Method

The last developments of the EGS4 code system [3] for low energy scattering, and for polarization established the code system as one of the best tools for synchrotron based x-ray simulations. The modular structure of the low scattering photon transport routines, developed by the KEK EGS group [4], enabled us to prepare compound cross sections with form factors and scattering functions as H_2O, air, RNA (as a polymer of $C_5O_5H_7$-P), Lucite, and polypropylene.

The PRESTA (Parameter Reduced Electron-Step Transport Algorithm) [5], an essential procedure for electron transport, was included in every user code in this study due to high sensitivity of dose absorption to secondary electrons at the low energy photon transport. The photoelectron direction distribution was simulated due to the Sauter's angular distribution equation for relativistic electrons [6].

The EMF_MAC.MOR macro was used in order to simulate the electromagnetic field in order to provide absorbed dose confinement in the cell culture application. This EMF_MAC.MOR macro was developed by Bielajew in order to simulate high-energy electron and photon beam dose deposition for radiotherapy [7].

3 Applications

3.1 X-ray Microbeam Radiotherapy

X-ray microbeam radiotherapy (MRT) is a therapy method based on inducing a high dose to an array of narrow regions inside a treated tissue. In the animal experiment stage, the MRT was tested for several brain tumor cases on rats. Other animal experiments were performed in order to ascertain normal brain tissue survival, and therefore the sparing of brain development disorders under the radiotherapy conditions. The MRT parameters such as microbeam array dimensions and spacing were investigated for peak-to-valley absorbed dose ratio

optimization [8]. The dose profile for a synchrotron - produced microbeam was simulated using the EGS4 code system including the low-energy code additions. The experimental results from a MOSFET monitoring micro-dosimeter at 1-μm resolution along 100-μm profile provided a verification for accuracy of the simulations as shown in Figure 1.

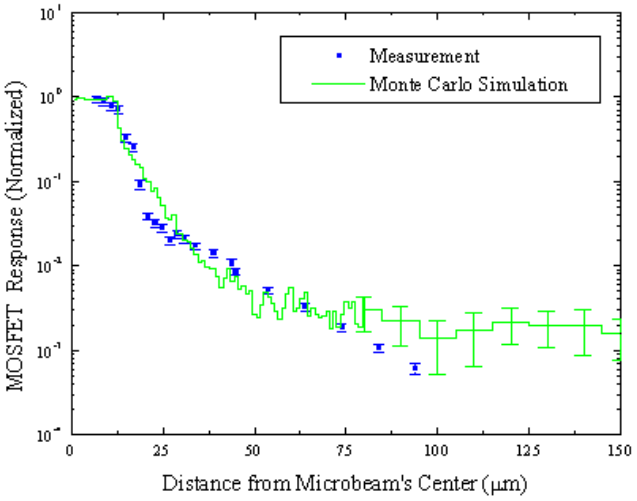

Fig. 1. A comparison of the MOSFET experimental results with the EGS4 simulation results along the microbeam profile up to 100 μm.

3.2 Microbeam with Magnetic Confinement for Cell Culture Simulation

The radiation influence on cell damage and on cell survival is an important issue in therapy treatment studies. X-ray is one of the most common radiation sources to which humans are exposed, from medical treatments, from radiographic imaging, and from radiation working environments. We used the x-ray microbeam method in order to pinpoint the response of every individual cell inside a culture to a given radiation field. A low-energy x-ray source was chosen in order to apply appropriate LET (linear energy transfer) in a cell culture. The simulation included a 3-mm thickness cell culture placed in front of a low energy synchrotron x-ray microbeam (NSLS-beam-line X15). A narrow exposure profile along the whole object was essential in order to extract the cell death in slices along the sample depth.

In case of low energy x-rays, secondary photoelectrons can be emitted in an almost perpendicular direction due to the Sauter angular distribution. A 6-T magnetic field parallel to the x-ray beam direction was included to direct the energy deposition from electron transport along the original beam direction. A comparison of the beam profile with a 0.5-mm thickness central slice, with and without a magnetic field is shown in figure 2. It was essential to check the beam shape confinement along the cell culture depth when adding a magnetic field to the simulation setup. The results of the simulation with the magnetic field are presented in figure 3, which provides an image of the microbeam profile along the sample depth.

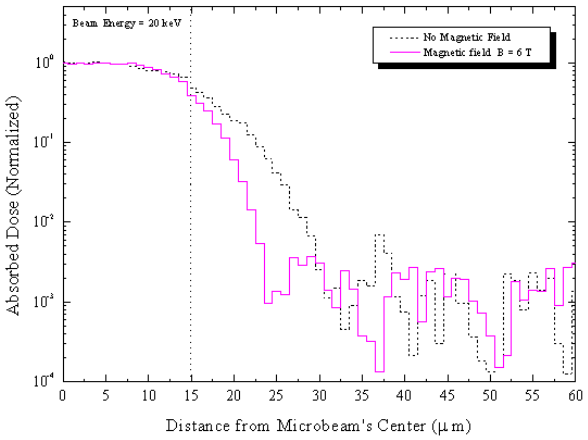

Fig. 2. The profile shape of central slice's absorbed dose for a 30 μm x-ray microbeam, with and without a magnetic field.

3.3 Synchrotron x-ray RNA footprinting

The need of a high LET radiation source with high intensity for x-ray RNA footprinting was recognized since 1993 [9]. The dose absorption in an RNA sample is highly depended on the source spectrum. The characteristics of x-ray generator were investigated in order to develop an available, and cheaper alternative source. The prepared RNA sample is a solution that was put into a polypropylene "Eppendorf" tube (0.5 ml) inside its conic shaped-end sealed by a 1 mm cover made of the same material. We compared the total absorbed dose, and the energy deposit spectra in an RNA sample from a synchrotron x-ray beam and from an x-ray generator source. The flux from the NSLS X9A beam-line was

of the order of 2×10^{11} photons $mm^{-2}s^{-1}$, and the calculated flux of an x-ray generator with 50 kV, 250 mA was of the order of 2.5×10^{8} photons mm^{-2} s^{-1}. The RNA sample inside the conic tube-end absorbed 72.7%, while the tube cover absorbed 24.2% of the beam energy, and the rest escaped or were absorbed by the tube's walls. The differences between the synchrotron beam and the generator source were as followed: spectral shape, polarization, rays divergence, and aperture dimensions.

Three x-ray tube source energies at 50 kV, from different target materials, were simulated in order to optimize the deposited energy on the RNA sample. The absorbed energy results versus the tube targets are summarized in table 1.

Comparisons of the normalized source spectrum and deposited spectrum on the RNA sample are presented for the synchrotron beam and for x-ray tube with Mo target (Figure 4).

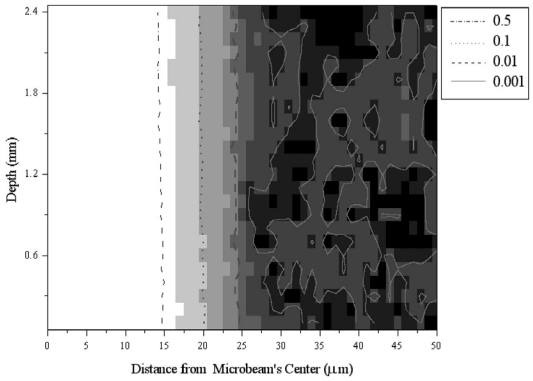

Fig. 3. Simulation results of 2-D image of the absorbed dose on 0.5 mm thickness cell culture slices that were exposed to a 30 μm microbeam (20 keV), with a longitudinal magnetic flux of 6 T.

Table 1. The simulations results of x-ray tubes with three target materials: the deposited energy in the RNA sample region, in the sample cover, and the escaped energy to other regions. (The statistical error is of the order of 0.1%.)

Target	Photon Energy	RNA	Cover	Escaped
Material	(keV)	(%)	(%)	(%)
Cu	9.0	36.7	16.9	46.4
Mo	17.0	46.1	2.6	51.3
Ag	25.5	35.8	0.8	63.4

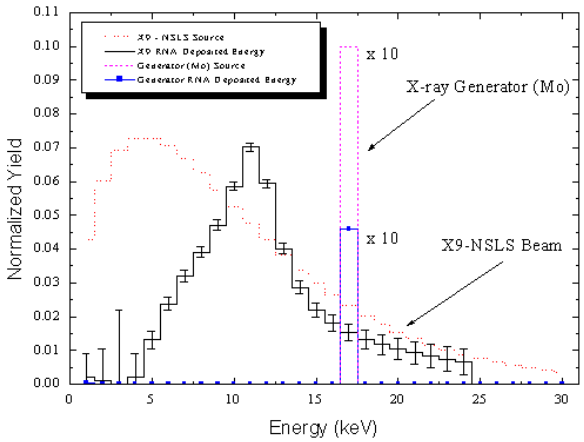

Fig. 4. Spectral distribution of the NSLS X9-A beam source (calculated using ref. [10]), the x-ray tube source line, and the deposited energy on the RNA sample for each source

4 Conclusion

The MRT studies provided a highly spatial resolution measurement of dose distribution along a microbeam profile for 35-200 keV source energies. The comparison of the EGS4 simulation to such an experimental result enabled us to simulate and plan future experiments.

The simulation of cell culture 3-D image reconstruction was essential to set up an experiment that includes the needed electromagnet (6-T). The resolution (presented in figure 1), and the simulated results (presented in figure 2) indicate a possibility of measuring the profile change due to the magnetic field. Knowing the accurate shape of absorbed dose distribution close to the incident beam will provide a confident interpretation of the cell survival effected by well-defined radiation exposure.

The cover of the RNA sample was found to play an important rule in the energy deposition being in front of the source beam, and absorbing a significant fraction of the incident photon flux.

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