Development of an x-ray irradiation port for biomedical applications at the CUEBIT facility

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Development of an x-ray irradiation port for biomedical applications at the CUEBIT facility

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Abstract. Because of the importance of x-ray interactions in modern medicine, efforts must be made to combine the fields of biology and physics. This paper reviews the development of an x-ray irradiation port that allows us to study the interaction of x-rays generated by highly charged ions with biological material, such as stem and cancer cells. Our goal is to better understand these interactions in order to improve the techniques of x-ray therapy by narrowing and specifically selecting the range of radiation energies applied. Using the Clemson University Electron Beam Ion Trap (CUEBIT), the generation of quasi-monochromatic x-rays from highly charged ions is possible. In order to maintain the integrity of the cells being studied, the cell culture needs to be oriented horizontally during the irradiation process. This poses a problem, as the highly charged ion beam generated at the CUEBIT is also oriented horizontally. Therefore, we have designed a system that employs a quadrupole bender that directs the ion beam vertically, which allows for the production of x-rays directly under the cell culture. The experimental station consists of a vacuum chamber that attaches to the end of the beam line. This chamber houses the quadrupole bender, a beryllium window for generating x-rays, and the interface between the beryllium window and the cell culture. X-rays must transmit through the bottom of a flask before they interact with the cells. Hence, we implement a procedure to replace the bottom of the flask with a thin layer of Mylar, allowing x-rays to penetrate through easily. We will use this system to study the effects of monochromatic x-rays on stem cells, cancer cells, and their associated proteins.

1. Introduction

At the Clemson University Electron Beam Ion Trap (CUEBIT) facility, multiple disciplines have combined their efforts to understand how radiation interacts with biological material with the primary goal of developing better imaging and therapy technologies. The development of a practical and effective experimental apparatus is the first step in the advancement towards this goal.

The application of ionizing radiation to control or kill malignant cells has been studied since 1896, and the mechanisms of action are well understood. Radiation therapy works through the creation of free radicals that induce cell death due to events such as double-stranded DNA breaks. Oxygen acts as a radiosensitizing agent, which increases the effectiveness of radiation therapy by boosting the amount of free radical production. However, cancer cells exist in a state of low oxygen concentration known as hypoxia. Therefore, healthy tissues in normal oxygen-rich states are more susceptible to free radical production. This is a problem because external beam radiation therapy – the most common form of radiotherapy – sends radiation through superficial, oxygen rich, healthy tissue to reach the target area. Currently, radiation technologies irradiate cells with a broad spectrum of x-ray energies in a multi-treatment process called fractionation. Given that many bonds between low-Z elements exist in cancerous and healthy tissue, statistically at least some of the x-rays will damage healthy tissue. Even though fractionation allows the healthy tissue to recover, it is not perfectly preventative of serious healthy tissue damage [1]. The development of new techniques and technologies are paramount for the advancement towards safe and more effective radiation therapies.

It has been shown that radiation can damage many different types of cells through a cascade of physical, chemical and biological processes [2,3]. Since stem cells are an integral part of the regeneration and healing processes in the body, a secondary goal of our research is to understand how ionizing radiation affects the differentiation and proliferation of stem cells.

The two hypotheses of this research are: (1) soft, monochromatic x-rays can damage cancer cells and (2) these x-rays can pause the cell cycle of stem cells. The production of soft, quasi-monochromatic x-rays is possible at the CUEBIT facility. Thus, the effects that quasi-monochromatic x-rays have on cancer and stem cells will be tested here using the apparatus discussed in this paper.

2. Development of the x-ray irradiation port:

The CUEBIT produces highly charged ions by passing a high-energy electron beam through a cloud of noble gases, stripping them of their atoms through impact ionization. These ions are then transported down the beam line where additional experiments can be conducted. In order to study the effects of radiation on cell cultures, an experimental apparatus that attaches to the end of the beam line and produces x-rays directly at the cell culture is imperative.

The beam line at the CUEBIT is oriented horizontally with respect to the floor. For the purposes of this research, a horizontal beam line makes it considerably more difficult to test biological samples. The cell culture dish must be sitting upright to support a cell culture with nutrients for an extended period of time. A quadrupole bender is used to bend the horizontal ion beam 90 degrees upwards. This allows the beam to focus on a beryllium window perpendicularly under the cell culture dish.

X-rays are produced via hollow atom decay during recombination at the beryllium window. An interface between the beryllium window and cell culture dish was made that holds the bottom of the dish approximately 1 mm above the window. Thus, the x-rays will not be significantly absorbed by particles in the atmosphere. A custom cell culture dish was developed in order to allow soft x-rays to transmit through with optimal transmission. A schematic of the x-ray irradiation port and its constituent parts can be seen in Figure 1.

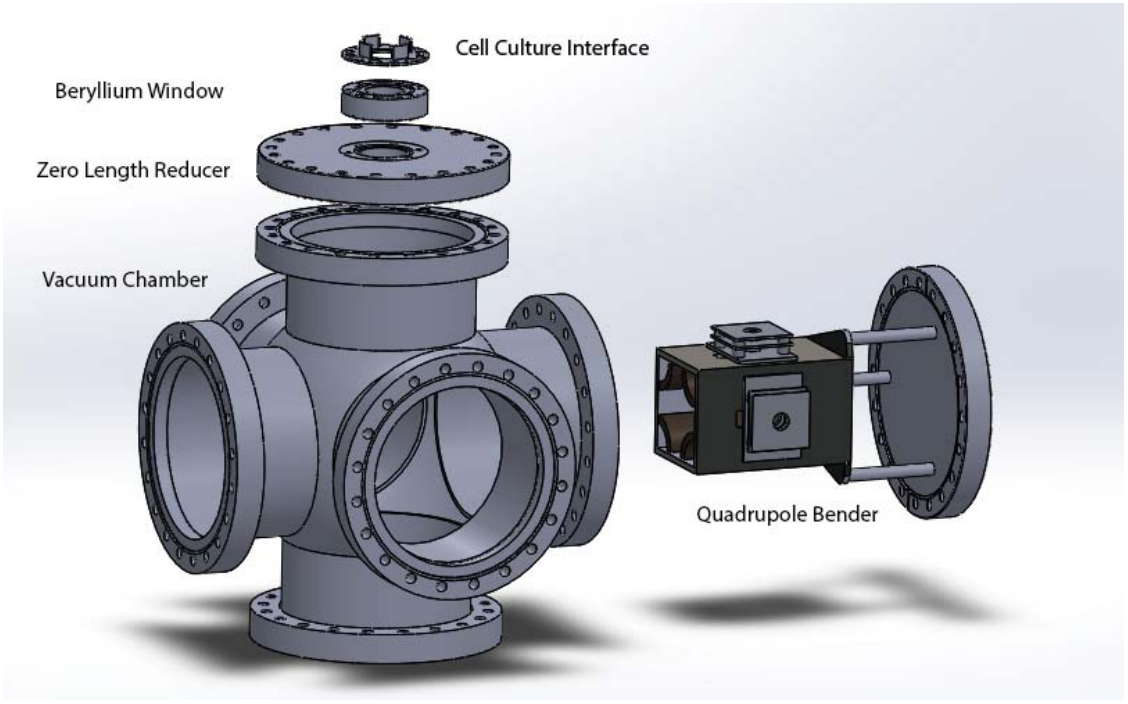

Figure 1. X-ray irradiation port and constituent parts.

2.1 Vacuum Chamber

The vacuum chamber is designed to achieve ultrahigh vacuum pressures on the order of $1.0*10^{-9}$ mbar. This allows the transport of ions through the chamber with minimum recombination. The vacuum chamber houses the quadrupole bender, which must be placed precisely with respect to the ion beam. The chamber has multiple attachment ports that can be used for spectroscopy or beam line imaging.

2.2 Quadrupole Bender

The quadrupole bender used was developed by DREEBIT [4]. It consists of four electrodes of equal potentials and alternating polarities. The incoming highly charged ions in the energy range of about 1*Q keV to 20*Q keV are repelled by the positive electrodes and attracted by the negative electrodes, thus the ions are bent around the first negative electrode by 90 degrees. Q represents the charge of the incoming ions. By changing the voltages applied to the electrodes, different ion beams can be used.

2.3 Beryllium Window

After the beam is bent upward, it is focused onto a 125 μm thick beryllium window, which acts as the barrier between ultrahigh vacuum and the lab's atmosphere. The window is welded to a conflat flange that is attached to the vacuum chamber. Thus, it is grounded and acts as an infinite electron source. As the ions approach the window, they pick up electrons off its surface forming hollow atoms [5]. These electrons will cascade into the lower orbitals late in the decay process, releasing quasi-monochromatic x-rays in all directions. X-rays transmit through the beryllium window and cell culture dish with minimal absorption.

2.4 Cell Culture Interface

The cell culture interface is designed to hold the cell culture close to the beryllium window (approximately 1mm). This allows the x-rays to reach the cell culture with little absorption with

atmospheric particles. It attaches to the flange that supports the window and has a hollow cylindrical port that houses the cell culture dish.

2.5 Custom Cell Culture Dish

Several experiments were performed to determine if x-rays would transmit through cell culture dishes. Using a x-ray fluorescence setup, a range of x-ray lines were directed through standard and custom made cell culture dishes. X-ray lines originated from fluorescing a sample holder, covered with multivitamin powder, by a broadband pyroelectric x-ray source [6]. The results of these experiments reveal that soft x-rays are not capable of transmitting through a typical plastic or silicone based cell culture dish. Therefore, a custom six-micrometer Mylar-bottomed cell culture dish was designed and tested. This experiment confirmed that soft x-rays would transmit through with low absorption. Figure 2 shows the x-ray spectrums after transmission through (a) plastic and (b) Mylar bottom dishes.

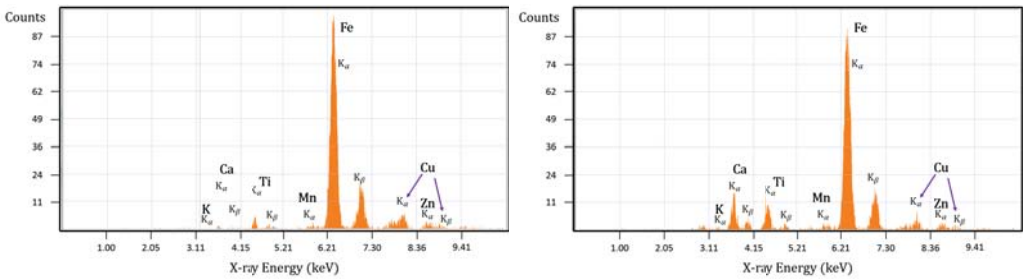

Figure 2. X-ray transmission through plastic (left) and Mylar (right).

3. Conclusion

The development of the x-ray irradiation port at the CUEBIT facility has created much interest in medical and biological physics. Many experiments are being developed in order to better understand how we can use this technology for biological applications. However, preliminary experiments must be performed. The irradiation port will be assembled with an x-ray spectrometer in place of the cell culture to determine the spectra produced with different ion charge states. Additionally, the ion beam collimators must be adjusted to focus the beam onto the beryllium window, which will maximize x-ray production.

Although the production of monochromatic x-rays is possible with simpler technologies, the CUEBIT provides several advantages. The main advantage is that the energy in the admitted x-rays is stored and transported in the potential energy of the highly charged ions. Additionally, charged particles are easy to manipulate, transport, and store. Lastly, at the time of x-ray generation, other radiation – electrons and photons – are generated, which allows for the determination of the exact position of x-ray production.

Computer simulations will also be used to aid with analysis of the results from cell irradiations. With Monte Carlo simulations, the tracks of particles through the biological material can be understood exactly through statistical methods. More developments need to be made in modeling biological material to a high degree of accuracy in current simulation software in order for the results to be meaningful.

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