Nuclear Instruments and Methods in Physics Research B 267 (2009) 2403–2410

Contents lists available at ScienceDirect

Nuclear Instruments and Methods in Physics Research B

journal homepage: www.elsevier.com/locate/nimb

Cell irradiation setup and dosimetry for radiobiological studies at ELBE

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ARTICLE INFO

Article history:
Received 8 October 2008
Received in revised form 22 April 2009
Available online 10 May 2009

PACS:
87.53.−j
87.53.Bn
87.55.−N
07.85.Fv
29.20.Ej
41.60.−m

Keywords:
Radiobiology
Cell irradiation
Dosimetry
Radiochromic film

ABSTRACT

The radiation source ELBE delivers different types of secondary radiation, which is used for cell irradiation studies in radiobiological research. Thereby an important issue is the determination of the biological effectiveness of photon radiation as a function of photon energy by using low-energetic, monochromatic channeling radiation (10–100 keV) and high-energetic bremsstrahlung (up to 40 MV). Radiobiological studies at the research facility ELBE demand special technical and dosimetric prerequisites. Therefore, a cell irradiation system (CIS) has been designed, constructed and installed at the beam line. The CIS allows automatic irradiation of a larger cell sample number and the compensation of spatial inhomogeneity of the dose distribution within the beam spot. The recently introduced GafChromic® EBT radiochromic film model has been used to verify the cell irradiation dose deposition achieving a dose uncertainty of <5%. Both, the installed cell irradiation system and the developed dosimetric procedure based on the use of the EBT film have been experimentally tested at ELBE. The biological effectiveness of 34 MV bremsstrahlung with respect to 200 kV X-rays from a conventional X-ray tube has been determined. An RBE value of 0.75 has been measured in good agreement with literature.

1. Introduction

The basic device of the radiation source ELBE [1,2] is a superconducting electron linear accelerator which provides an electron beam of high brilliance and low emittance with maximum electron energy of 40 MeV and a high average beam current of 1 mA. The electron beam is used for the production of different types of secondary radiation which are applied for several research topics. The primary electrons can also be used for experiments.

The different types of radiation are applied for radiobiological research as one important issue. There the determination of the biological effectiveness of ionizing photon radiation as a function of photon energy [3–5] represents a major scientific objective. Very intense, low-energetic, quasi-monochromatic, and energy tunable (10–100 keV) channeling radiation (CR) is generated by channeling of relativistic electrons in diamond crystals [6] at the radiation physics beam line at ELBE. Additionally, high-energetic bremsstrahlung of up to 40 MV photon energy can be delivered.

The present work is part of radiobiological studies which are related to photon radiation applied in medical application such as mammography screening and radiotherapy. In order to compare radiation qualities, the relative biological effectiveness (RBE) has to be introduced. It is defined by the fraction of the dose delivered by a reference radiation quality to the dose delivered by a given radiation quality, whereas both radiation qualities are responsible for the same biological effect. The general basis of radiobiological experiments is RBE determination by measuring of dose–effect curves for *in vitro* cell systems.

Usually radiobiological studies are performed on conventional high-voltage X-ray tubes or medical acceleration facilities. Both sources deliver broad polychromatic bremsstrahlung with a high photon flux. Thus, therapeutic dose values (few Gy per daily fraction) can be delivered in a sufficiently small irradiation duration (dose rate ≈1 Gy/min) to be independent from repairing processes in human cells. Due to the high reproducibility of beam parameters of conventional radiation sources, a large number of samples can be irradiated in stable conditions in order to cope with the biological diversity. Considering the dosimetry, a standardized radiation field is used. All changes in the radiation geometry resulting in differences of beam absorption, scattering or dose build up effect are taken into consideration by applying tabled correction factors. In practical irradiation experiments, cell samples are irradiated at a vertical beam and the delivered dose is controlled by presetting a certain irradiation duration.

Cell irradiation experiments at the research facility ELBE demand special technical prerequisites which mainly arises from the use of the intense CR. The intensity and the pointing of the

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0168-583X/$ - see front matter © 2009 Elsevier B.V. All rights reserved.
doi:10.1016/j.nimb.2009.04.015

ELBE beam show temporal variations which have to be monitored and taken into account. But also the complex tuning and optimization of the flexible electron beam line by the operators has to be mentioned. Both influence the reproducibility of irradiation experiments. Moreover, the ELBE beam provides a very small divergence, which leads to an increased spatial inhomogeneity of the dose distribution within the beam spot. For this reason the dose has to be measured for each irradiated sample. As a basic and cost efficient instrument self-developing radiochromic film dosimeters (model GafChromic® EBT Prototype A, henceforth referred to as EBT) have been used. Their high spatial resolution, low energy dependence and near tissue-equivalence make them highly suitable for measurements of dose distributions in a wide photon energy range and in radiation fields with high dose gradients [7–9]. The EBT films were applied to quantitatively measure the dose delivered to each individual cell sample and on-line dose rate measurement (ionization chambers) was applied for experimental control.

For the reason of radiation protection regulations after switching of the beam, the cell samples can be taken out of the experiment room only after a waiting time of 20 min. Thus, the irradiation of a larger sample number requires an automatized irradiation procedure for which a cell irradiation system (CIS) has been designed, constructed and installed at ELBE. Spatial inhomogeneity of the dose distribution within the beam spot can be compensated by a special motion feature of the CIS in the case where simple beam scattering methods are not possible (limited intensity and strong attenuation of low-energetic CR). Supplementary, the CIS allows the use of various sample sizes with different geometries according to the biological endpoint to be investigated. For testing a procedure to spatially homogenise the delivered dose over the area of a single cell sample, the EBT films have been applied.

In the following the installed cell irradiation setup at ELBE and the developed dosimetric procedure based on the use of the EBT film will be presented. Finally, first experimental results demonstrating the feasibility of the developed methods will be discussed in detail.

2. Irradiation setup at ELBE

The elements of the radiation physics beam line at ELBE and the design of the CR source have already been described in detail in [6,10]. A schematic drawing of the beam line parts essential for the radiobiological studies is shown in Fig. 1. The electron beam is focused into the target chamber where different target positions are available. The generation of highly intense CR with photon energies in the range of 10–100 keV is realized by introducing diamond crystals (40,...,200 μm thick) [6]. High-energetic, polychromatic bremsstrahlung up to 40 MV is produced by insertion of foils made of aluminum for practical reasons. After passing the target chamber, the photon beam is separated from the electrons by a bending magnet. The photon beam leaves the beam line through a vacuum window of beryllium (19 mm in diameter, 100 μm thick) and is available for experiments at the irradiation site where the cell irradiation system (CIS) is situated. Along the beam line, two electron beam position monitors (BPM) are installed in front of the target area and in the beam dump for beam setting and electron beam current determination. Further beam monitoring devices especially dedicated to electron beam transmission measurements in CR experiments are discussed in [10].

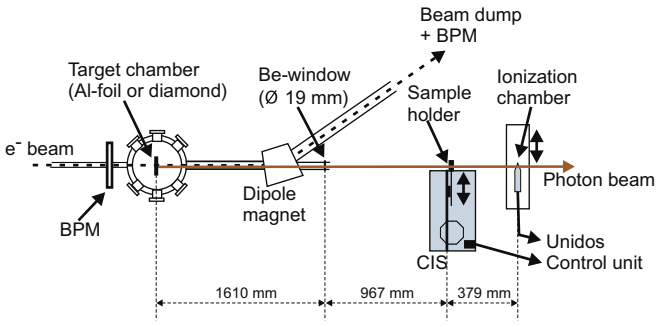

Fig. 1. Schematic drawing of the irradiation site and beam line elements essential for radiobiological studies in the radiation physics cave at ELBE.

It should be mentioned that incomplete electron beam transmission to the beam dump due to scattering of electrons to the walls of the beam line [11] results in an uncontrolled source of bremsstrahlung and neutron background. Due to variations in the beam setting in conjunction with unavoidable electron scattering in the target and, correspondingly, with production of background radiation, the measurement of the electron beam current is not sufficiently sensitive for estimation of photon flux at the irradiation site. Therefore, ionization chambers or alternatively photodiodes placed down the cell sample are used to measure the primary photon flux and to control cell irradiation experiments.

2.1. Cell irradiation system

An automated irradiation system for extensive routine use including user-friendly operation has been designed and constructed in collaboration with IFE-Automatisierungs GmbH and Intronik (both Dresden, Germany). It allows the irradiation of a larger number of cell samples by taking into account geometrical and spectral peculiarities of the radiation source and special cell culture conditions [12], respectively. For illustration, a picture of the CIS is shown in Fig. 2. The CIS consists of a sample supply unit, a control unit and a personal computer. To prevent radiation damages to the control unit, it is placed outside the irradiation site. From the PC console, placed also outside the irradiation room and connected to the control unit, the irradiation procedure is software controlled. Up to 27 cell samples can be positioned in the turnable stack box, transported to the beam position and irradiated separately with a given dose value. To provide defined environment conditions during the irradiation procedure until the moment the samples can be returned to the cell laboratory (about 2 h), the stack box is covered with a plastic lid. Furthermore, a vessel is situated below the samples which can be filled with ice or water at a certain temperature depending on the requirements of the studied biological endpoint. Several cell sample geometries are manageable. All of them can be transported and irradiated from the same stack box (illustrated right in Fig. 2).

The motion of the samples into starting position is provided by two axis, one moves horizontally and the other along the elevator. Both are independently driven by stepper motors. The angle between both axis amounts to 52.5°. This aims at a maximum distance between the beam position and the stack box in order to minimize the influence of background radiation on the cell samples remaining in the stack box. A changeable beam aperture allows additional flexibility in the irradiation geometry, particularly in the case of low-energetic photons.

2.2. Scanning procedure for dose homogenisation

Despite the low electron beam emittance, the photon beam exhibits a significant divergence. This is due to the spread of the electron beam in the target which strongly depends on target thickness and electron energy. Additionally, photon scattering on parts of the beam line and associated beam attenuation leads to a confined beam spot in the plane perpendicular to the beam axis. The spot size corresponds to the diameter of the beryllium vacuum