Applied Radiation and Isotopes 115 (2016) 227–234

Contents lists available at ScienceDirect

Applied Radiation and Isotopes

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

Facility for gamma irradiations of cultured cells at low dose rates: design, physical characteristics and functioning

Giuseppe Esposito [a,b], Pasquale Anello [a], Ilaria Pecchia [a], Maria Antonella Tabocchini [a,b], Alessandro Campa [a,b,*]

[a] Health and Technology Department, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Roma, Italy
[b] INFN Roma1, Gruppo Collegato Sanità, Viale Regina Elena 299, 00161 Roma, Italy

HIGHLIGHTS

- A gamma irradiation facility for chronic exposures of cells was set up at the Istituto Superiore di Sanità.
- The dose rate uniformity and the percentage of primary 662 keV photons on the sample are greater than 92% and 80%, respectively.
- The GEANT4 code was used to design the facility.
- Good agreement between simulation and experimental dose rate measurements has been obtained.
- The facility will allow to safely investigate different issues about low dose rate effects on cultured cells.

ARTICLE INFO

Article history:
Received 4 August 2015
Received in revised form
9 June 2016
Accepted 18 June 2016
Available online 24 June 2016

Keywords:
Gamma irradiation facility
Chronic exposures
Cell cultures
GEANT4 simulations
EBT3 GafChromic films

ABSTRACT

We describe a low dose/dose rate gamma irradiation facility (called LIBIS) for in vitro biological systems, for the exposure, inside a CO_2 cell culture incubator, of cells at a dose rate ranging from few μGy/h to some tens of mGy/h. Three different ^{137}Cs sources are used, depending on the desired dose rate. The sample is irradiated with a gamma ray beam with a dose rate uniformity of at least 92% and a percentage of primary 662 keV photons greater than 80%. LIBIS complies with high safety standards.

1. Introduction

Ionizing radiation has always been naturally present in our environment. It comes from outer space, from the ground, and even from within our own bodies. It is present in the air we breathe, in the food we eat, in the water we drink, and in the construction materials we use to build our homes. Exposure of the population to ionizing radiation at low dose rates is therefore unavoidable (Hutchison and Hutchison, 2004; IAEA, 2005; Khan et al., 2012). Furthermore, by now the medical use of radiation has become an important part of modern healthcare, both for diagnostic and for therapeutic procedures. However, notwithstanding the clear clinical advantages, there is some risk of adverse radiation effects. The computation of the risk of detrimental health effects of ionizing radiation at high doses is now well established; in contrast the evaluation of the effects of low doses, or of prolonged exposure at low dose rates, has not yet reached the same level of knowledge (see, e.g., (Morgan and Bair, 2013) and references therein). In this context, the study of the biological effects induced by the exposure to ionizing radiations at low doses and at low dose rates is of great importance for public health. Specifically, it may have implications for the applicability of the linear no threshold model in extrapolating radiation risk data to the low-dose region (ICRP, 2007).

Carrying out long time experiments at very low doses/dose rates is, at present, a hot topic for the scientific radiation protection research community. Radiobiological responses in these exposure scenarios have been scarcely investigated so far, primarily due to the lack of facilities allowing this type of exposure in controlled conditions. For in vitro studies on the radiation induced

* Corresponding author at: Health and Technology Department, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Roma, Italy.
E-mail addresses: giuseppe.esposito@iss.infn.it (G. Esposito), pasquale.anello@iss.it (P. Anello), ilaria.pecchia@iss.it (I. Pecchia), antonella.tabocchini@iss.it (M.A. Tabocchini), campa@iss.infn.it (A. Campa).

http://dx.doi.org/10.1016/j.apradiso.2016.06.018
0969-8043/

damage in cellular systems following protracted exposure to ionizing radiation, experiments must be done under well controlled conditions: dose and dose rate are to be measured with great accuracy and kept as uniform as possible on the sample; physiological conditions must be guaranteed for the duration of the experiment, that can last days or even several weeks, by maintaining the proper values for parameters such as temperature, humidity and CO_2 concentration.

Nowadays, some facilities for exposure of samples at different dose rates are already in operation. Among them, the Canadian Nuclear Laboratories apparatus, the Sandia gamma facility and the Tunisian facility are used for calibrating nuclear radiation instrumentation, irradiating personnel dosimetry badges, space technology development, military systems vulnerability testing, nuclear reactor component development, preservation of foodstuff, sterilization of medical devices. They are not used for radiobiological experiments. In Europe there are two irradiation facilities for irradiation of cells at low dose rates, one at the Stockholm University (SU), Sweden, and another at the Public Health England (PHE), UK. In this paper we describe the design, physical characteristics and functioning of a new facility; it nicely complements the two already existing, since it presents several innovative important features. They can be summarized in the following points: *i*) the Cesium sources are inside the cell culture incubator; *ii*) the whole range of possible dose rates is obtained without the use of filters; *iii*) it allows to perform irradiation experiments with cell cultures at dose rates down to 2 μGy/h, i.e., only one order of magnitude higher than the natural background. The first two points are important because they allow to change as little as possible the energy of the photons incident on the cell sample. This could be relevant because the variation of the energy also involves a variation of the photon beam quality and, possibly, of its biological effectiveness (see, e.g., (Hunter and Muirhead, 2009)). The third point is even more important since it allows to obtain radiobiological data on cell cultures over a range of dose rates up to now inaccessible for the experiments. Our facility, called LIBIS (Low dose/dose rate gamma Irradiation facility for in vitro BIological Systems) was set up at the Istituto Superiore di Sanità (ISS), Italy. It allows the exposure, inside a CO_2 cell culture incubator, of cultured cells to low gamma doses at a dose rate ranging from few μGy/h to some tens of mGy/h.

Among the limited data sets dealing with low/very low dose rate effects, we want to mention the experiments carried out at the Stockholm University facility using endothelial cells (HUVEC) that have been chronically exposed to dose rates of 1.4, 2.4 and 4.1 mGy/h for 1, 3, 6 and 10 weeks. The results have shown modulation of proinflammatory response, premature senescence and associated proteomic changes (Yentrapalli et al., 2013a, 2013b; Ebrahimian et al., 2015). Other studies were carried out for period of times lasting some months in an extremely low radiation environment at the underground Gran Sasso National Laboratory of the National Institute of Nuclear Physics (INFN), Italy. These long term experiments on cultured cells have shown that environmental radiation contributes to the development and maintenance of cellular defense mechanisms (Fratini et al., 2015). Use of LIBIS can help to investigate the dose rate dependence of the capability of in vitro biological systems to develop stress response mechanisms. Finally, LIBIS may be used in the field of biodosimetry, allowing to extend investigation of the dose rate dependence of micronuclei induction and chromosome aberrations (Bhavani et al., 2014; Bakkiam et al., 2015; Tamizh Selvan et al., 2015) to very low dose rate values.

2. Design of the facility

2.1. Gamma-ray sources

To cover the wide dose rate range from few μGy/h to some tens of mGy/h, three ^{137}Cs sources with very different activities were ordered from the chosen supplier (Eckert & Ziegler Nuclitec GmbH, Braunschweig, Germany).

^{137}Cs decays with a half-life of 30.05 years by β^- emission to the ground state of ^{137}Ba (emission energy 1175.63 keV, emission probability 5.64%) and via the 662 keV isomeric level of ^{137}Ba ($^{137\,m}$Ba) (emission energy 513.97 keV, emission probability 94.36%). The following decay of $^{137\,m}$Ba (half-life of 2.55 min) yields a gamma ray with an energy of 661.657 keV (emission probability 90%), an X-ray with an energy of about 32 keV (emission probability 9%) and Auger electrons (emission probability 1%). Therefore, from the decay of ^{137}Cs we have gamma rays with energy of about 662 keV, with an emission probability of 84.92%, plus β^- particles, X-rays and Auger electrons (Bureau International des Poids et Mesures, 2006).

The three sources are extended sources, with the emitting volume constituted by a cylinder with a diameter of 4 mm and a height of 4 mm. The sources contain the radionuclides as a pellet of solid Cesium-ceramic doubly encapsulated in welded stainless steel. The temperature of 37 °C and the high level of humidity inside the cell culture incubator have no effect on the ^{137}Cs sources, that are mechanically stable, insoluble in water and can be used in a wide range of temperature from −40 °C up to +80 °C. As of August 24, 2012, the total activities of the sources are 37 MBq, 740 MBq and 18.5 GBq, respectively. The sketch of a source is shown in Fig. 1. The β^- particles and the Auger electrons are readily stopped by the 1.4 mm thick stainless steel layer encapsulating the source (ICRU, 1984). Considering the value of the mass attenuation coefficient, μ/ρ, for the stainless steel and for the energy of 32 keV, it can be seen that only about 0.07% of the X-rays with energy of 32 keV cross the stainless steel layer. The dose rate incident on the cells is, tehrefore, almost exclusively due to the 662 keV photons, while the contribution of the 32 keV X-rays is extremely low. In the following, in the section dedicated to the description of the GEANT4 simulations, the contributions to dose rate are quantified.

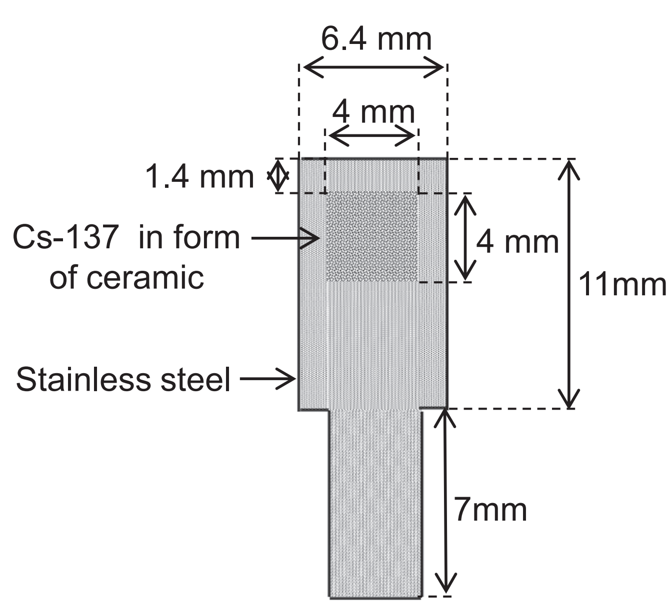

Fig. 1. Sketch of the ^{137}Cs sources (manufacturer: Eckert & Ziegler Nuclitec GmbH).