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Dosimetry for radiobiology experiments at GANIL

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ABSTRACT

Mainly encouraged by the increasing application of ion beams for cancer treatment (hadron-therapy) including carbon beams, the use of heavy ion facilities for radiobiology is expanding rapidly today. As an alternative to dedicated centers for treatment and medical research, accelerators like GANIL offer the possibility to undertake such experiments.

Since 20 years, CIMAP, reinforced 15 years ago by the biological host laboratory LARIA, has been receiving researchers in radiobiology and assisted them in performing experiments in different fields such as hadron-therapy, space radioprotection and fundamental biological and physico-chemical mechanisms. We present here a short description of the beam line and the on-line equipments that allow the automatic irradiation of up to 24 biological samples at once.

We also developed an original on-line beam monitoring procedure for low ion flux (low dose rates) based on the measurement of the K-shell X-rays emitted from a thin iron foil. This detector is calibrated on an absolute scale before each experiment by counting etched tracks on an irradiated CR39 polymer plate. We present the performances and limits of this method and finally give typical fluence (dose) uncertainties for a standard irradiation in radiobiology.

1. Introduction

The spectacular development of radiobiology during the last decades is largely due to advances in hadron-therapy and therapeutic hopes it raises in the treatment of cancers. Hadron-therapy is indeed an innovative technique based on the use of heavy ion beams or protons for tumor treatment in either replacement of or addition to widely practiced X-rays treatments.

Unlike X-rays, the energy deposition of the hadrons can reach a maximum and be very well localized in-depth. This ballistic exploitation and the resulting accuracy of the well known Bragg curve gives strength to this method, as it seems more appropriate to treat internal localized tumors in the vicinity to radiation-sensitive organs which would be considerably affected by the radiation field of less localized energy deposition by X-rays [1].

Although the idea of using proton beams for radiotherapy has been suggested very early in the 1940s by Robert Wilson [2], the first real clinical treatment centers (exclusively for clinical applications) were born in 1990 (LLUMC, Loma Linda University Medical Center). Their number is now increasing rapidly and expected to exceed 50 in 2015 [3] with a result of 110,000 patients treated worldwide (85% in protons).

Heavy ions present both higher dose deposition capacities and better ballistic properties and in particular, carbon ions appear to have some significant clinical benefits [4]. Until a few years ago, carbon treatment centers were not numerous and mostly localized in two countries (HIMAC, HIBTM, NIRS in Japan and GSI in Germany).

But with the advent of new generations of low cost turnkey accelerators, dedicated to industrial use, treatment center projects are multiplying (CNAO, HIT, MEDAUSTRON, ARCHADE, only to mention Europe) [5]. Pending the construction of these new centers, the demands of beam time for research purposes are increasingly important, which mainly explains the use of structures originally designed for other applications. Thus, at GANIL (Grand Accélérateur National d'Ions Lourds, Caen, France) a quota of beam time is intended for interdisciplinary (i.e. non nuclear) research, including radiobiology. The laboratory CIMAP (Centre de recherche sur les Ions, les MAtériaux et la Photonique) undertakes

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the interdisciplinary research at GANIL and manages, through its so called CIRIL[1] platform and together with the biology laboratory LARIA (Laboratoire d'Accueil et de Recherche avec les Ions Accélérés, CEA), the hosting of experiments in radiobiology [6].

The GANIL accelerator can provide various beams, from carbon to uranium, at maximum energies ranging from 95 MeV /A for light ions down to 24 MeV/A for uranium. This diversity allows expanding the activities to space radiation biology studies and the study of fundamental processes. On the other hand, cyclotrons supply only a fixed energy[2], but which can be reduced afterward by beam degraders.

In Part 2 we describe the beam line and instruments that have been developed for radiobiology experiments. This adaptation of a physics machine to biological context with its specific constraints is reinforced by the presence of LARIA since 2003. Part 3 is dedicated to the monitoring of low beam intensities and the description of dosimetry carried out for each experiment. The proposed method aims to be not only compatible with the specificities of a large nuclear physics facility, but also to guarantee a good repeatability which is of a great interest for experiments sometimes spaced by more than a year. An evaluation of standard uncertainties will be given.

2. Beam line and equipments

2.1. Beam line

The radiobiology experiments take place in the D1 cave on the so called IRRABAT beam line, which is also the name of the diagnostic and experiment vacuum chamber used in a standard way for high energy irradiations. At the end of the line, after crossing a stainless steel window of 25 μm thickness, an automated sample holder of 24 positions is installed. It allows handling and processing in a single irradiation run a set of 4 lines with 6 flasks each, in order to limit the number of time consuming access into the cave. Vertical and horizontal motions are controlled by two step-motors allowing a precise positioning of the samples in front of the beam.

The optics of the line was adapted to focus the beam behind IRRABAT, just on the position of the flasks. The standard characteristics of the beam are the following ones[3]: a spotlight on the target of 13×13 mm^2 size, a deflection angle (semi angle with the medium beam axis) of 10 mrad in horizontal direction and 15 mrad in vertical direction, an emittance of 5×5 π.mm.mrad and a resolution in energy $\Delta W/w$ of 0.007 (see Figs. 1A and 2).

With the help of two fast scanning magnets, the beam is swept horizontally at a frequency of 425.8 Hz and vertically at a frequency of 4.4 Hz. Both frequencies are chosen to avoid that one is a multiple of the other. In this way, no spatial structure (like Lissajous figure) is artificially created, which would damage the homogeneity of the dose deposition. The maximum reachable scanning surface is 60×60 mm^2, allowing a maximal irradiation field large enough for a 25 cm^2 flask. A couple of horizontal and vertical slits delimit accurately the irradiation field area. This data is used in the calculation of the fluence. Upstream of the line, a thin Ta foil can be inserted into the beam path in order to smooth and homogenize the beam spot, if needed.

At the beginning of each experiment the radiation field defined by both the amplitude of scanning and the position of the slits (Fig. 1B), is visually controlled by irradiating (with a dose of usually around 8 Gy) a Gafchromic EBT2 type film, placed on a flask in the sample holder. Until now, these films were only used for checking the size and position of the radiation field, but it might be possible in the future to use them for an additional dosimetry by exploiting the optical density variations of the film. Some teams are working on this topic [7–9].

The precise beam spot position depends on each upstream beam tuning, so the zero beam position has to be adjusted by use of set of horizontal and vertical steerers. This zero position is placed out of the irradiation area (that is "in the slits"), where the scanning amplitude is zero. This allows, on the one hand, setting the reversal point of the sweeping out of the area to be irradiated, so as not to impair the homogeneity of the dose deposition, and, on the other hand, protecting the sample in case of failure of the scanning magnets.

2.2. Biological side: LARIA facility

The radiation-biology research laboratory LARIA embedded at GANIL hosts experiments in biology thanks to a partnership with CIMAP. The biology platform operated by LARIA includes a comprehensive tissues culture room, a molecular biology laboratory and a proteomic laboratory allowing hosted teams to perform various canonical assays in the radiation biology field. Furthermore, the platform may be adapted for special requirements if needed. The automatic biological sample holder may be used with 12.5 and 25 cm^2 flasks, tubes (0.5; 1.5; 2 and 15 ml), lab-tek™ chamber slide, 8 cm^2 culture dishes, 96-well plates (36 wells irradiated).

Fields of interest of platform users are either radiation protection of space travelers (healthy tissues) or cancer treatment (tumors and surrounding healthy tissues). During the late 15 years, multiple ions were used with an emphasis on carbon ions. To date, 20 peer-reviewed articles of radiation biology were published with data obtained at GANIL on the IRRABAT beam line, as summarized in the table of Annex 1.

3. Dosimetry

3.1. Method and main results

The typical dose rates used during a radiobiology experiment are of the order of few Gy/min (equivalent in water), this implies, for a ^{12}C beam of 75 MeV/A, fluxes of about 3 10^5 ions/(s·cm^2) which, considering the typical radiation fields, corresponds to $\approx 10^7$ ions/s. This intensity is far too low to be correctly measured and monitored by the standard methods applied at GANIL for non-biological samples. The latter are based on current measurements for monitoring the beam intensity via Faraday cups, and the secondary electron emission of a thin metallic foil [10]. The alternative method developed in the laboratory is based on the measurement of the emitted K-shell X-rays when the beam passes through a thin metallic foil.

Dosimetry, or calibration of this X-ray detector, is divided into two stages:

1. Calculation of the expected X-ray count rate. This step may be optional, since it does not belong to the calibration process itself, but it saves a considerable amount of time by adjusting immediately the different parameters of the detector to the right range of fluence.
2. Calibration of the whole detector and acquisition chain by an absolute measurement of the fluence by means of a CR39 polymer sheet track-etched detector.

3.1.1. Set-up

A thin metallic (Fe) foil (from 5 up to 25 μm thick and tilted with respect to the beam axis) is placed inside the IRRABAT chamber (item 'a' on Fig. 3). A 25 μm thick stainless steel exit window (item 'b' on Fig. 3) 15 cm downstream, separates the high vacuum in the beam line

[1] CIRIL: Centre Interdisciplinaire de Recherche avec des Ions Lourds; www.cimap.ensicaen.fr.

[2] The tuning of the cyclotrons to a new energy takes time on the experiment. It is generally an option which is not retained by the experimenters.

[3] These values might slightly change from an experiment to another