Preliminary results of proton beam characterization for a facility of broad beam *in vitro* cell irradiation

A.-C. Wéra^{a1}, K. Donato^b, C. Michiels^c, Y. Jongen^b and S. Lucas^a

^a *Laboratoire d'Analyses par Réactions Nucléaires (LARN), University of Namur-FUNDP*

Rue de Bruxelles, 61, B-5000 Namur, Belgium

^b *Ion Beam Application, Chemin du Cyclotron 3, B-1348 Louvain-la-Neuve, Belgium*

^c *Unité de Recherche en Biologie Cellulaire (URBC), University of Namur-FUNDP*

Abstract

The interaction of charged particles with living matter needs to be well understood for medical applications. Particularly, it is useful to study how ion beams interact with tissues in terms of damage, dose released and dose rate.

One way to evaluate the biological effects induced by an ion beam is by the irradiation of cultured cells at a particle accelerator, where cells can be exposed to different ions at different energies and flux.

In this paper, we report the first results concerning the characterization of a broad proton beam obtained with our 2 MV tandem accelerator. For broad beam *in vitro* cell irradiation, the beam has to be stable over time, uniform over a $\sim 0.5 \text{ cm}^2$ surface, and a dose rate ranging from 0.1 to 10 Gy/min must be achievable. Results concerning the level of achievement of these requirements are presented in this paper for a 1 MeV proton beam.

¹ Corresponding author: A.-C. Wéra, Rue de Bruxelles 61 – 5000 NAMUR-Belgium, +3281 72 54 79, +3281 72 54 74 (fax), anne-catherine.wera@fundp.ac.be

Introduction

The interaction of charged particles with living matter has become increasingly interesting for medical applications like radiotherapy, radioprotection and space radiobiology [1-7]. In this field, particle accelerators are helpful due to the wide range of available ions, energies and flux. Dose fractionation can be also studied with an accelerator. Usually, two types of configuration are found: micro/nano beams and broad beams. A microbeam can precisely target a defined point on a cell or a group of cells. In this way, cytoplasm and/or nucleus irradiations can be performed [8-10]. However, cell recognition software, cell alignments and beam scanning need to be developed and subsequently makes the system very expensive. Moreover, focalised beam lines are generally operational for only two or three type of ions. On the other hand, broad beams [11, 12] allow the use of a wide range of ions. Thousands of cells can be irradiated simultaneously and additional stresses, like temperature effects, can be minimized. Unfortunately, with broad beam, particles Poisson distribution leads to dose error. With these set-ups studies like clonogenic assays or immunofluorescence can be performed and precious information can be inferred, especially for hadrontherapy.

In 2007, the LARN laboratory (Laboratoire d'Analyses par Réactions Nucléaires) decided to develop a cheap *in vitro* irradiation station using broad beam. This paper reports preliminary results obtained for a proton beam. Cell irradiation experiments require the beam to possess certain properties. In our set-up, the beam must have a spatial uniformity of $\pm 5\%$ over an approximately 0.5 cm^2 surface and be stable during the irradiation. Indeed, for the same experiment, a homogeneous dose must be deposited within the cells and the dose rate must be constant. In this paper, we present the set-up, beam uniformity, beam stability and dose rate achievable with our system. Results of cell irradiation will be presented elsewhere.

Materials and Methods

LARN facility

The LARN accelerator is a 2 MV Tandem accelerator (High Voltage). It consists of three sections: a dual source injecting system, a high voltage accelerating tube, a switching magnet with 5 beam lines. Due to two different sources, particles from Hydrogen to Uranium can be accelerated. Beam energy is determined by the terminal voltage, adjustable from 0.15 to 2 MV.

Once particles are accelerated, they enter the selected beam line. The irradiation beam line is equipped with a square collimator (1x1 cm²) and a pumping station, without any additional optical elements.

Characterization set-up

To perform radiobiological studies with a broad particle beam, the beam must be monoenergetic and homogeneous at least over an approximately 0.5 cm² surface in the air. These beam characteristics were measured with the set-up presented in Figure 1. It consists of a vacuum vessel with a square collimator, coupled to a turbomolecular pumping system, a specially designed irradiation head and a PIPS (Passivated Implanted Planar Silicon) particle detector collimated with a 0.5 mm aperture mounted on a X-Y moving table. The detector is used to measure the flux to evaluate the stability and uniformity of the broad beam. The irradiation head includes an 8 µm Kapton foil maintained between two stainless steel cylinders. This head has two purposes: it acts both as an exit window for the beam and as a substrate for the cells to be irradiated in air. In our configuration, a window, 1.8 cm in diameter, seals the exit for more than 10 hours working with 1 MeV proton beam.

Dose and dose rate assessment

Basic studies in radiobiology and particularly survival fraction studies, are performed at doses ranging from 0.1 to 10 Gy [3,7, 14-17] and with a dose rate ranging from 0.1 to 10 Gy/min. This range of dose rates also allows us to study low dose rates and low dose hypersensitivity [17-19]. For an ion beam, the dose rate can be related to the flux through the formula:

$$\dot{D} = 1.6 \cdot 10^{-9} \frac{LET \phi}{\rho} \quad (\text{Gy/s})$$

Where $\dot{D}$ is the dose rate (Gy/s), LET is the linear energy transfer (keV/ μm), ϕ is the flux (particles. $\text{s}^{-1}.\text{cm}^{-2}$) and ρ is the density of the cells (g/ cm^3). Taking into account the voltage range of our accelerator and the energy loss in the 8 μm exit window, the LET of a proton hitting a monolayer of cells can be adjusted from 10 keV/ μm (terminal voltage: 1.9 MV) to 50 keV/ μm (terminal voltage: 305 kV) according to SRIM [13] calculations ($\rho_{\text{cells}}=1\text{ g/cm}^3$). The LET yields a maximum relative biological effectiveness (RBE) at 30 keV/ μm [15, 16], which corresponds to 500 kV at the terminal voltage. The beam properties presented in this paper are obtained with this terminal voltage value.

Results and discussion

Stability and spatial uniformity of the proton beam

Beam stability and spatial uniformity were checked with the set-up presented in Figure 1. Figure 2 presents the proton beam stability for a given dose rate for more than 10 minutes. Standard deviation was 2.6 %. Conversion between flux and dose rate was achieved by employing the equation above with a LET=30 keV/ μm and $\rho_{\text{cells}}=1\text{ g/cm}^3$. Proton beam spatial uniformity is presented in Figure 3. Dose rate was measured every millimetre, line by line, by moving the collimated PIPS detector with the X-Y table over a 12 mm excursion. One can

recognise a clear 1x1 cm² collimated beam. The irradiation field with a dose rate variation below $\pm 5\%$ is 8x8 mm², large enough for broad beam *in vitro* cell irradiation.

Dose rate assessment

Dose rate variation was studied with the same set-up (Figure 1). The beam flux was tuned by tuning the accelerator source ioniser current. Dose rate ranging from less than 0.1Gy/min to more than 10Gy/min can be achieved with a variation in the ioniser current of about 3 A. Figure 4 shows the dose rate versus ioniser current. Dose rates ranging from 0.26 to 15.9 Gy/min are presented in this figure.

Conclusion and future developments

The results presented in this paper concerned a 1 MeV proton beam. These show that the LARN facility can be adapted for in vitro cell irradiation with a broad proton beam. Indeed, dose rates ranging from 0.1 to 10Gy/min are achievable by varying the source ioniser current. A stable and spatially uniform beam over a 8x8 mm² surface is easily obtained. Cell irradiations are currently performed.

Acknowledgements

We would like to thank Y. Morciaux, A. Nonet and L. Lambotte for their technical support. C. Michiels is a senior research associate of the Belgian Fund for Scientific Research (F.R.S.-FNRS). K. Donato was supported by the LEONARDO program.

References

- [1] U. Amaldi, Nucl. Phys. A 654 (1999) 375c-399c
- [2] U. Amaldi, G. Kraft, Rep. Prog. Phys. 68 (2005) 1861-1882
- [3] G. Chuanling, W. Jufang, J. Xiaodong, J. Xigang, L. renmin, W. Wei, L. Wenjian, Nucl. Instr. Meth. B 259 (2007) 997-1003
- [4] R. Orecchia, A. Zurlo, A. Loasses, M. Krengli, G. Tosi, S. Zurrada, P. Zucali, U. Veronesi, Eur. J. Cancer 34 (1998) 459-468
- [5] E.A. Blakely, Phys. Med. 17 (2001) 50-58
- [6] M. Durante, Heavy, Radiot. Oncol. 73 (2004) 158-160
- [7] Y. Furusawa, M. Aoki, M. Durante, Adv. Space Res. 30 (2002) 877-884
- [8] M. Folkard, K. Prise, G. Schettino, C. Shao, S. Gilchrist, B. Vojnovic, Nucl. Instr. Meth. B 231 (2005) 189-194
- [9] M. Folkard, K.M. Prise, A.G. Michette, B. Vojnovic, Nucl. Instr. Meth. A 580 (2007) 446-450
- [10] C. Shao, Y. Furusawa, Y. Kobayashi, T. Funayama, Nucl. Instr. Meth. B 251 (2006) 177-181
- [11] M. Belli, R. Cherubini, G. Galeazzi, S. Mazzucato, G. Moschini, O. Sapor, G. Simone, M.A. Tabocchini, Nucl. Instr. Meth. A 256 (1987) 576-580
- [12] P. Scampoli, M. Casale, M. Durante, G. Grossi, M. Pugliese, G. Gialanella, Nucl. Instr. Meth. B 174 (2001) 337-343
- [13] J.F. Ziegler, J.P. Biersack, U. Littmark, Pergamon, New York, 1985
- [14] J. Besserer, J. de Boer, M. Dellert, C. Gahn, M. Moosburger, P. Pemler, P. Quicken, L. Distel, H. Schüssler, Nucl. Instr. Meth. A 430 (1999) 154-160
- [15] M. Folkard, K.M. Prise, B. Vojnovic, H.C. Newman, M.J. Roper, B.D. Michael, Int. J. Radiat. Biol, 69 (1996) 729-738
- [16] J.A. Shuff et al, Nucl. Instr. Meth B 187 (2002) 345-353
- [17] L. Enns, K.T. Bogen, J. Wizniak, A.D. Murtha, M. Weinfeld, Mol. Cancer Res. 2 (2004) 557-566
- [18] P. Lambin, Revue de l'ACOMEN, 4 (1998) 301-314
- [19] K.M. Prise, G. Schettino, M. Folkard, K.D. Held, LANCET Oncol, 6 (2005) 520-528

Figures

Figure 1: Experimental set-up for broad beam characterization. 1) Beam, 2) Pumping system, 3) Irradiation head, 4) 0.5mm collimated PIPS detector, 5) X/Y axes, 6) Stainless steel cylinders, 7) 8 μ m Kapton foil (exit window)

Figure 2: Proton beam stability versus time

Figure 3: 1MeV proton beam uniformity map

Figure 4: Dose rate and flux measurement of a 1 MeV proton beam versus source ioniser current