Dosimetric studies for the irradiation of biological samples with protons at the 3 MV Tandem accelerator (National Centre of Accelerators, Seville)

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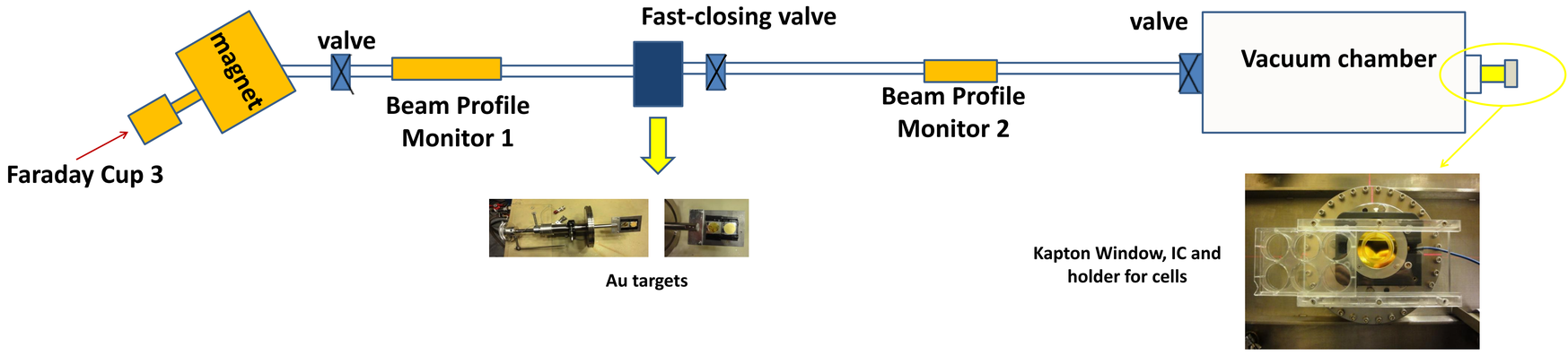
Abstract

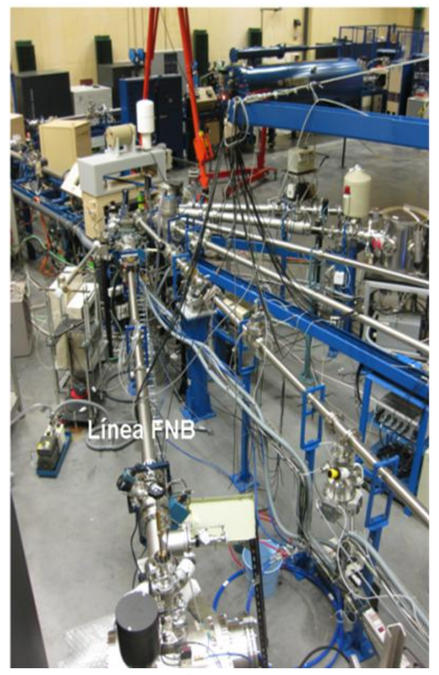
The study of the DNA damage due to ionizing radiation is of great interest for the scientific community. In order to understand the correlation between the exposure to different kinds of radiation (with different values of linear energy transfer, LET) and the DNA damage produced, many studies have been carried out. Here we present the modifications carried out on the Basic Nuclear Physics beam line at the 3MV Tandem accelerator installed at the National Centre of Accelerators (CNA) in Seville, Spain, in order to perform dosimetry studies and cell culture irradiation with low energy proton beams. An important goal of this work is to provide proton beams with sufficiently low and homogeneous intensity in a wide area, in order to assure a uniform dose delivery onto the whole cell sample surface.

Experimental techniques:

- **Beam line at 30 degrees after the switching magnet of the 3MV Tandem accelerator at CNA.**
- **Au target of 5.4 mg/cm² thickness to scatter and obtain a homogenous beam profile onto the cell samples.**
- **Kapton window (diameter of 44mm and thickness of 50µm).**
- **Ionization chamber (IC) with two air gaps of 6.5mm and V_{IC}=400V. With this IC calibrated, the delivered dose can be monitored directly in front of the biological samples.**
- **After going thorough the IC, the protons continue towards a movable sample holder with six irradiation positions.**

Beam line scheme:



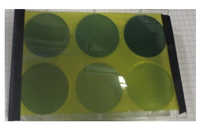


Beam line

Beam diagnostics with Gafchromic EBT3 films

RadioChromic film calibration for absolute dose quantification

Radiochromic characteristics



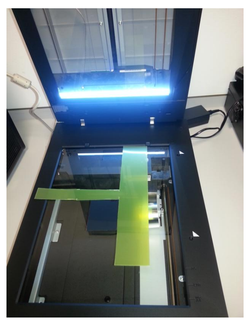
Polyester 125 µm
Active layer 28 µm
Polyester 125 µm

EBT3 radiochromic film. *Left:* irradiated film with different doses; *right:* transversal section of the EBT3

Characteristics:

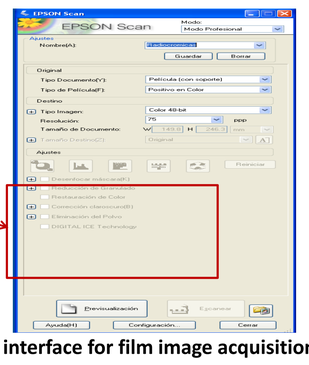
- **Direct coloration by the absorption of energetic radiation**
- **No chemical, thermal or optical development.**
- **Radiochromic reaction: solid-state polymerization, where the film turns blue proportionally to radiation dose**

Radiochromic films analysis: scanner and calibration



EPSON perfection V700 photo scanner

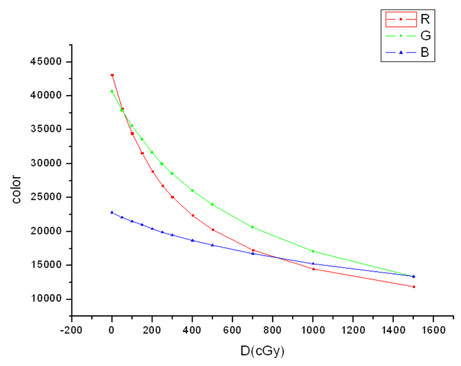
No colour corrections activated



PC interface for film image acquisition

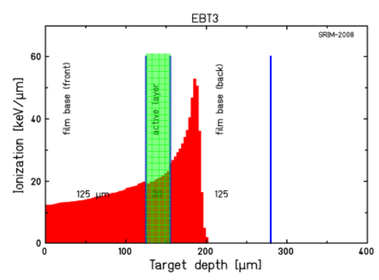
- **Transmission mode**
- **48-bit RGB (Red Green Blue)mode.**
- **No colour correction activated.**
- **Tiff image acquired.**
- **75 dpi (dots per inch resolution).**

Scanner response for films irradiated by 6 MV photons produced by a clinical Linac



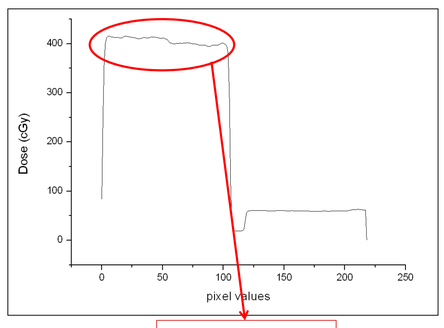
Under the condition of a source to surface distance (100cm) and 1.5 cm of solid water above the film, **100MU** delivered by the Linac correspond to **100cGy**

RadioChromic films are calibrated for absolute dose measurements when irradiated by photons



For protons in the plateau region of the Bragg curve (but not in the peak), the dose calibration with photons, in a first preliminary approach, is also valid for protons.

Au target of 5.4 mg/cm²



Homogeneity better than 5%

Proton beam profile after the absolute calibration in dose

IC dosimetry

- **The fluence F of the protons in front of the biological samples is proportional to the charge output of the chamber and can be determined from the calculated energy loss in the two air gaps .**
- **The dose deposited at a given depth in the sample is proportional to the fluence F and the specific energy loss dE/dx (1).**

$$D_p(Gy) = 1.602 * 10^{-9} * F\left[\frac{p}{cm^2}\right] * \frac{dE}{dx}\left[\frac{keV}{\mu m}\right] * \frac{1}{\rho}\left[\frac{cm^3}{g}\right] (1)$$

(1) where dE/dx is the stopping power and ρ is the density of the medium.

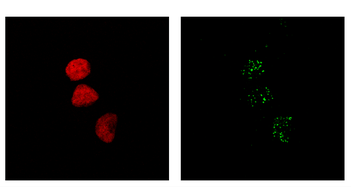
Dose results: film vs Ionization Chamber

Q (nC)	D_{IC} (Gy)	D_{film} (Gy)	D_{IC}/D_{film}
210	0.53	0.46	1.15
405	1.02	0.92	1.11
598	1.51	1.39	1.08
807.9	2.04	1.98	1.03
1198.5	3.03	2.91	1.04
1606.24	4.05	3.94	1.03

$D_{IC}/D_{film} \approx 1 - 1.1$

Cell sample irradiation: preliminary results

MCF-7 line of human breast cancer ***in the medium of the culture***



Cells irradiated with energy depositions out of the Bragg peak region and with different dose values

Confocal microscope analysis

Depth profiles (step of 15 nm, cell thickness 7-10 µm)

GOAL: to study the damage produced in the cell nuclei at different depths

***Top*: cell samples irradiated. *Bottom left*: foci images of cells; *bottom right*: foci images of the damage produced in the cell nuclei**

Conclusions and perspectives

- **A homogeneous and flat beam profile achieved by using a gold target for scattering (5.4mg/cm2);**
- **Calibration of the Gafchromic EBT3 film response in absolute dose for protons in the plateau region of the Bragg curve;**
- **First irradiations of cell cultures were performed.**

Further steps:

- **Irradiation and analysis of further biological samples;**
- **Calibration in dose of the EBT3 films for higher LET conditions (as it happens when the Bragg peak is placed at the active layer);**
- **Dosimetric analysis and irradiation of cells in the region of the Bragg peak (RBE study).**

Bibliography

(1) A. Niroomand-Rad et al. "Radiochromic film dosimetry", medical physics, vol 25,2093-2115, November 1998

(2) N. Sinenian et al. "The response of CR-39 nuclear track detector to 1-9 MeV protons" March 2012, PSFC/JA-11-46

(3) M. Müller "Physical and biological characterization of light ionizing radiation", Diploma thesis, December 2004

(4) D. Guirado et al. "Low dose radiation hyper-radiosensitivity in multicellular tumour spheroids", The British Journal of radiology, 85, 1398-1342, 2012