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Microdosimetry on nanometric scale with a new low-pressure avalanche-confinement TEPC

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Abstract. The tissue equivalent proportional counter (TEPC) is the most accurate device for measuring the microdosimetric properties of a particle beam, nevertheless no detailed information on the track structure of the impinging particles can be obtained, since the lower operation limit of common TEPCs is about 0.3 μm . On the other hand, the pattern of particle interactions is measured by track-nanodosimetry, which derives the single-event distribution of ionization cluster size at the nanometric scale. Anyway, only three nanodosimeters are available worldwide. A feasibility study for extending the performances of TEPC down to the nanometric region was performed and a novel avalanche-confinement TEPC was designed and constructed. This detector is constituted by a cylindrical chamber, based on a three-electrode structure, connected to a vacuum and gas flow system to ensure a continuous replacement of the tissue equivalent gas, thus allowing to simulate different biological site sizes in the range 300-25 nm. This TEPC can be calibrated by exploiting a built-in alpha source and a miniaturized solid-state detector as a trigger. Irradiations with photons, fast neutrons and two hadron beams demonstrated the good performances of the device. A satisfactory agreement with FLUKA simulations was obtained.

1. Introduction

The interest in hadron therapy, based mainly on protons and carbon ions for treating radio-resistant cancers and malignant tumours close to critical organs, has been growing during the last years [1]. Ion beams provide a better dose conformation and show superior radiobiological properties with respect to conventional radiation therapy. Since ionization generated in ion therapy is markedly localized and non-uniform against depth, significant variations on the radiation quality and consequently differences in the biological effectiveness across the Bragg curve are present [2]. Nevertheless, the present radiation- treatment planning procedures are based on the measurement of the absorbed dose, which is a macroscopic and average quantity that does not take into account neither the stochastics of particle interactions in the target volume nor the track structure of ionizing charged particles, which is crucial for the initiation of the radiation damage [3]. The standard dosimetric approach can be integrated with methodologies and instruments provided by microdosimetry, which aims at measuring the statistical fluctuations of the local energy imparted at the micrometric level, and track-nanodosimetry, which is devoted to the description of the pattern of particle interactions in nanometric volumes.

The tissue equivalent proportional counter (TEPC) is the most accurate device for measuring the microdosimetric properties of a particle beam, but it is capable of simulating site sizes in the



micrometric domain down to about 0.3 μm when operated in pulse-height mode [4]. Nevertheless, it is widely accepted today that radiation damage is initiated at the DNA level and the severity of the damage is closely related to the radiation track structure, which causes inhomogeneous interaction patterns at the nanometric scale [5]. Probability distributions of such interaction patterns, which are measured by track-nanodosimetry, show a trend similar to the cellular inactivation cross-sections [6]. However, only three nanodosimeters are available worldwide, showing stringent limitations: complexity, dimension and associated lack of transportability. This technological hurdle could be partially overcome by developing a microdosimeter capable of simulating tissue sites down to the nanometric region. Since the lower operation limit of single-wire TEPCs is about 300 nm in order to maintain an acceptable energy resolution, it is necessary to modify the geometry of the sensitive volume by embedding a third electrode for confining the electronic avalanche within a defined region. An extensive study, based on a prototype described elsewhere [7], allowed designing and developing a new low-pressure avalanche-confinement TEPC capable of measuring microdosimetric distributions in simulated sites in the range 300-25 nm.

2. The avalanche-confinement TEPC

The cylindrical sensitive volume of the new avalanche-confinement TEPC (13 mm in diameter and length) houses three electrodes biased independently: a central anode wire (graphite), a cylindrical cathode shell (conductive plastic A-150 type) and a helix (gold-plated tungsten), which surrounds the anode and subdivides the sensitive volume into an external drift zone and an internal multiplication region. Two aligned cavities embed, respectively, a removable ^{244}Cm alpha source and a very compact solid-state detector: this configuration allows calibrating the TEPC by also varying the simulated site size and the polarization of the three electrodes (Figure 1). It guarantees that only signals due to alpha particles with a straight path inside the sensitive volume, i.e. the drift region, are collected [8]. A customized and transportable vacuum and gas flow system guarantees vacuum conditions and ensures a continuous replacement of tissue equivalent gas inside the chamber. Dimethyl ether (DME: $(\text{CH}_3)_2\text{O}$), which can be considered as a tissue-equivalent gas apart from the lack of nitrogen, is the selected filling gas for this TEPC.

Irradiations with photons emitted by a ^{137}Cs source confirmed that the operating parameters of the device, i.e. the bias voltages of the electrodes, do not affect the microdosimetric information measured by the detector, which depends on the cavity size and on the radiation field only. Moreover, the TEPC response in the range 0.3 μm -25 nm against a fast neutron field produced by a calibrated ^{241}Am -Be source and quasi-monoenergetic neutron beams produced through the $^7\text{Li}(p,n)^7\text{Be}$ reaction on a LiF target was assessed experimentally. The comparison between measured distributions and FLUKA simulated spectra shows a rather good agreement also at low site sizes [9].

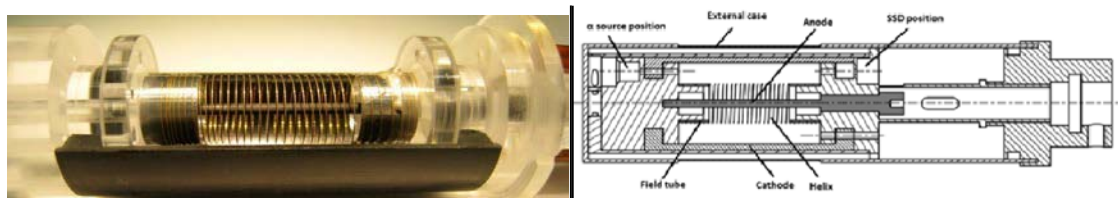


Figure 1. The avalanche-confinement TEPC: the calibration alpha source and the solid-state detector (SSD) are indicated in the cross-sectional view.

3. Response against 62 MeV/u carbon ion and helium ion beams

The avalanche-confinement TEPC was characterized preliminarily against a 62 MeV/u carbon ion beam. A set of PMMA foils with different thicknesses was used to reproduce different depths across the Bragg peak. Several configurations were tested by varying both the simulated site size in the range 300-25 nm and the depth across the Bragg peak of the delivered beam [10]. Figure 2 shows the dose distributions obtained for a simulated site of 300 nm at a depth 6.50 mm, 6.76 mm and 7.09 mm in

PMMA. At 6.50 mm the carbon peak is slightly shifted at lower lineal energy values with respect to the one at 6.76 mm, but the edge is the same. At 7.03 mm, the spectrum changes completely: the primary carbon contribution is no more present and that due to fragments, which is barely visible at 6.50 mm and 6.76 mm, becomes predominant. This depth is beyond the Bragg peak. The microdosimetric spectra obtained at eight different points across the Bragg peak are shown in Figure 3 for a 25 nm simulated site. The distributions shift towards higher y values as depth increases (from 1.76 mm to 6.76 mm), according to the beam slowing-down. In contrast, at 7.29 mm in depth, which is downstream of the Bragg peak, the distribution changes dramatically due to the contribution of fragments. The experimental set-up was also simulated with Monte Carlo simulations performed with the

FLUKA code in order to compare experimental and simulated microdosimetric spectra in site sizes equal to 300 and 25 nm. The obtained results are in good agreement, showing that this code is capable of reproducing microdosimetric spectra of a carbon beam down to 25 nm in simulated site [11]. Nevertheless, it should be stressed that these simulations refer to carbon beam only and further comparison with experimental data measured with other particles is required.

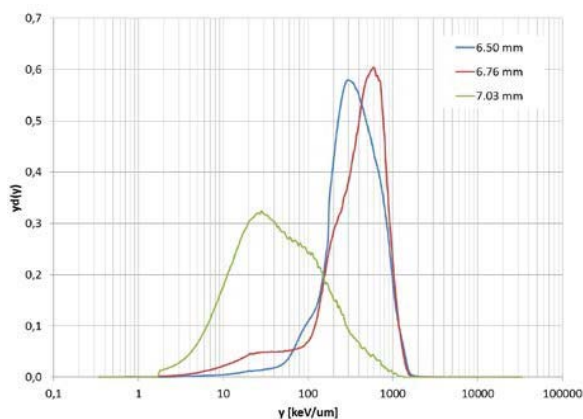


Figure 2. Carbon microdosimetric spectra obtained at 6.50, 6.76 and 7.03 mm in PMMA for a 300 nm simulated site.

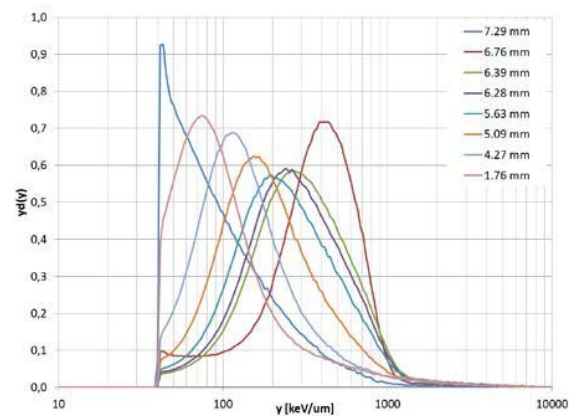


Figure 3. Carbon microdosimetric spectra obtained at different depths in PMMA from 1.76 mm to 7.29 mm for a 25 nm simulated site.

A very recent characterization was performed by irradiating the TEPC with a 62 MeV/u alpha particle beam. The experimental response of the microdosimeter for different simulated site sizes in the range 300-25 nm at seven points across the depth dose distribution was assessed. Figure 4 shows the microdosimetric spectra obtained for a 300 nm site at five different depths in PMMA. The distributions shift towards higher lineal energy values as depth increases, according to the beam slowing-down. In Figure 5, the comparison of the spectra obtained at different simulated site sizes at the same depth (24.31 mm in PMMA) is shown. The alpha edge does not change position, while a slight shift of the main peak towards higher lineal energy values can be observed with decreasing the site size. FLUKA simulations of all studied irradiation conditions are still ongoing, but a first good agreement was obtained for the 300 nm site size.

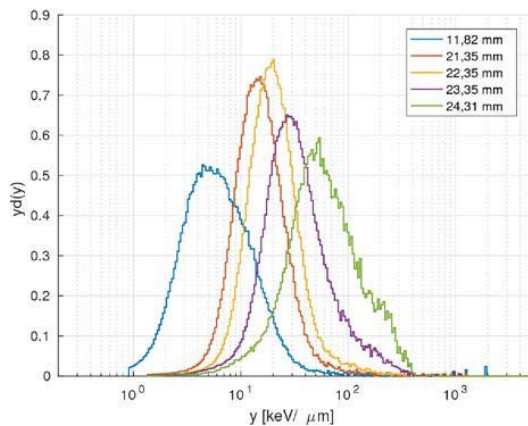


Figure 4. Helium microdosimetric spectra obtained at different depths in PMMA for a 300 nm simulated site.

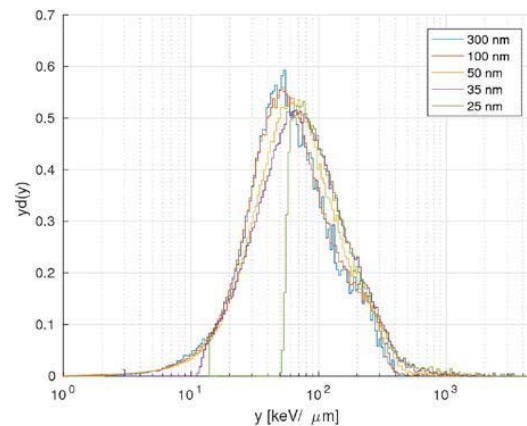


Figure 5. Helium microdosimetric spectra for different simulated site sizes in the range 300-25 nm at 24.31 mm in PMMA.

4. Conclusions

The irradiation campaigns with different neutron beams and low-energy hadrons (helium and carbon ions) give confidence about the capability of this novel avalanche-confinement TEPC of measuring microdosimetric distribution at simulated site ranging from 0.3 μm down to 25 nm. Nevertheless, further irradiations with other particles are necessary to study deeply the charge collection efficiency of the TEPC at low simulated site sizes (down to 25 nm). Moreover, further comparisons between FLUKA simulation and experimental data measured with other particles are foreseen.

5. Acknowledgments

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