MICRODOSIMETRY AT NANOMETRIC SCALE WITH AN AVALANCHE-CONFINEMENT TEPC: RESPONSE AGAINST A HELIUM ION BEAM

D. Mazzucconi[1,2,*], D. Bortot[1,2], S. Agosteo[1,2], A. Pola[1,2], S. Pasquato[1,2], A. Fazzi[1,2], P. Colautti[3], V. Conte[3], G. Petringa[4], A. Amico[4] and G. A. P. Cirrone[4]
[1]Politecnico di Milano, Dipartimento di Energia, via La Masa 34, Milano, Italy
[2]INFN, Sezione di Milano, via Celoria 16, Milano, Italy
[3]INFN, Laboratori di Legnaro, viale dell'Università 2, Legnaro (Padova), Italy
[4]INFN, Laboratori Nazionali del Sud, via Santa Sofia 62, Catania, Italy

*Corresponding author: davide.mazzucconi@polimi.it

The tissue-equivalent proportional counter (TEPC) is the most accurate device for measuring the microdosimetric properties of a particle beam but, since the lower operation limit of common TEPCs is ~0.3 μm, no detailed information on the track structure of the impinging particles can be obtained. The pattern of particle interactions at the nanometric level is measured directly by only three different nanodosimeters worldwide: practical instruments are not yet available. In order to partially fill the gap between microdosimetry and track-nanodosimetry, a low-pressure avalanche-confinement TEPC was designed and constructed for simulating tissue-equivalent sites down to the nanometric region. The present paper aims at describing the response of this TEPC in the range 0.3 μm–25 nm to a 62 MeV/n ^{4}He ion beam. The experimental results, for depths near the Bragg peak, show good agreement with FLUKA simulations and suggest that, for smaller depths, the distribution is highly influenced by secondary electrons.

INTRODUCTION

The interest for hadron therapy has been growing during the last three decades[1]. The assessment of the biological effective dose of clinical hadron beams is based on absorbed dose measurement. This is a macroscopic quantity which is not adequate for describing the energy deposition process at the micrometric level, because it takes into account neither the stochastics of particle interaction in the target volume nor the track structure of ionizing charged particles, which affects radiation damage to the DNA[2]. The main branches that aim at describing the local energy deposition are: microdosimetry, which characterizes the statistical fluctuations of the local energy imparted at the micrometric level, and track-nanodosimetry, devoted to the description of the pattern of particle interactions at the nanometric level.

The tissue-equivalent proportional counter (TEPC) is the most accurate device for measuring the microdosimetric properties of a particle beam and it is capable of simulating site sizes in the micrometric domain. Since the lower operation limit of standard TEPCs operating in the pulse-height mode is about 0.3 μm[3], no detailed information on the track structure can be obtained. On the other hand, the pattern of particle interactions at the nanometer level is measured by track-nanodosimetry, which assesses the single-event distribution of ionization cluster size for site dimensions from a few nanometers up to tens of nanometers. Nanodosimetric probability distributions show a trend similar to the cellular inactivation cross-sections[4]. Anyway, only three nanodosimeters are available worldwide and they cannot be easily transported[5–7].

In order to fill the gap between standard TEPCs and nanodosimeters, a low-pressure avalanche-confinement TEPC capable of simulating tissue-equivalent sites down to the nanometric region was designed and constructed[8]. This detector consists of a cylindrical chamber which houses a three-electrode structure and is connected to a vacuum and gas flow system to ensure a continuous replacement of the tissue-equivalent gas inside the chamber. Adjusting the gas pressure allows it to simulate different biological site sizes. Several irradiations with photons from ^{137}Cs source, fast neutrons and 62 MeV/n carbon ions demonstrated the capability of this TEPC of performing microdosimetric measurements for simulated site size from 0.3 μm down to 25 nm[9].

The present paper aims at describing the response of this newly developed TEPC when operating in the site size range of 300–25 nm and exposed to a 62 MeV/n ^{4}He ion beam. The experimental results are compared with Monte Carlo simulations performed with the FLUKA code.

THE AVALANCHE-CONFINEMENT TEPC

The TEPC has a transportable vacuum and gas flow system that guarantees vacuum conditions and ensures a continuous replacement of tissue-equivalent gas inside the chamber[10]. In such a way, the high purity required for stable gas gain during irradiation is preserved. Dimethyl ether (DME: $(CH_3)_2O$) is the selected filling gas for this avalanche-confinement TEPC: it can be considered as a tissue-equivalent gas, apart from the lack of nitrogen[11].

The sensitive volume of the detector is cylindrical (13 mm in diameter and length) and contains three electrodes biased independently: a central graphite anode wire (1 mm in diameter), a plastic cylindrical cathode shell (A-150 type, 13 mm in internal diameter and 1 mm in thickness) and a helix (gold-plated tungsten, 100 µm in diameter), 6 mm in diameter. This helix surrounds the anode wire and subdivides the sensitive volume into an external drift zone and an internal multiplication region. Two field tubes (stainless steel, 6 mm in diameter) are employed both for sustaining the helix and for defining the sensitive volume, thus avoiding any distortion of the electric field, while two insulating Rexolite caps enclose the chamber. Two aligned cavities house, respectively, a thick removable ^{244}Cm alpha source, sealed by a mylar layer, and a miniaturized solid state detector: this configuration allows calibrating the TEPC by also varying the simulated site size and the potentials applied to the three electrodes. It guarantees that only signals due to alpha particles with a straight path inside the sensitive volume are collected[8]. The microdosimeter is inserted into an aluminum case 0.2 mm in thickness, which is insulated from the cathode shell with a thin Rexolite cylinder 0.5 mm in thickness.

IRRADIATION SET-UP

The TEPC was irradiated with a 62 MeV/u ^{4}He ion beam accelerated by the cyclotron of the INFN-LNS laboratories, in Catania (Italy). The beam line is shown schematically in Figure 1. In particular, the primary helium beam passes through a 15 um tantalum foil and, 12 cm downstream, it is extracted from vacuum to air through a 50 µm kapton window. Particles then pass through a PolyMethylMethAcrylate (PMMA) ripple-filter set at 22 cm (for obtaining a wider Bragg peak) and a PMMA slab ending at 182.5 cm from the TEPC axis at 192 cm. Different positions across the Bragg peak can be simulated by modifying the thickness of the PMMA slab. Figure 1 shows also the depth-dose profile that is obtained using this beam line. The black points in the figure stand for the positions at which the spectra were acquired. The depth of the points is intended as the sum of the thickness of the PMMA foil and the intrinsic tissue-equivalent thickness of the TEPC. By considering the ratios of the mass stopping powers of the materials composing the TEPC with respect to PMMA for helium ions in the range 62–1 MeV/n, the overall intrinsic thickness of the

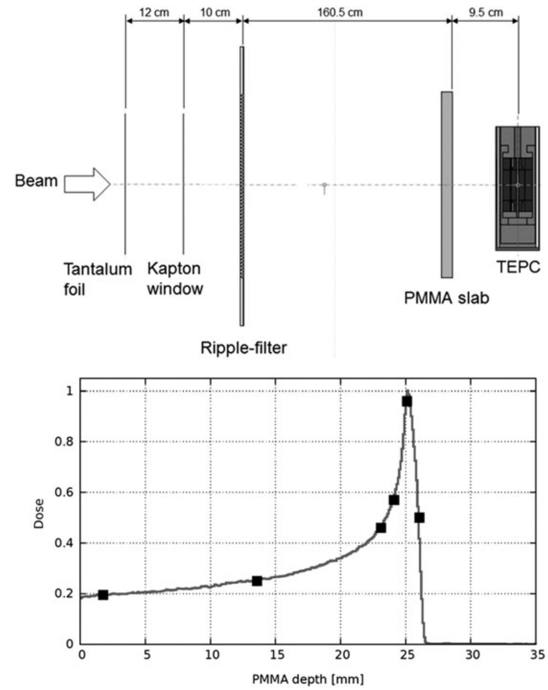

Figure 1. Schematic representation of the irradiation set-up at INFN-LNS laboratories. The measurement positions are indicated in the depth-dose profile.

TEPC walls is estimated equal to 1.76 mm PMMA equivalent.

In the following, microdosimetric spectra across the Bragg peak are referred to the PMMA foil thickness only.

CHORD-LENGTH DISTRIBUTION

The sensitive region of the developed TEPC is characterized by an unconventional shape due to the relative big diameter (6 mm) of the helix if compared with the cathode diameter (13 mm). As a consequence, the avalanche occupies a significant region of the interacting volume, and the sensitive volume in which all the generated electrons undergo equal amplification (drift region) should be considered of a hollow cylindrical shape. This feature leads to a different particle track distribution with respect to conventional cylindrical TEPCs. Thus, the conventional chord-length distribution for cylindrical TEPCs (solid cylinder shape) does not adequately describe the chord-length distribution for the actual hollow cylindrical shape of the sensitive volume. Moreover, the straight helium beam is far from the isotropic field that is considered conventionally for assessing the mean chord length for microdosimetric spectra. A deeper and complete discussion on the chord-length probability distribution for this TEPC can be found in[12]. The resulting probability distributions for this TEPC are different with respect to the cylindrical TEPC and can be found in[12]. The following microdosimetric spectra will be presented by considering the actual distribution which is characterized by a mean chord length equal to 0.612d, where d is the simulated site size.

MICRODOSIMETRIC SPECTRA

Microdosimetric spectra referred to 300 and 35 nm simulated sites for different thicknesses of the PMMA slab are plotted in Figure 2. The microdosimetric distribution shifts towards higher lineal energies following the reduction in energy of the primary beam.

The He-edge is visible when measuring with a 24.31 mm PMMA slab and at 35 nm, the effect of the reduced gas gain, that results in a higher threshold in terms of lineal energy, is observed.

FLUKA simulations were performed in order to make a comparison with the experimental distributions. The generation and transport thresholds were set by subdividing the detector regions into shells. In particular, the electron production and transport thresholds were set to 1 keV in the sensitive region and in all the surrounding regions (e.g. cathode wall, anode, helix) and to 10 keV in the other detector regions that are not directly adjacent to the sensitive zone (e.g. aluminum case and surrounding air).

Comparisons between FLUKA simulations and experimental data for two different sites with a 24.31 mm PMMA foil are plotted in Figure 3. FLUKA can reproduce with a good agreement the distributions even for smaller sites. Nevertheless, comparisons for smaller depths point out some discrepancies between FLUKA simulations and experimental data. These differences are due to the FLUKA 1 keV electron transport threshold that is the lowest actual limit for this code.

In Figure 4 (top), experimental data referring to 24.31 mm of PMMA for different site diameters are compared. It should be noted that the edge of the

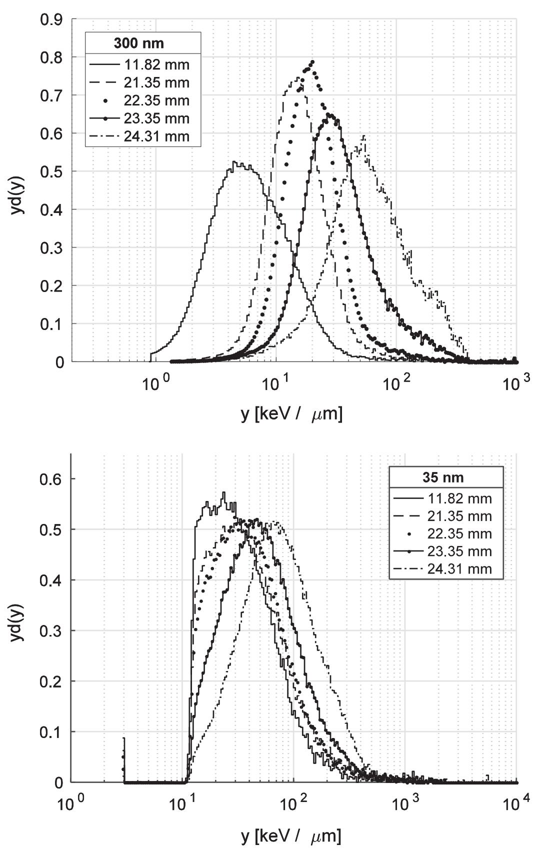

Figure 2. Microdosimetric distributions for 300 (top) and 35 (bottom) sites at different depths across the Bragg peak.

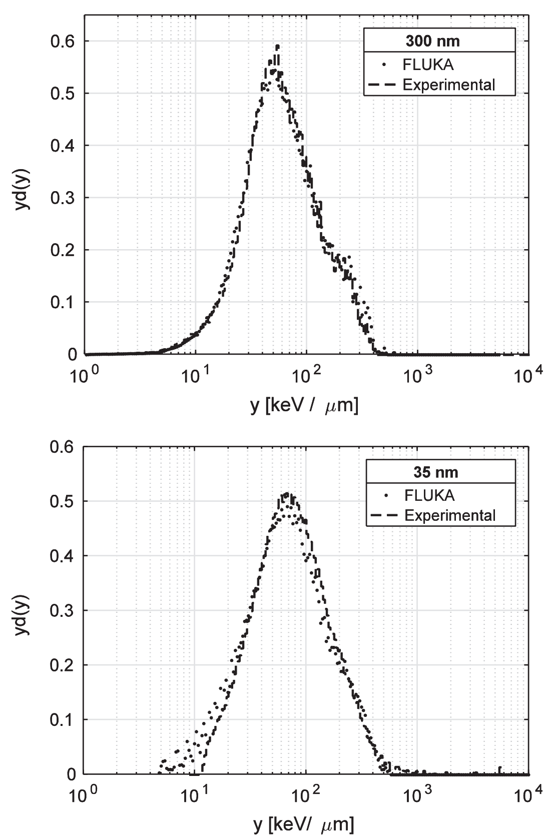

Figure 3. Comparison between experimental spectra and FLUKA simulations for 300 (top) and 35 (bottom) nm site employing 24.31 mm of PMMA.

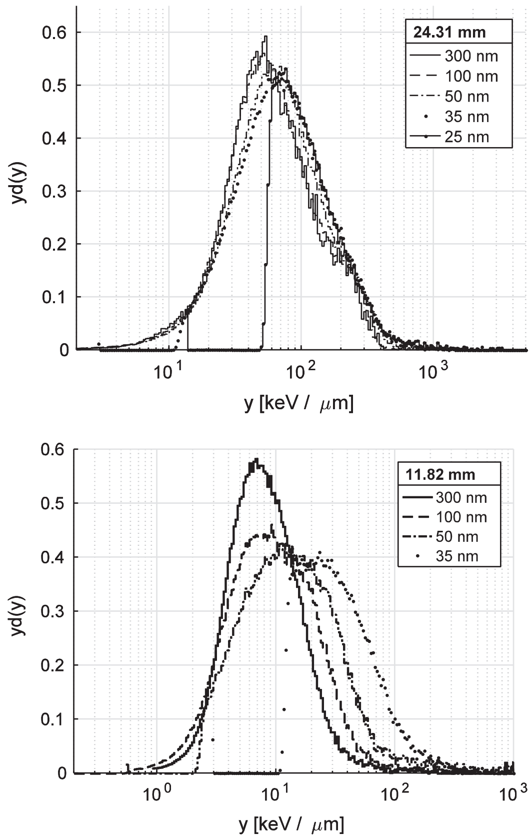

Figure 4. Comparison between different simulated site spectra for 24.31 (top) and 11.82 (bottom) mm of PMMA.

microdosimetric spectrum is almost independent of the simulated site although a slight shift on the main peak is observed. The shift, as the site is smaller, becomes considerable if the same comparison is done for smaller depths, as shown in Figure 4 (bottom), where spectra for a 11.82 mm PMMA slab are compared.

This trend can be explained if the right side of the main peak is assumed to be given by secondary electrons behaving as exact stoppers. In fact, for smaller simulated sites, exact stoppers have smaller energy, therefore higher lineal energy. This behavior is the same observed by irradiating the TEPC with photon fields and changing the simulated site, as reported in(9) and(13).

CONCLUSIONS

The response of a new low-pressure avalanche-confinement TEPC against a 62 MeV/n ^{4}He ion beam was experimentally characterized at different site sizes in the range 300–25 nm. A satisfactory agreement between FLUKA simulations and experimental results was obtained only for higher depths across the depth-dose distribution. The acquired data highlight that for smaller depths the distribution is highly influenced by secondary electrons. Still a direct and systematic comparison with reference devices both in the micrometric and nanometric domains has to be performed and will be matter of future work. In particular, further irradiations with protons are foreseen to directly compare the obtained microdosimetric distributions at 0.3 μm with those measured by reference TEPCs.

ACKNOWLEDGEMENTS

This work was supported by the INFN—Scientific Commission V in the framework of the NADIR (biologically relevant NAnoDosimetry of Ionizing Radiation) experiment.

REFERENCES

1. Durante, M. and Loeffler, J. S. *Charged particles in radiation oncology*. Nat. Rev. Clin. Oncol. **7**, 37–43 (2010).
2. Weyrather, K. and Kraft, G. *RBE of carbon ions: experimental data and the strategy of RBE calculation for treatment planning*. Radiother. Oncol. **73**, S161–S169 (2004).
3. Hogeweg, B. *Gas gain characteristics of a tissue-equivalent proportional counter, and their implications for measurements of event size distributions in small volumes*. Proc. Fourth Symp. on Microdosimetry **5122**, 843–854 (1973).
4. Conte, V., Moro, D., Colautti, P. and Grosswendt, B. *Nanodosimetric descriptors of the radiation quality of carbon ions*. Radiat. Prot. Dosim. **166**, 214–218 (2015).
5. De Nardo, L., Alkaa, A., Khamphan, C., Conte, V., Colautti, P., Ségur, P. and Tornielli, G. *A detector for track-nanodosimetry*. Nucl. Instrum. Meth. A **484**, 312–326 (2002).
6. Garty, G., Shchemelinin, S., Breskin, A., Chechik, R., Assaf, G., Orion, I., Bashkirov, V., Schulte, R. and Grosswendt, B. *The performance of a novel ion-counting nanodosimeter*. Nucl. Instrum. Meth. A **492**, 212–235 (2002).
7. Pszona, S. and Gajewski, R. *An approach to experimental microdosimetry at the nanometer scale*. Radiat. Prot. Dosim **52**, 427–430 (1994).
8. Bortot, D., Pola, A., Agosteo, S., Pasquato, S., Introini, M. V., Colautti, P. and Conte, V. *A miniaturized alpha spectrometer for the calibration of an avalanche-confinement TEPC*. Radiat. Meas. **106**, 531–537 (2017).
9. Bortot, D., Pola, A., Agosteo, S., Pasquato, S., Mazzucconi, D., Fazzi, A., Colautti, P. and Conte, V. *A novel avalanche-confinement TEPC for microdosimetry at nanometric level*. Radiat. Meas. **103**, 1–12 (2017).
10. Bortot, D., Delbono, R., Sagia, E., Pola, A., Introini, M. V., Lorenzoli, M., Agosteo, S. and D'Angelo, G. *Development of a vacuum and gas flow system for a new*

avalanche-confinement TEPC. INFN-LNL Annual Report 2013 **240**, 154–155 (2014).

11. International Commission on Radiation Units and Measurements. *Microdosimetry*. ICRU Report 36 (1983).
12. Mazzucconi, D., Bortot, D., Pola, A., Agosteo, S., Pasquato, S., Fazzi, A., Colautti, P. and Conte, V. *Monte Carlo simulation of a new TEPC for microdosimetry at nanometric level: response against a carbon ion beam*. Radiat. Meas. **113**, 7–13 (2018).
13. Cesari, V., Colautti, P., Magrin, G., De Nardo, L., Baek, W. Y., Grosswendt, B., Alkaa, A., Khamphan, C., Ségur, P. and Tornielli, G. *Nanodosimetric measurements with an avalanche confinement TEPC*. Radiat. Prot. Dosim. **99**, 337–342 (2002).