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Mini-TEPC Microdosimetric Study of Carbon Ion Therapeutic Beams at CNAO

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Mono-energetic carbon ion scanning beams of 195.2 MeV/u at the Italian National Centre for Oncological Hadrontherapy (CNAO) have been used to study the microdosimetric features of an "active" carbon ion beam used in hadrontherapy. A 30x30 mm^2 area has been scanned by a 6 mm beam with scanning steps of 2 mm. A mini TEPC of 0.57 mm^3 has been used to perform measurements in a water phantom at different depths on the beam axis. The detector small size allowed for measuring, with good spatial resolution, also inside the relatively small Bragg peak region and inside the distal edge, where the radiation quality varies quickly. In spite of the high event rate (up to ~ 10^5 s^{-1}), no pile-up effects were observed. Results showed that the frequency-mean lineal energy scaled well with the absorbed dose. Moreover, the dose-mean lineal energy itself seemed to be a good descriptor of the radiation quality.

KEYWORDS: microdosimetry, mini tissue-equivalent proportional-counter (TEPC), carbon ions

I. Introduction

The ion beam radiotherapy is a technique that uses fast light ions (protons and carbon ions) to treat solid tumours. Its success is mainly due to the good ballistic properties of ions with respect to electrons, photons and neutrons. The ion finite range allows maximizing the tumour dose, while sparing the dose to the surrounding healthy tissues. Therefore, such a radiation therapy has therapeutic indications for solid tumours that are located close to critical healthy tissues. Nowadays, forty-nine therapeutic centres use ion beams to treat their patients [1]. Most of them use fast protons. At present, eight centres (2 in Europe, 4 in Japan and 2 in China) use carbon ions. Carbon ions have high relative biological effectiveness (RBE) and low oxygen enhancement ratio (OER) [2, 3]. These features make carbon ions suitable to treat tumours, which are low-LET radiation resistant. However, both the RBE the OER values change with the radiation quality, namely with the ion charge and velocity. Therefore, the radiation-field biological action varies with the spatial coordinates inside the treated volume. As far as the RBE and OER can be assessed from the radiation field quality, it should be known with high spatial resolution in order to optimise the therapeutic plan and its success. That is of specific utility when complex radiation fields, namely radiation fields with several radiation quality components, are used (IMPT for instance). The only available technique for such an aim is the experimental microdosimetry. Microdosimetric detectors measure the energy imparted $\boldsymbol{\varepsilon}$ by a single particle in a site of finite size, for instance 1 µm site (~ the chromosome thickness). In microdosimetry, the ratio $\boldsymbol{\varepsilon}/\bar{\boldsymbol{l}}$, where $\bar{\boldsymbol{l}}$ is the microdosimeter sensitive-volume mean-chord length, is called lineal energy $\boldsymbol{y}$. In a mixed radiation field, $\boldsymbol{y}$ events originate the frequency distribution $\boldsymbol{f(y)}$, the mean value of which is called frequency-mean lineal energy $\bar{\boldsymbol{y}}_{\boldsymbol{F}}$. $\bar{\boldsymbol{y}}_{\boldsymbol{F}}$ is proportional to the absorbed dose through the equation:

$$\boldsymbol{D} = \frac{\boldsymbol{k}}{\boldsymbol{d}^2}\boldsymbol{N}\bar{\boldsymbol{y}}_{\boldsymbol{F}} \tag{1}$$

where $\boldsymbol{N}$ is the event number and $\boldsymbol{d}$ the sensitive volume size and $\boldsymbol{k}$ a constant factor depending on the sensitive volume shape. The average value of the weighted distribution $\boldsymbol{d(y)}$ is called dose-mean lineal energy, $\bar{\boldsymbol{y}}_{\boldsymbol{D}}$. The two microdosimetric averages can be used as a radiation quality signature.

Microdosimetric detectors can be made of silicon [4], diamond [5] or organic gas. Gas counters have the advantage to amplify in proportional mode the ionization events produced by the imparted energy. Therefore, they are potentially able to detect a single ionization event, namely all the imparted energy $\boldsymbol{\varepsilon}$.

Various microdosimetric measurements of carbon ion beams were performed in the past with TEPCs (tissue-equivalent proportional counters). The most of them used the commercial gas counter LET ½ (Far West Technology, Inc., Goleta, CA, 93117), which is a relatively large detector of 1.07 cm^3 (a sphere of 12.7 mm of diameter). Therefore, in order to prevent pile-up effects, these counters were used in low-intensity ion beams or with rather cumbersome trigger and veto detection systems. They are not suitable for scanning beams used in the hadrontherapy clinical practice, where the fluence rates span a 10^4 –10^7 mm^{-2} s^{-1} range. The mini-TEPC developed by INFN Legnaro laboratories [6], which has a cylindrical sensitive volume of only 0.57 mm^3 (0.9 mm of diameter and height), was already successfully tested in intense therapeutic proton beams [7]. Therefore, in principle it could be used also in therapeutic carbon ion beams. Moreover, the small counter cavity allows to perform measurements in radiation fields with high dose-gradients with a spatial accuracy of about 0.1 mm.

The aim of this research was to test the ability of mini-TEPCs to properly measure microdosimetric spectra in an active carbon ion beam at different depths in a water phantom. For this study, the scanning therapeutic beam of the Italian national centre for oncological hadrontherapy (CNAO) [8] has been used.

II. Instruments and Methods

1. The CNAO carbon ion beam

At CNAO a fully active scanning delivery system is used. A treatment planning system (TPS) is used to calculate how to adequately cover the entire tumour volume, while sparring normal tissues and organs, using a very large number of beam spots. Every spot (6 mm of diameter at FWHM as an average over the whole energy spectrum) is characterized by the particles energy, the particles number and the position where it has to be placed. All spots with the same energy are grouped in slices and a synchrotron cycle is used to generate a beam with the right energy and dimension. With a couple of scanning magnets the beam is sent in the right position and, when the requested particles number is delivered for the first spot the beam is moved to the following spot position. When the last spot belonging to a slice has been delivered, the beam extraction is stopped and a new synchrotron cycle is generated. The sequence continues slice by slice until all spots are delivered. The control of the treatment is done in real time by the "dose delivery system", which is composed mainly by the monitoring system, that measure the beam intensity and position, and the scanning system. More detailed have been published elsewhere [9].

In order to simulate a TPS single-slice irradiation, a mono-energetic carbon ion beam of 195.2 MeV/u, which was enlarged by using two thin PMMA ripple filters, was used. The emerging beam has been calculated to have an average energy of 189.5 MeV/u and a FWHM (energy spread) of 0.28 MeV/u at the isocentre. The multi-spot scanning system was used to uniformly irradiate a 30 x 30 mm^2 surface. The surface was irradiated with equally-separated 225 spots, approximately lasting 0.04 s each. This procedure was repeated about 90 times, for a total of ~ 2,250 spots, to obtain the total absorbed dose to water of 10 Gy at the reference depth of 2 cm. The maximum fluence rate in a single spot was calculated to be about $2{\cdot}10^5$ s^{-1}mm^{-2}.

2. The microdosimetric detection system

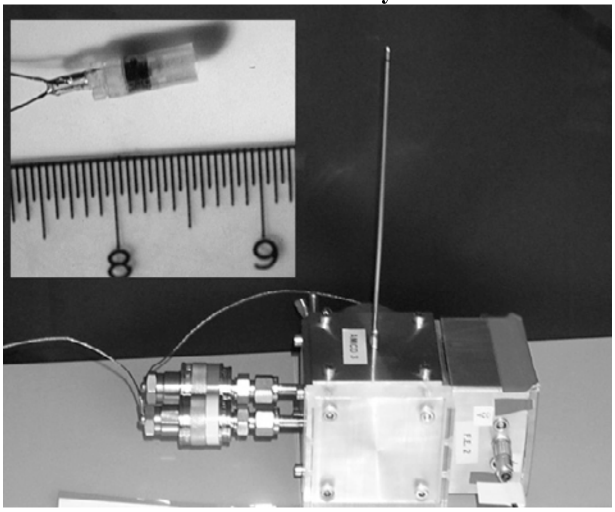

Figure 1: *The mini TEPC is shown in the up-left insert. It is placed inside the thin aluminum sleeve (the long stick in the figure).*

Measurements were performed with a cylindrical detector made of A-150 plastic, the cathode, and Rexolite® plastic, the insulators. The detector stands inside 2.7 mm diameter 16 cm long aluminium sleeve, which has a thickness of 0.2 mm (see figure1).

Measurements were performed with pure propane gas to prevent the response inaccuracy due to the uncertainty about the propane-based tissue-equivalent gas-mixture composition. The gas pressure value was set to simulate 1 μm-equivalent propane-TE site size. All the measurements were performed in gas-flow modality (1 cm^3/min) with the mini-TEPC filled with 454 mbar of propane at 21.8 °C of temperature.

The mini-TEPC is equipped with a homemade charge preamplifier of ~ 300 equivalent electrons of rms noise and a dynamic range of four and a half order of magnitude. The preamplifier is placed inside the aluminium box, on which the aluminium sleeve is inserted. Three spectroscopy linear amplifiers were used for conditioning and simultaneously amplifying the pulses coming from the preamplifier. The shaping times were set at 250 ns. The analogic pulses were digitized with three CAMAC-standard ADCs of 16k, 8k and 8k channels respectively. The CAMAC system was driven by a portable computer with Kmax® software.

3. The irradiation set up

Measurements were performed in a liquid water phantom, at the isocentre. The detector was placed on a rigid support, which could be moved along the beam axis with a precision of 0.1 mm. The thin rod containing the mini-TEPC was inserted in a PMMA cylinder of 24 mm outer diameter (see figure 2). The overall position uncertainty, mainly due to the PMMA window and cylinder thickness uncertainties, has been assessed to be 0.6 mm. The relative depth-dose profile has been measured with the Advanced Markus parallel-plate ionization chamber (model 34045, PTW, Freiburg, Germany).[8].

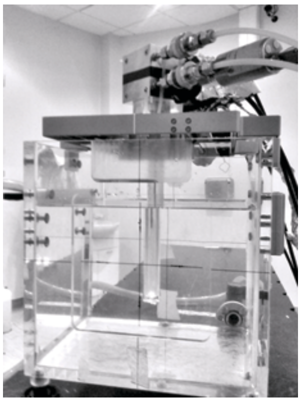

Figure 2: *The water phantom used during measurements at CNAO. The detector was placed upside down inside a PMMA cylinder that is immerged in the water.*

4. Data processing

Every microdosimetric spectrum is the result of two measurements: one measurement at low gas gain (600 V) and the second one at higher gas gain (750 V). The two spectra were calibrated with a ^{137}Cs source. More details about the calibration procedure have been published elsewhere (10). The spectra at different gas gains were joined together superimposing the common spectral parts. This "photon calibrated" spectrum has been eventually re-calibrated by using the carbon-edge value, which has been determined with the same procedure explained in reference 10. The carbon edge corresponds to the maximum energy transferred in 1 µm site of liquid water, namely 931 keV/µm, which corresponds to a lineal energy value of 1,397 keV/µm.

III. Results and discussion

Because of the electronic noise, the experimental spectra had a low detection threshold of 0.2-0.3 keV/µm. Therefore, all the spectra were extrapolated down to 0.01 keV/µm by using the linear best-fit of 0.2-0.5 keV/µm data .

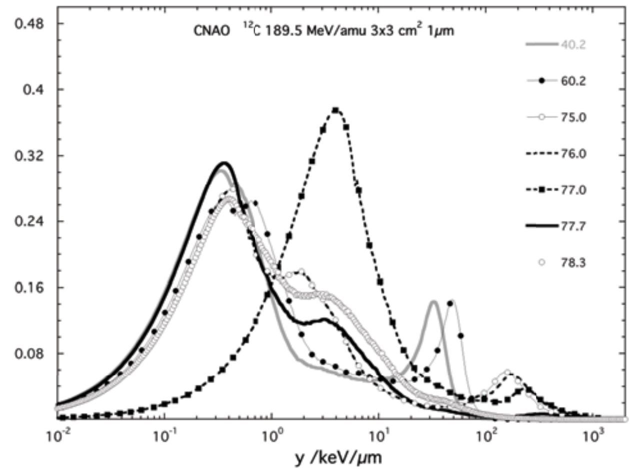

Figure 3: *Microdosimetric frequency distributions at different depths in the water phantom.*

In figure 3, the frequency distribution multiplied by the y is plotted against log(y). In such a representation, equal visual areas under the curve mean equal relative contribution to the total event number. In the proximal edge, the carbon ion events give rise to roughly Gaussian peaks in the 10 – 100 keV/µm region. In the Bragg peak region, carbon ion events give rise to broader and lower peaks in the region 10^2 – 10^3 keV/µm. Figure 3 shows also that at any depth the event majority has sizes less than 10 keV/µm. Such small events are likely due to lighter ions emerging from nuclear reactions.

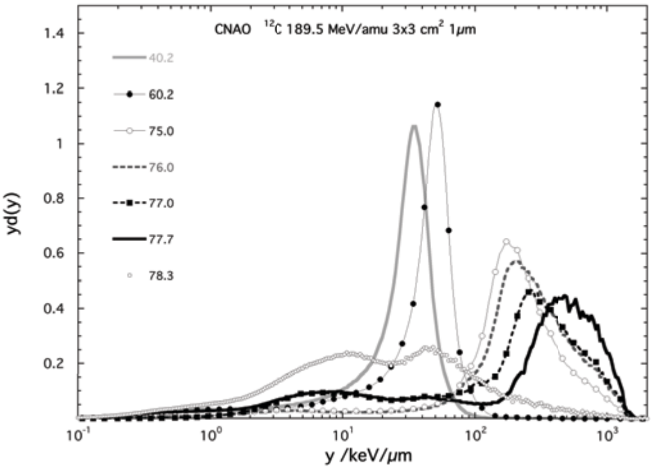

Figure 4: *Microdosimetric dose-weighted distributions at different depths in the water phantom.*

In figure 4, the dose-averaged lineal energy multiplied by y-value is plotted against log(y). In such a representation, equal visual areas under the curve mean equal contribution to the total absorbed dose. Differently from the frequency distributions, the dose distributions are almost everywhere dominated by carbon ion events, which give rise to roughly-Gaussian peaks of 10 – 100 keV/µm in the proximal edge and to broader peaks of 100-1000 keV/µm in the Bragg peak region. However, in the Bragg peak distal edge (78.3 mm of depth), where the primary carbon ion beam is quickly vanishing, low y-values events due to light ion from nuclear reactions become dominant.

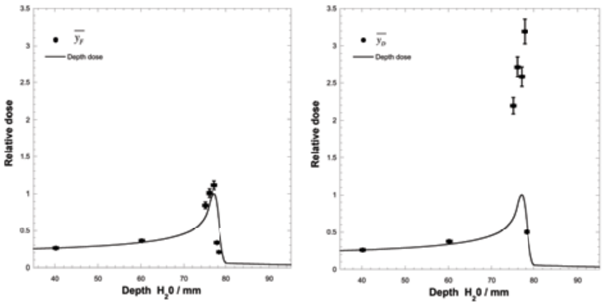

Figure 5: *Comparison of relative absorbed dose (line) with the microdosimetric relative mean-values (full dots). Left side: frequency-mean lineal energy. Right side: dose-mean lineal energy.*

In figure 5, the frequency-mean and the dose-mean lineal energy values are superimposed to the relative absorbed dose curve. For sake of comparison, the microdosimetric values have been scaled to match the absorbed-dose relative value at 40.2 mm of depth. Figure 5 shows that the frequency-mean values scale rather well with the absorbed dose, according to equation 1. On the contrary, the does-mean values are much higher than the relative absorbed-dose values in the Bragg peak region. At the Bragg peak, the $\bar{y}_D$ value is 3.2 times higher.

IV. Conclusion

For the first time, microdosimetric measurements have been performed in a carbon ion scanning beam, at the CNAO hadrontherapy facility. In spite of the high counting rate, no spectral distortion, due to pile-up events, were observed. Moreover, the frequency-mean values at different depths scales rather well with the relative absorbed dose values, this being a further indication of the accuracy of measured spectra. The $\bar{y}_D$ values do not scale with the absorbed dose. They are much higher in the Bragg peak region. The increase factor is not far from the expected RBE values in the Bragg peak [12]. Discussing about the use of microdosimetric data in radiobiological models is not the aim of this paper. However, CNAO microdosimetric data suggest that mini-TEPCs are able to monitor the quality of carbon-ion active-beams used in the modern hadron therapeutic centres.

Acknowledgment

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References

1) Hadrontherapy facilities worldwide in operation. www.ptcog.ch,updated 09-Nov-2014)
2) Raju MR, Amols HI, Bain E, Carpenter SG, Cox RA, Robertson JB, "A heavy particle comparative study. Part III. OER and RBE", Br. J. Radiol., **51**, 712-719 (1978)
3) Curtis SB, "The OER of mixed high- and low-LET radiation", Radiat Res **65**, 566-572 (1976).
4) S. Agosteo, G.A.P. Cirrone, P. Colautti, G. Cuttone, G. D'Angelo, A. Fazzi, M.V. Introini, D. Moro, A. Pola , V. Varoli. "Study of a silicon telescope for solid state microdosimetry: Preliminary measurements at the therapeutic proton beam line of CATANA" Radiat. Meas. **45**, 1284-1289 (2010).V. Cesari et al., *Nanodosimetric measurements with an avalanche confinement TEPC*, Radiation Protection Dosimetry 99(1-4): 337-342 (2002).
5) S.Rollet, M.Angelone, G.Magrin, M.Marinelli, E.Milani, M.Pillon, G.Prestopino, C.Verona, G.Vrrona-Rinati. "A novel microdosimeter based upon arificial single crystal diamond", Nucl.Sci. IEEE Trans. 59, 2409-2415 (2012).Meas. **45**, 1284-1289
6) L. De Nardo, V.Cesari, G.Donà, G.Magrin, P.Colautti, V.Conte and G.Tornielli, "Mini-TEPCs for radiation therapy", Rad. Prot. Dos. **108**, 345-352 (2004).
7) L. De Nardo, V. Cesari, N. Iborra, V. Conte, P. Colautti, J. Héreault, G. Tornielli, P. Chauvel. "Microdosimetric assessment of Nice therapeutic proton beam biological quality, Physica Medica **XX**, 71-77 (2004).
8) S. Rossi, "The National Centre for Oncological Hadrontherapy (CNAO): Status and perspectives", Physica Medica **31**, 333-351 (2015). Doi: 10.1016/j.ejmp.2015.03.001.
9) S. Giordanengo, M.A. Garella, F. Marchetto, F. Bourhaleb, M. Ciocca, A. Mirandola, V. Monaco, M.A. Hosseini, C. Peroni, R. Sacchi, R. Cirio, M. Donetti, "The CNAO dose delivery system for modulated scanning ion beam radiotherapy" Med Phys. **42**, 263-275 (2015). doi: 10.1118/1.4903276
10) Mirandola A, Molinelli S, Vilches Freixas G, Mairani A, Gallio E, Panizza D, Russo S, Ciocca M, Donetti M, Magro G, Giordanengo S, Orecchia R. *Dosimetric commissioning and quality assurance of scanned ion beams at the Italian National Center for Oncological Hadrontherapy*. Med Phys. 2015 42(9):5287-300.
11) Conte, D. Moro, B. Grosswendt, P. Colautti. *Lineal energy calibration of mini tissue-equivalent gas-proportional counters (TEPC)*, in Multidisciplinary Applications of Nuclear Physics With Ion Beams. AIP Conference collection, 2013, pp. 171 -178.
12) IAEA 2008. *Relative Biological Effectiveness in Ion Beam Therapy*. Technical report 461