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THE TOP-IMPLART PROTON LINEAR ACCELERATOR: INTERIM CHARACTERISTICS OF THE 35 MEV BEAM

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ABSTRACT

In the framework of the Italian TOP-IMPLART project (Regione Lazio), ENEA-Frascati, ISS and IFO are developing and constructing the first proton linear accelerator based on an actively scanned beam for tumor radiotherapy with final energy of 150 MeV. An important feature of this accelerator is modularity: an exploitable beam can be delivered at any stage of its construction, which allows for immediate characterization and virtually continuous improvement of its performance. Currently, a sequence of 3 GHz accelerating modules combined with a commercial injector operating at 425 MHz delivers protons up to 35 MeV. Several dosimetry systems were used to obtain preliminary characteristics of the 35 MeV beam in terms of stability and homogeneity. Short-term stability and homogeneity better than 3% and 2.6%, respectively were demonstrated; for stability an improvement with respect to the respective value obtained for the previous 27 MeV beam.

INTRODUCTION

The Italian National Agency for New Technologies, Energy and Sustainable Economic Development (ENEA), the National Institute of Health (ISS) and the Regina Elena National Cancer Institute (IFO) are carrying on, within the TOP-IMPLART project funded by Regione Lazio, the development and construction of the first proton linear accelerator for radiotherapy based on an actively scanned beam. Currently, four accelerating modules driven by a 10 MW klystron deliver protons with energy up to 35 MeV.

One of the peculiarities of the TOP-IMPLART accelerator is its intrinsically extendable modularity: it can deliver an exploitable beam any time while under construction. The immediate characterization and virtually continuous improvement of its performance is thus possible even for energies far from those suitable for therapy treatments. The interest in the low energies currently available is mainly focused on *in vitro* and *in vivo* radiobiological studies, in particular on the therapeutic potential of the unique (for hadrontherapy) pulsed structure of the beam. However, the dosimetric characterization of the beam is required before starting these investigations. As no similar accelerator is currently available on the market, upgrades are in progress to improve its performance until the final energy will be reached. At the present stage, efforts are addressed at optimizing the beam parameters such as stability or homogeneity with a view to its use in radiotherapy applications. A previous dosimetric characterization at 27 MeV energy showed that the reproducibility of the beam was 5% and the uniformity 4% within a 16 mm circular surface(1). Since the operation of the fourth structure, improvements in the RF line have been introduced to enhance beam stability by installing a new klystron/modulator system and implementing resonant frequency feedback control systems on the accelerating structures; a further dosimetric characterization of the beam was considered necessary in order to evaluate the effect of the upgrade of the accelerating systems, and define the current performances of the beam for radiobiological studies in terms of these two parameters.

MATERIALS AND METHODS

Detectors and holders

Measurements were performed in free air using a 2D ionizing chamber(2) (built at the ISS), EBT3 Gafchromic films (Ashland ISP Advanced Materials, NJ, USA), measured with an EPSON Expression 10000XL/PRO color scanner(3); a silicon diode (SD), high-doped p-type stereotactic field detector (Hi-pSi), SD, mod. DEB050 (Scanditronix, Belgium)(1), connected to a Keithley electrometer mod. 6517A with no polarizing voltage; MOSFET detectors (Best Medical, Ottawa ON, Canada); nominally pure LiF crystals (MacroOptica Ltd., Russia)(4); alanine dosemeters (Gamma Service, Leipzig Germany)(1), measured with a Bruker ELEXSYS spectrometer operating in X-band and equipped with a high sensitive SHQ cavity and a microDiamond detector, mD, mod. 60019 (PTW-Freinburg, Germany)(5), connected to a Keithley electrometer mod. 6517A with no polarizing voltage.

The 2D-IC actually measures the x and y projections of the beam simultaneously: each point of the x-projection represents the mean value of the charge collected by the strip parallel to the y-axis passing through that point (the same holds for the y-profile). This ionizing chamber is intended to be tested as a monitor chamber of the beam, therefore, in each irradiation, it was always kept in front of the other dosemeters at a distance of about 15 cm from them and to a distance of about 160 cm from the beam exit. Its response was also compared with that of EBT3 films when evaluating the homogeneity of the beam profiles. Nevertheless, the 2D-IC measurement modality prevents the direct comparison between the EBT3 profiles and the 2D-IC projections. The images of the films were therefore resampled on the 2D-IC and then properly projected on the two axes, assuming that the absorbed dose scales with the film optical density according to the following function[(3)]:

$$D = a\times netOD + b\times netOD^3$$

where a=1 and b=3 were used as preliminary uncalibrated values (driven by the typical ratio around 3 of the corresponding calibrated quantities for EBT3). For irradiations, two *ad hoc* dosemeter holders of PMMA were custom-made (Figure 1). They were mounted on a track united with the 2D-IC to place the detectors along the beam axis and reproduce their position effortlessly in different irradiation sessions. One of the dedicated holders was for both SD and mD. It is a parallelepiped (6.5x1.5x2.5) cm^3, two holes at the opposite ends of the larger faces allow the right positioning of SD or mD along the beam axis (see figure 1); the other PMMA holder, having the same dimensions, allows several dosemeters to be irradiated simultaneously. Three alanine pellets were housed at the vertices of an equilateral triangle, at the center of the beam; LiF crystals were positioned below the alanine in correspondence of the triangle base; SD and mD detectors were housed close to the other two sides of the triangle. No dedicated holders were made for MOSFETs or EBT3 films, which were placed on the other detector holders, when used.

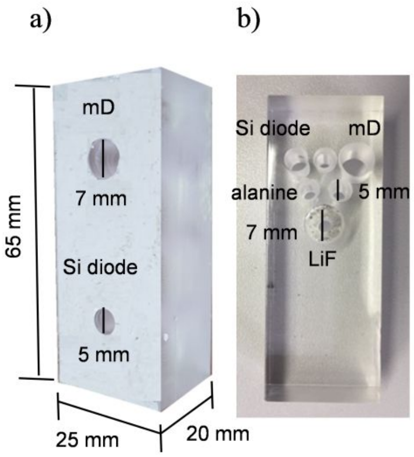

Figure 1. Dedicated PMMA dosimeter holders used to irradiate a) silicon diode or microDiamond and b) several dosimeters simultaneously.

Alanine and LiF crystals detectors were calibrated in ^{60}Co source at the Italian Primary Laboratory (ENEA-INMRI Casaccia). The microDiamond detector was provided with the calibration in ^{60}Co by the PTW in 2017; the MOSFET detector was calibrated at IFO hospital in a 6 MV beam against an ionization chamber calibrated at the Italian Primary Laboratory, in both cases following the IAEA TRS-398 protocol. The EBT3 film sheets came from a non-calibrated batch. The Si diode is no longer calibrated because of its extensive use in protons.

The 2D ionization chamber has not been calibrated yet using a reference standard condition, as it is still under test. As a first step it was characterized against alanine in the TOP-IMPLART protons, by comparing the 2D charge responses in the top-flat central region corresponding to the area covered by the alanine pellets sitting behind the chamber, at different doses, dose rates and different times. The two detector responses differ by less than 3%; this variation includes the uncompensated effects on the chamber due to temperature (<3 Celsius degree) and pressure (<10 hPa) variability during the measurements.

In each run, at least two dosimetry systems were simultaneously irradiated. Routinely adopted for calibration of clinical photon beams, alanine and mD dosemeters were here used for dose measurements. Measured dose was evaluated using the ^{60}Co calibration. For the remaining dosimetry systems only the relative dosemeter response was acquired during the experimental irradiation runs; for the purposes of this work, no correction factor was applied to the detector response to take into account for the different calibration beam used.

Irradiations

The pulsed structure of the proton beam is currently characterized by a beam current from 0.5 to 35 μA, with 3 μs pulse duration and repetition frequency in the (10-50) Hz range. The main characteristics of the beam are summarized in Table 1. Details on the beam line have been reported elsewhere[(1)]. An integral ionization chamber, mounted right after the proton extraction segment, measures the output charge and is used during the irradiations to turn-off the beam when a preset amount of particle charge is reached. The total dose delivered is therefore not affected by pulse instabilities[(1)]. As the beam spot diameter at the pipe exit window is ~2 mm and the active scanning beam system has not been implemented yet, a lateral spread of single spot was obtained, performing all irradiations with the detectors placed at 175 cm from the window exit, in free air. The energy of the protons at the detector surface was (31.00 ± 0.03) MeV. It was measured by irradiating a polished LiF crystal of (10x10x1) mm^3, placing the larger face parallel to the proton beam direction. In this irradiation geometry, the proton beam generates a spatial distribution of stable F^2 and F^{3+} color centers whose concentrations with depth are proportional to LET[(2)]. The visible photoluminescence of color centers allowed using an optical fluorescence microscope to acquire the photo-luminescent LET profile stored in the crystal. The beam energy was estimated by comparing such experimental LET profile with the one provided by SRIM code simulations in the same experimental conditions. The uncertainty of the energy estimation is related to the uncertainty of the measured Bragg peak depth in the crystal, which depends on the spatial resolution of the microscope.

At 31 MeV, all the detectors used were working in the transmission conditions of the beam. Irradiation was performed both with and without an aluminum collimator of 16 mm diameter and 10 mm thick, placed in front of the 2D-IC ~7 cm away from it.

Beam stability

The stability of the 35 MeV nominal energy beam was investigated using 2D-IC, mD, Si diode, MOSFETs, LiF crystals and alanine. In particular, the short-term stability was evaluated measuring the reproducibility, in terms of percentage coefficient of variation (CV%, defined as the standard deviation to the mean ratio, expressed as a percentage), of the detector response of 10 repeated irradiations (i.e. 10 measurements/run) under the same experimental conditions. For alanine, the mean value of the signal of three pellets irradiated simultaneously was used in each irradiation. Runs were performed at three different dose-rates.

Currently, because of the continuous upgrade of the accelerator components, no indication can be given as for the long-term stability of the beam. Indeed, in the irradiation sessions over several months beam parameters were changed according to the improvements to the accelerator structures.

Beam homogeneity

Beam homogeneity of the laterally spread single spot was evaluated both with 2D-IC and EBT3 films. Measurements were done with and without the aluminum collimator. The collimator was housed on a rectangular frame positioned along the beam axis; when it was removed a larger proton field was available, shaped on the frame dimensions. The measurement without collimator was always performed at the beginning of each irradiation session in order to verify beam position with respect to dosemeter position. The collimator was specifically used to better evaluate the homogeneity on the circular surface assumed suitable for radiobiological experiments. As already mentioned, no dedicated holder was made for homogeneity investigation. Pieces of EBT3 film were positioned on the multi-dosemeter holder perpendicularly to the incoming beam.

Homogeneity was evaluated as CV% of the net pixel value (NPV) along the diameters drawn on x and y axes, for different diameter lengths.

Dose measurements

Dose measurements were done with alanine and mD detectors in different measurement runs.

Custom-made holders were used for the two detector types (see Figure 1). No collimator was positioned along the beam axis for dose measurements. Alanine pellets and microDiamond were positioned in air with their detector surface at the same distance from the beam exit (175 cm). Therefore, taking into account the density and thickness of the detector sensitive and coating materials, detector reference points were at the water-equivalent depth of 1.5 mm and 1.0 mm for alanine and mD, respectively. Three consecutive irradiations were repeated under the same experimental conditions for both dosimetry systems. The mean value of the signal of the three irradiations was used for dose determination. Three alanine pellets were used in each irradiation and three pellets were replaced after each irradiation. An average dose rate of 7.6 Gy/min was used. For both detectors, ^{60}Co calibration was used for dose determination in protons.

RESULTS AND DISCUSSION

Beam stability

All detectors were used for short-term stability evaluation of the beam. In the first measurement run, mD was housed in the dedicated holder and irradiated along with 2D-IC. In the second measurement run, the mD was replaced with the SD. A MOSFET was included and positioned on the SD holder close to the detector. From run 3 to run 6, mD was used instead of SD. These irradiations were carried out with the collimated beam. In the last measurement run, the collimator was removed in order to have a larger beam and the multi-dosemeter holder (see Figure 1) was mounted on the track. In this set up all the detectors were positioned for the measurement. Table 2 shows the results of all seven measurement runs. Specifically, in all runs but run 4, all detectors indicated a short-term stability of the beam better than 3%. This finding was always confirmed in several irradiation sessions with the same detectors over a period of about six months. The worse performance of MOSFET, mD and 2C-IC was probably due to the adopted high dose rate, about twice as high as for the other runs. This aspect has to be further investigated. However, because of the large value of the CV% of the MOSFET, the consistency between that detector and mD or 2D-

IC results was also investigated through Bland Altman plot. This analysis revealed no significant difference among the detectors results.
For LiF crystals two values are shown, related to the green and red photoluminescence signals simultaneously emitted, under blue light excitation, by the F_3^+ and F_2 color centers, respectively[(4)].

Beam homogeneity

Figure 2 shows the profiles of the beam in both configurations, with and without aluminum collimator. In both cases, EBT3 films were irradiated at about 4 Gy. Although the entire profiles are presented, due to the non-linear response of the EBT3 film vs. dose, the homogeneity evaluation was restricted to the region in which an approximation to linear behaviour of the film response vs. dose could be assumed.

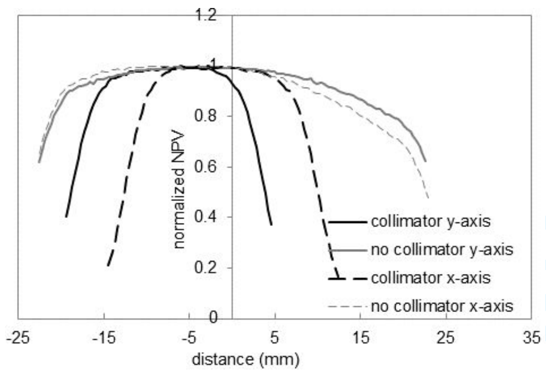

Figure 2. Homogeneity of the laterally spread spot measured by EBT3 film, along the x-axis (dashed line) and the y-axis (solid line). Measurements obtained with (black line) and without (gray line) the aluminum collimator with films placed at about 175 cm away from the beamline exit. In order to compare the profiles, each curve was normalized to its maximum value.

Specifically, the analysis was restricted to the region around the maximum value over which response variations of film were less than 5%. The results of beam homogeneity are reported in Table 3. With the collimator, homogeneity was better than 3.3% on circular surfaces with diameter of less than 17 mm. The comparison with the data obtained after removal of the collimator reveals an apparent incongruity. This is due to the different portions of the beam which were analyzed in the two configurations. The analysis on the large field was done in order to estimate the maximum homogeneity attainable in a region having the same dimensions as the collimator. The finding in that configuration proved that the region selected in the measurement with collimator was in a different part of the field. This means that the center of the aluminum collimator was not aligned with the beam axis. As it is possible to see from figure 2 in which the distances from beam axis are indicated.
At the current low energy of the protons and with the collimator placed far from the detectors, no significant dosimetric impact of scattered protons is expected[(6)].
The results obtained with EBT3 films were confirmed with 2D-IC, with EBT3 profiles reprocessed according to the method described in the Materials and Methods Section. Figure 3 shows the comparison of the 2D-IC and reprocessed EBT3 film data, for irradiation with collimator. Despite the approximations assumed in the above analysis, a good agreement was found, both in terms of shapes (Kolmogorov-Smirnov test probabilities on both x and y larger than 0.99996) and overall

response (ratio of integrals of 2D-IC / reprocessed EBT3 = 1.0084 and 0.987 for x and y profiles integrals, respectively).

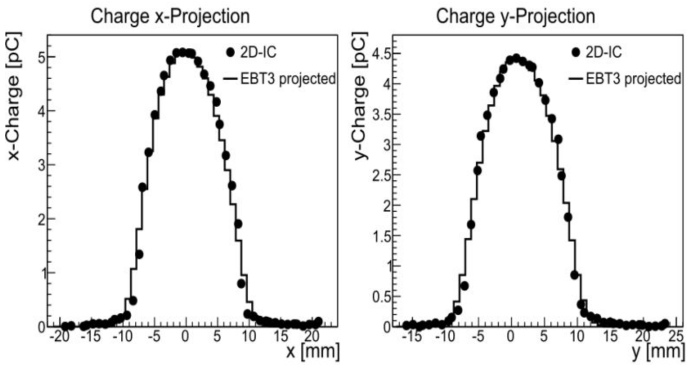

Figure 3. Comparison of the 2D-IC and reprocessed EBT3 film data, in irradiation with aluminum collimator.

Dose measurements

As three alanine pellets are used for each irradiation, it was not possible to place any pellets overlapping the mD position. Therefore, a difference in dose assessment is expected between the two detectors. It could match the beam homogeneity value on the circular surface defined by the alanine pellets (13 mm diameter). Specifically, a contribution to the difference up to 1.7% (corresponding to the 14.5 mm diameter, in Table 3) has to be considered.

In addition, a difference in dose assessment is also expected due to the different position of the alanine and mD reference points. An evaluation of this contribution was done using a SRIM code simulation of the energy loss in water of 31 MeV beam. It showed that a difference of about 2.6% between the dose measured with the two detectors had to be expected.

Doses of (10.45±0.15) Gy and (10.62±0.08) Gy were measured with alanine and mD, respectively. The uncertainty is the standard deviation of the measurements. The two values agree within 1.6%.

CONCLUSIONS

This work focuses on the performance, in terms of stability and homogeneity, of the 35 MeV proton beam delivered by the TOP-IMPLART linear accelerator under construction in Italy. The investigation shows that the current stability of the beam is better than 3 %, an improvement with respect to 27 MeV energy (5%)[(1)], comparing measurements performed at the same dose rates. Further investigations will be done using high dose rate values. Also the homogeneity of the beam, within 2.6% in a 16 mm diameter circular surface, showed an apparent improvement with respect to the performance at the lower energy (4% at 27 MeV)[(1)] over the same area. However, this result has to be evaluated in the light of the dosimeter position with respect to the beam exit: 100 cm at 27 MeV and 175 cm at 35 MeV. Therefore, considering the beam divergence, no significant improvement in the beam homogeneity can be clearly evidenced. These results highlight the positive influence of the changes introduced in the accelerator structure in terms of stability of the beam. The delivered dose was measured with alanine and microDiamond detectors, which agree within 1.6%. This result confirms the good features of the microDiamond to be used also for dose assessment in low-energy protons with the advantage of an on-line dose measurement.

A full dosimetric characterization of the beam at this stage of accelerator construction is still in progress, but this preliminary investigation has indicated the suitability of this beam for radiobiological experiments to study the therapeutic potentialities of the peculiar pulsed structure of the beam at the currently available energies, which are more appropriate for this kind of measurements.

FUNDING

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Table 1. Current parameters of the 35 MeV proton beam.

Parameter	Value
Beam current	0.5-35 μA
Pulse duration	3 μs
Pulse repetition frequency	10-50 Hz
Charge/pulse	112 pC (max)
Number of particles/pulse	7E8 (max)
Number of particles/sec	3.5E10 (max)
Spot size at the beam exit	2 mm

Table 2. Short-term stability of the beam, expressed as percentage variation coefficient, in different measurement runs (R#).

Detector	R1	R2	R3	R4	R5	R6	R7
microDiamond	1.65		1.14	3.25	0.73	1.38	0.98
2D-IC	1.89	1.63	1.38	3.50	0.77	1.02	1.23
MOSFET		2.03	1.66	4.64	1.71	1.51	1.51
Silicon diode		1.38					2.51
LiF crystal							1.98(F_3^+)
							3.12(F_2)
alanine							1.49

Table 3. Beam homogeneity evaluation for different diameters of the circular surface, expresses as CV% of the NPV along the diameters drawn on x and y axes, with (second column) and without (third column) collimator.

Diameter (mm)	Collimator	No collimator
14.5	1.7	
16.0	2.6	
17.0	3.3	0.6
25.0		1.9