Physica Medica 30 (2014) 559–569

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Original paper

Proton range monitoring with in-beam PET: Monte Carlo activity predictions and comparison with cyclotron data

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ARTICLE INFO

Article history:
Received 19 January 2014
Received in revised form
3 April 2014
Accepted 6 April 2014
Available online 29 April 2014

Keywords:
Hadron therapy
In-beam PET
Treatment quality monitoring
Cyclotron

ABSTRACT

Goal: Proton treatment monitoring with Positron-Emission-Tomography (PET) is based on comparing measured and Monte Carlo (MC) predicted β^+ activity distributions. Here we present PET β^+ activity data and MC predictions both during and after proton irradiation of homogeneous PMMA targets, where protons were extracted from a cyclotron.

Methods and materials: PMMA phantoms were irradiated with 62 MeV protons extracted from the CATANA cyclotron. PET activity data were acquired with a 10×10 cm^2 planar PET system and compared with predictions from the FLUKA MC generator. We investigated which isotopes are produced and decay during irradiation, and compared them to the situation after irradiation. For various irradiation conditions we compared one-dimensional activity distributions of MC and data, focussing on $\Delta w50\%$, i.e., the distance between the 50% rise and 50% fall-off position.

Results: The PET system is able to acquire data during and after cyclotron irradiation. For PMMA phantoms the difference between the FLUKA MC prediction and our data in $\Delta w50\%$ is less than 1 mm. The ratio of PET activity events during and after irradiation is about 1 in both data and FLUKA, when equal time-frames are considered. Some differences are observed in profile shape.

Conclusion: We found a good agreement in $\Delta w50\%$ and in the ratio between beam-on and beam-off activity between the PET data and the FLUKA MC predictions in all irradiation conditions.

Introduction

Radiotherapy plays an important role in modern cancer treatment, with about 50% of all cancer patients receiving radiotherapy [1]. The main challenge in radiotherapy is how to deliver high dose to the tumour region, while minimizing dose to healthy tissue. Proton therapy is a promising radiotherapy technique, because it offers the possibility to deliver high dose in well-defined volumes (Bragg-peak). However, the steep dose gradients make proton therapy much more sensitive to treatment uncertainties than conventionally used X-ray therapy. Indeed, uncertainties in patient positioning, proton range and anatomical changes can cause dose distortions, possibly impairing the beneficial effects of charged particle therapy.

For this reason, it is highly desirable to monitor the effectively delivered dose, or at least the particle range in patients. PET imaging is a non-invasive way of in-vivo verification of the dose delivered to the target volume. During ion beam irradiation, various β^+ emitting isotopes (^{15}O, ^{11}C, ^{13}N, etc) are generated in the patient. These β^+ annihilations can be detected with a PET system during or after the irradiation, depending on the half-life of the β^+ emitting isotope. Since dose and β^+ activity result from different physics processes, the relation between them is indirect, as shown in Fig. 1. By measuring the β^+ activity in a certain time-frame, and by comparing it to planned β^+ activity from Monte Carlo simulations,

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http://dx.doi.org/10.1016/j.ejmp.2014.04.003
1120-1797/

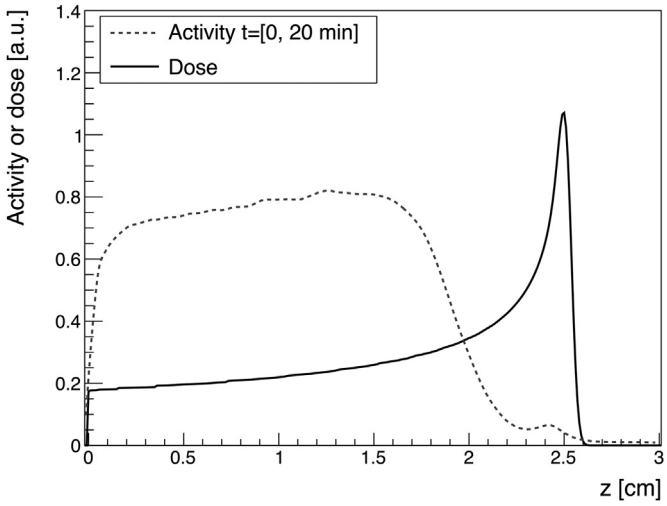

Figure 1. Simulated Bragg peak and activity 1-D profile along the *z*-direction (beam direction) of 58 MeV protons on a PMMA target, obtained with a FLUKA Monte Carlo simulation of 800 M protons.

it is possible to verify whether the dose was delivered correctly. If large differences are found between the measured and planned β^+ activity distributions, the treatment can be adjusted. For more details about in-vivo proton range verification we refer to recent review papers by Knopf and Lomax [2] and Zhu and El Fahkri [3].

There are different PET data-taking strategies. In '*offline PET data acquisition*', data are acquired after patient irradiation with a commercial PET-CT scanner outside the treatment room, and PET data are usually acquired after a CT scan. Although the method is economically attractive, biological washout and patient movement limit the use of this method. Essentially only the β^+ activity from ^{11}C (half-life 20 min) can be detected. This method has been clinically applied in several treatment centres, see for instance references [4–8]. Another strategy is so-called '*in-room PET data acquisition*'. Here a full-ring PET detector is installed inside the treatment room [9,10]. The main advantage with respect to offline imaging is that signal washout is greatly reduced, as it allows for detection of activity from ^{15}O (half-life 2 min). This isotope is produced in abundance in human tissue during irradiation. Also, no repositioning of the patient is necessary. Disadvantages include a slower patient throughput and problems with co-registration of PET and CT images. Another promising strategy is '*in-beam PET data acquisition*'. Here a PET detector is integrated in the beam-delivery system [11–15]. The advantage is that data can be taken not only after, but also *during irradiation*, so problems related to washout and patient motion are minimized. One of the main technical difficulties is the integration into the beam delivery system. Dual-head PET systems [13,15,16] are relatively easy to install, but have limited angular coverage, resulting in low sensitivity and artifacts in reconstructed images. Time-of-flight techniques are proposed to counterbalance these issues [17]. PET systems with more efficient geometries have been developed and include a dual-ring [18] and a full-ring [19] PET, cut at a slant angle. Apart from geometrical issues, another important challenge of in-beam PET is to take advantage of the full irradiation time interval, i.e., to include not only data acquired after irradiation of during beam-pauses, but also during beam extraction [20]. In fact, background from random coincidences tends to paralyze the PET detectors, and advanced techniques are required for background suppression [21].

In this last context, a compact planar PET prototype has been developed and built in Pisa, which can be installed in the beam delivery system. This system is capable of acquiring data during ('*beam-on*') and after ('*beam-off*') particle irradiation, as was demonstrated recently [15,22] for proton irradiation with the CATANA (Center for Hadron Therapy and Advanced Nuclear Applications, Centro di AdroTerapia e Applicazioni Nucleari Avanzate) cyclotron. Including data acquired during irradiation was seen to improve the quality of range measurements in PMMA with respect to data acquired only after irradiation. It was also shown that 'beam-on' data alone were enough to give precisions in range determination better than 1 mm when at least 5 Gy was delivered [15].

A crucial issue for a successful application of PET to detect range deviations is reliable Monte Carlo predictions of the expected particle range. From the treatment plan, the time course of the delivery, and the planning CT scan, the activity map and particle range can be predicted in any time-frame. Although analytical approaches can offer a fast solution for this purpose [23,24], Monte Carlo predictions are considered more accurate [25]. The validation of PET modelling against experimental data has been performed in the past with various Monte Carlo generators [26–37]. Since beam-background at cyclotrons was considered a major limitation, none of these studies include range measurements performed during target irradiation with a cyclotron. Also, since PET dose verification is generally more relevant for deep-seated tumours, most studies focus on high energies. However, range verification can be desirable also when irradiating more superficially located tumours, such as for instance ocular tumours and head-and-neck tumours.

The scope of this work is to present 'in-beam' PET proton range verifications with data acquired both during and after cyclotron irradiation with 62 MeV protons, and to compare these PET data to Monte Carlo predictions. More precisely, we use a set of PET β^+ activity data acquired during and after PMMA phantom irradiation from the CATANA cyclotron, partly reported previously [22], and compare the measured range with those predicted by the FLUKA Monte Carlo generator [38,39]. We investigate what β^+ emitting isotopes are formed, and present Monte Carlo predictions and measurements of the proton range under different irradiation conditions. In particular, we will show that range monitoring can be performed also during irradiation, despite the large beam backgrounds. Different to most previous studies, we focus on verifying the proton range, and do not intend to perform a detailed validation of the predicted activity map. This is on one hand because our detector has partial angular coverage only, resulting in image artefacts, and on the other hand because we did not perform a full signal propagation, as would be necessary for this purpose. In contrast to several previous studies performed with FLUKA in this context for protons [27–29,31,32], where proton track length was folded with external experimental cross section data, we have now used directly the prediction of newly developed FLUKA models [40,41]. These models have been benchmarked with up-to-date experimental nuclear cross section data. The present study therefore also helps to improve our understanding of the involved nuclear processes.

Methods and materials

PET system

We used a planar PET system developed at INFN (National Institute of Nuclear physics, Istituto Nazionale di Fisica Nucleare) and the University of Pisa, previously described in Refs. [15,22,42,43]. It consisted of two planar 10×10 cm^2 detector heads, each composed of four modules of 5×5 cm^2 each, which