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Simulation of proton range monitoring in an anthropomorphic phantom using multi-slat collimators and time-of-flight detection of prompt-gamma quanta

Patricia Cambraia Lopes[a,b,c], Paulo Crespo[b,d,*], Hugo Simões[b,d], Rui Ferreira Marques[b,d], Katia Parodi[c,e], Dennis R Schaart[a,f]

[a] Department of Radiation Science and Technology, Delft University of Technology, Delft, The Netherlands
[b] Laboratório de Instrumentação e Física Experimental de Partículas, Coimbra, Portugal
[c] Heidelberg Ion-Beam Therapy Center, Heidelberg University Clinic, Heidelberg, Germany
[d] Physics Department, Universidade de Coimbra, Coimbra, Portugal
[e] Department of Medical Physics, Ludwig-Maximilians-Universität München, Munich, Germany
[f] Holland Proton Therapy Centre (Holland PTC), Delft, The Netherlands

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ABSTRACT

Prompt-gamma (PG) imaging has the potential for monitoring proton therapy in real time. Different approaches are investigated. We focus on developing multi-slat collimators to image PG quanta, aiming at optimizing collimator performance to detect deviations in treatment delivery. We investigated six different multi-slat configurations, which have either optimal (analytical) intrinsic spatial resolution at fixed efficiency, or otherwise; at different distances from the proton pencil-beam axis (15 cm–35 cm). We used Geant4 to simulate irradiations of the head (energy: 130 MeV) and pelvis (200 MeV) of an anthropomorphic phantom, with and without physiologic/morphologic or setup changes of clinical dosimetric relevance. The particles escaping the phantom were transported through each of these multi-slat configurations and the gamma counts profiles were recorded at the collimator exit. Median filtering was applied to the registered PG-profiles to mitigate the effects of septa shadowing and statistical fluctuations. Time-of-flight discrimination was used to enhance the signal-to-background ratio, which appeared crucial for 200 MeV irradiations. Visual detection of the artificially introduced changes was possible by comparing the PG to the depth-dose profiles. Moreover, 2 mm range shifts could be detected in the head irradiation case using a simple linear regression fit to the falloff of the PG-profile. The influence of changes in complex, patient-like dose distributions on the PG-profiles obtained with multi-slat collimation is first studied in this work, which further gives insight on collimator design optimization and highlights its potential and simplicity for detecting proton treatment deviations over a wide range of Bragg peak positions.

1. Introduction

Proton therapy is a form of radiotherapy (RT) that uses proton beams to destroy solid tumors. The potential of proton RT over conventional (photon) RT is that it can deliver a high dose to the tumor with less overall dose to healthy-tissues, a factor very important to reduce the side effects of irradiation. This high dose conformity is enabled by the fact that protons release a large amount of their energy in a highly localized region, the Bragg peak (BP), just before they stop [1]. This makes proton therapy well suited for treating e.g., deep-seated and pediatric tumors.

Despite these physical advantages, treatment plans in proton therapy are often sub-optimal in clinical practice due to the relatively large uncertainty in the particle range *in vivo* [2]. Particle range strongly depends on tissue composition, density, and heterogeneities. The main causes of range uncertainty are related to: (1) the conversion of X-ray computed tomography (CT) data to proton interaction data [3]; and (2) patient morphological/anatomical and/or physiological changes occurring during the course of the therapy. Such changes may include, e.g., edema of the irradiated region [4], tumor regression [5], and filling of empty cavities due to inflammation and/or increased tissue permeability leading to edema.

Prompt-gamma (PG) imaging has been suggested for *in vivo* monitoring of proton therapy delivery, range verification in particular [6,7].

* Corresponding author.
E-mail address: crespo@lip.pt (P. Crespo).

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This technique is based on the detection of gamma quanta originating from proton-nuclear interactions within the body, which are emitted promptly and can escape from the patient. Compared to PET imaging of 511 keV gamma rays resulting from positron-emission decay of proton-induced radioactive nuclides [5,8–11], PG imaging does not rely on delayed emission and therefore is unaffected by biological processes (e.g., activity washout). Moreover, it may provide real-time feedback on the treatment delivery, on a pencil-beam basis.

PG rays are single photons, therefore Compton cameras [12–15], mechanically collimated cameras, PG spectroscopy [16], and timing spectroscopy [17] are currently being investigated to resolve spatial information. The scope of this work is mechanical collimation, which has the advantages of relative simplicity of implementation and compactness, as well as the possibility to provide complementary information beyond the particle range. Prompt-gamma profiles can be obtained by simple projection of the object onto the image plane, without Compton reconstruction. Moreover, full-energy deposition is not required, unlike in spectroscopy measurements where only few energy-resolved lines are usually targeted [16,18–22]. Kelleter et al. [21] present an experimental spectroscopy study. However, no variation in the distal fall-off of the Bragg peak is exploited. Zarifi et al. [22] present a Geant4-based Monte Carlo study with sub-millimeter range resolving power. However, the influence of a detection system (diminishing the counting statistics) is not taken into account, together with a validation of the prompt gamma yield, which has been shown to vary between the Geant4 Monte Carlo code in respect to the MCNPx and Fluka packages [23].

In pencil-beam scanning (PBS), the lateral position of the proton pencil beam is well known already, so obtaining information on the dose distribution along the beam direction is more important. Different types of collimators have been investigated, such as the multi-slat or multi-slit collimator [24–26], the pinhole collimator [27], and a one-dimensional pinhole denoted as knife-edge slit [28–30]. Multi-slat collimators are made of multiple plates ('slats') made of a high-density material such as tungsten. The slats are typically placed perpendicular to the pencil-beam direction, although tapered configurations can also be used [31]. Previous studies have shown that collimated PG profiles correlate well with the distal dose falloff, both in simulations [23,29] and experiments [25,28–30,32,33]. Although the results are encouraging, the aforementioned works are proof-of-principle studies focused mostly on comparing collimated PG profiles to pristine Bragg peak distributions in homogeneous phantoms and/or phantoms with simple artificial inserts of different materials. Smeets et al. [34] have considered a multi-slat camera operated without the shifting time-of-flight (TOF) method, which results in (n,γ) reactions that disturb the optimum profile distribution. In addition, they compared two cameras (knife-edge slit vs multi-slat) with a weight limit being imposed on both, which may not allow optimal multi-slat camera operation. Heterogeneities are also not considered in that study. The first *in vivo* results of PG imaging have been recently reported using a knife-edge slit collimator, obtained during brain irradiation with pencil beam scanning [35] and passive beam collimation [36]. Krimmer et al. [37] provide a thorough review of prompt-gamma-based range verification.

In this work, we focus on developing multi-slat collimators that accept photons emitted at right angles from the beam axis, for proton therapy verification on a per-pencil-beam basis, and considering clinical realistic scenarios. Potential advantages in regard to the knife-edge slit collimator in this case, are that the multi-slat collimator allows for simultaneous imaging of the whole proton path and not only the dose falloff, due to the constancy of its geometric performance throughout its field of view (FOV).

There is still little knowledge on the optimal properties of a multi-slat collimator for PG imaging. Although the potential of multi-slat PG imaging has been inferred to some extent from PG measurements using a single collimated detector scanned parallel to the beam axis [32,33], these studies give little insight into the signal-to-background ratio in a full-scale system. Min et al. [25] took a first step towards optimizing a multi-slat collimator based on Monte Carlo simulations, but considered only one fixed distance between the phantom and the collimator and did not apply TOF background discrimination (due to (n,γ) reactions).

We perform Monte Carlo (Geant4) simulations of the PG profiles registered by various multi-slat configurations, upon proton irradiations of an NCAT (NURBS-based cardiac-torso) anthropomorphic phantom [38]. We study the viability of using a multi-slat collimated gamma camera, from the clinical deviation in dose delivery until its detection in the imaging system. The alterations in dose delivered in an anthropomorphic phantom studied in this paper correspond to real questions that arose in clinical situations, which some of the authors have experienced on the German heavy ion pilot project (GSI Darmstadt) (despite being then in the context of carbon ions). For example, it was sometimes wondered whether an undershoot or an overshoot was occurring during fractionated irradiation in the brain (possibly due to repeated damage to brain vascularization). One possible mechanism responsible for inducing such question was the fact that the images were obtained by in-beam PET, where washout was thought to play a major role. Here, washout plays no effect; therefore, this paper presents for the first time the advantage of imaging prompt gammas that are washout-free, taking into account a human phantom.

The simulated PG profiles obtained with different multi-slat collimators are compared to determine which collimator performs best. Furthermore, the influence of simple signal-processing options such as TOF discrimination, energy selection, and median filtering are studied. The detector system was not simulated on purpose, in order to give emphasis on the effect of the collimator itself, without compromising the different results that would be obtained by choosing one or other type of detector. By using a digital anthropomorphic phantom connected to simulations with a multi-slat collimation system, this work tries to estimate whether such a system may be useful in real clinical scenarios.

2. Methods

In the following section we briefly describe how the multi-slat configurations for further study were selected. Section 2.2 subsequently describes the Monte Carlo simulation framework, Section 2.3 the NCAT case studies, and Section 2.4 the post-processing of the simulation data.

2.1. Definition of multi-slat collimator configurations

The optimum slat height, slat thickness, and slit aperture (Fig. 15, Appendix A) for multi-slat collimators at different distances from the beam axis, were determined as previously explained by Cambraia Lopes et al [39], using Eqs. (1) and (2), that give its *effective point resolution*, $R_{eff}^{multi-slat}$, and its *effective 2D efficiency*, $g_{eff}^{multi-slat}$ at the beam axis:

$$R_{eff}^{multi-slat} \approx d(l_{eff} + b)/l_{eff},\ l_{eff} = l - 2/\mu \quad (1)$$

$$g_{eff}^{multi-slat} \approx d^2/[2\pi l_{eff}(d + t)], \text{with}\, t = [6d/\mu]/[l-(3/\mu)] \quad (2)$$

where l is the slat height, d the slit aperture in the beam direction, b the distance between the beam axis and the front surface of the multi-slat collimator, t is the slat thickness, and l_{eff} is the effective collimator height, used to account for septa penetration [40], and calculated based on the linear attenuation coefficient $\mu = 7.9 \times 10^{-2}\,\text{mm}^{-1}$ for 5 MeV photons in tungsten [41]. The derivation of the *effective 2D efficiency* is shown in Appendix A.

Here we study collimators at distances between the beam axis and their front surface (b) of 15 cm, 25 cm, and 35 cm, which are compatible with typical treatment scenarios. The applicability of one or another distance in practice will depend on the irradiated site, angle of incidence, and the size of the patient. For e.g., for pelvis or thorax irradiations, the minimum achievable value of b may be higher than for