A MC tool for CT-based calculations of dose delivery and $\beta^+$-activation in proton therapy

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Abstract. The feasibility and value of offline PET/CT imaging for in-vivo, non-invasive verification of proton beam delivery is currently under investigation at Massachusetts General Hospital, Boston. Within this project we have developed a Monte Carlo framework for CT-based calculation of dose and irradiation induced positron emitter distributions using the FLUKA Monte Carlo code. Particle transport in the patient is performed on the CT grid, taking into account realistic tissue composition as well as the correlation between CT numbers and stopping power ratio to water as used by the commercial treatment planning system (XiO, Computerized Medical System Inc.). Positron emitter production is computed by combining during runtime proton fluence with experimental and evaluated cross-sections for all the major reaction channels yielding measurable tissue activation. In this paper we describe our dedicated implementation which might be easily generalised for use in other proton therapy centres or extended to include further activation reaction channels, provided that initial beam information or experimental cross sections are known. Further, we present clinical examples for calculation of delivered dose and irradiation induced PET activation.

1. Introduction

Therapeutic proton beams activate positron emitters, pre-dominantly $^{11}$C and $^{15}$O, in patients. Detection of this irradiation induced activation via positron emission tomography (PET) may offer a valuable tool for in-vivo, non invasive verification of the beam delivery in proton therapy (cf. [1], [2] and references therein). In particular, the possibility to extract range information from the activated tissue may enable a safe reduction of the margins as well as an increase of the beam angle options (e.g., including portals directly stopping in front of critical structures) in treatment planning, potentially resulting in an even more improved conformality of proton treatments.

Following detailed pre-clinical phantom experiments [3], clinical studies have been started at Massachusetts General Hospital (MGH) to address feasibility and value of PET/CT (positron emission tomography / computed tomography) imaging directly after proton treatment [4]. Delivered dose and induced $\beta^+$-activity are however different quantities. For useful clinical interpretation, PET measurements have to be compared with corresponding PET images calculated on the basis of the planned treatment, as already done in clinical routine for in-beam PET verification of carbon ion therapy at GSI Darmstadt, Germany [5,6]. Due to the limitation of the proton induced $\beta^+$-activation to target fragmentation in combination with the pronounced lateral scattering of proton beams, detailed
modelling of particle transport in the patient with realistic description of the tissue composition is advisable for PET calculations in proton therapy [2]. Thus, within our project we have developed a Monte Carlo (MC) framework for CT-based calculation of dose and irradiation induced positron emitter distributions using the FLUKA transport code [7]. This paper reviews our dedicated implementation, requiring customization of few user-oriented routines and some extra code development, which is now included in the standard FLUKA distribution since the 2006.3 release. Examples of clinical applications are also reported.

2. Material and methods

Initial proton beam phase space information (i.e., individual proton energy, position and direction) at the exit of the treatment head prior to the entrance in the patient is obtained from a separate Geant4 [8] based Monte Carlo (MC) simulation. This models with sub-millimetre accuracy the gantry-equipped beam delivery of the Francis H. Burr Proton Therapy Center of MGH, including the patient- and field-specific beam modifiers [9]. Starting from this phase space information, particle transport in the patient is achieved using the FLUKA Monte Carlo code. This is a general purpose MC transport code, which was originally developed for high energy physics, but has been extended since 1991 to cover also the lower energy range of therapeutic interest. Furthermore, it was recently upgraded with a new algorithm allowing for efficient particle transport in CT voxel geometries for radiation protection purposes [10]. In proton therapy, FLUKA was already successfully employed by various groups for dosimetric and radiobiological applications [11]. Moreover, it was demonstrated to be an adequate tool for accurate description of in-beam and offline PET phantom studies [2,3,12].

In our MC CT-based implementation, information on the elemental tissue composition and mean density is obtained from a segmentation of the CT scan into 27 Hounsfield Units (HU) intervals, 24 of which are taken from the work of [13], extended with 3 more intervals to higher CT numbers to include metallic implants of Titanium [14, 3]. As suggested in [14], a dedicated code implementation was performed to enable introduction of scaling factors for nuclear and electromagnetic processes (cf. new option CORRFACT in the FLUKA manual). This allows accounting for the continuous dependence of the mass density on the HU values within each HU interval, which is defined in the MC as a unique material sharing the same composition and a mean density (corresponding to the HU value at the center of the considered interval). The electromagnetic scaling factor is furthermore adjusted in order to force the program to reproduce the same dependence of the relative stopping power ratio to water versus HU as used by the treatment planning system [14, 3]. This guarantees reproduction of the same range predicted by the planning system, which is of utmost importance for in-vivo range verification based on the comparison between measured and Monte Carlo calculated PET images.

Whereas dose is calculated using standard FLUKA utilities, positron emitter production is calculated by combining proton fluence with experimental and evaluated cross sections, as proposed elsewhere [12]. Besides the main (p,pn) interactions on C and O leading to the production of $^{11}$C and $^{15}$O, further reaction channels on N, O, Ca, P yielding $^{11}$C, $^{15}$O, $^{13}$N, $^{38}$K and $^{30}$P were included. A more detailed description of our specific implementation is given in a separate paper [15].

3. Results

Examples of MC calculated dose delivery and corresponding main yield of $^{11}$C and $^{15}$O positron emitters are shown in figures 1-2 for one single oblique portal of a cranial tumor patient treated at the Francis H. Burr Proton Therapy Center at MGH Boston. The dose distribution is compared with the calculation of the commercial analytical treatment planning system (XiO, Computerized Medical Systems Inc.), which employs the pencil beam algorithm described elsewhere [16]. The activity distribution resulting from the MC predicted production of positron emitters is shown in figure 3 for two different imaging scenarios, i.e. for the same acquisition time of 5 min starting 15 min or immediately after completion of a 60 s long irradiation. This choice would correspond to the usage of a remote or an in-room PET scanner, respectively.
Figure 1. Comparison between treatment plan (left) and MC (right) calculated dose distributions for an oblique portal delivering 909 mGy to a clivus chordoma patient. The color bar shows dose levels in mGy, whereas the CT numbers (black-white scale) were arbitrarily rescaled for display purposes.

Figure 2. MC calculated production of $^{15}$O (left) and $^{11}$C (right) for the same portal of figure 1. The colour bar shows the number of produced isotopes for delivery of the prescribed dose.
The comparison between the MC calculation and the planned dose distribution generally shows good agreement in terms of lateral field extension and beam range. Exceptions are found in cases more sensitive to the limitations of analytical pencil beam algorithms, like in the presence of air/tissue interfaces or metallic implants [4]. When normalizing both calculations to the prescribed dose delivery, minor differences are also found in terms of absolute dose values because of the different computational approach. MC calculation in fact keeps into account a realistic composition of the patient tissue based on the stoichiometric calibration of the CT scan [13]. Differently, the commercial treatment planning system computes dose deposited to water, accounting for the patient density by means of a proper adjustment of the beam penetration depth. Hence, the former MC approach provides a more accurate calculation of the dose deposited to tissue, especially in the presence of high density and high Z materials. A more detailed dosimetric comparison is however beyond the purpose of this work and is subject of ongoing research at MGH, where a dedicated Geant4 based implementation is used for daily clinical MC dose calculations [17] and an inter-comparison between the two MC codes is planned.

Activity distributions calculated by means of the developed FLUKA based approach are generally found in good agreement with offline PET/CT images measured 13 to 20 min after proton irradiation at MGH [4]. The examples reported here indicate the capability of the model to predict the effects of different imaging regimes, resulting from the time dependent contribution of the produced isotopes to the total activity. In particular, the selected data show the dominant contribution from $^{15}$O for acquisitions taken immediately after irradiation, while long-lived emitters like $^{11}$C and $^{13}$N are the main isotopes determining the activity detected 15 min after treatment delivery. The different imaging scenario, e.g. for in-room or off-site PET equipment, clearly affects the signal intensity and spatial distribution for the same duration of the PET acquisition. Hence, MC offers a very useful tool to investigate the impact of different acquisition schemes on the achievable accuracy for PET monitoring, as discussed in more detail elsewhere [15].

4. Discussion and conclusion
A tool for patient- and field-specific Monte Carlo calculation of dose and positron emitter distributions induced by therapeutic proton beam irradiation has been developed at MGH using the FLUKA transport code, starting from available proton beam phase-space information at the treatment head exit prior to entrance in the patient. A customisation of the FLUKA utilities for processing of the patient CT has been performed to allow for assignment of elemental tissue composition based upon literature
data and calculation of the proton range in the patient in analogy to the commercial treatment planning system. Further modifications of the available user-oriented routines of the FLUKA code were done to allow for on-the-fly calculation of positron emitter production using experimental and evaluated cross-sections.

The MC results are generally found in good agreement with dose calculations of the treatment planning code XiO in use at MGH as well as with PET images measured after patient irradiation. The developed MC approach was tailored to the needs of the PET project at the Francis H. Burr Proton Therapy Center at MGH. Nevertheless, it can be easily adapted to use for other facilities, provided that the phase space beam information is known. This is particularly straightforward in the case of active beam delivery systems, which are increasingly used in new or under construction ion beam centres. Furthermore, the MC implementation can be also easily extended to include additional reaction channels of known cross-sections. Finally, it might be coupled to a new FLUKA feature for online evolution of the $\beta^+$-decay and transport of the resulting positron and annihilation photons, allowing for a complete simulation of PET signals measured by different detector arrangements. Similar investigations on the usage of FLUKA for PET studies are also ongoing for other ions species than protons such as $^3$He and $^{12}$C [18-20].

Acknowledgement
From Massachusetts General Hospital, Boston, the authors wish to thank J. Sisterson for providing literature data and useful discussion on experimental cross-sections and A. Trofimov for help with the handling and display of patient planning data. This work was supported by NCI Grant 5 P01 CA21239-25 for Proton Radiation Therapy Research

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