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Reliability of proton-nuclear interaction cross section data to predict proton-induced PET images in proton therapy

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Abstract

In-vivo PET range verification relies on the comparison of measured and simulated activity distributions. The accuracy of the simulated distribution depends on the accuracy of the Monte Carlo code, which is in turn dependent on the accuracy of the available cross sections data for β^+ isotope production. We have explored different cross section data available in the literature for the main reaction channels ($^{16}\text{O}(p,pn)^{15}\text{O}$, $^{12}\text{C}(p,pn)^{11}\text{C}$ and $^{16}\text{O}(p,3p3n)^{11}\text{C}$) contributing to the production of β^+ isotopes by proton beams in patients. Available experimental and theoretical values were implemented in the simulation and compared with measured PET images obtained with a high-resolution PET scanner. Each reaction channel was studied independently. A phantom with three different materials was built, two of them with high carbon or oxygen concentration and a third one with average soft tissue composition. Monoenergetic and SOBP field irradiations of the phantom were accomplished and measured PET images were compared with simulation results. Different cross section values for the tissue-equivalent material lead to range differences below 1 mm when a 5 min scan time was employed and close to 5 mm differences for a 30 min scan time with 15 min delay between irradiation and scan (a typical off-line protocol). The results presented here emphasize the need of more accurate measurement of the cross section values of the reaction channels contributing to the production of PET isotopes by proton beams before this in-vivo range verification method can achieve mm accuracy.

1. Introduction

The use of proton therapy to treat cancer has increased significantly in the last few years. The main advantages of protons are the dose maximum at the Bragg peak and the absence of dose distal to the Bragg peak. The accuracy in positioning the distal edge of the dose distribution is crucial for the complete irradiation of the tumor and for constraining the dose to organs at risk. Many different techniques have been proposed for in-vivo proton range verification (Parodi et al 2007a, Parodi et al 2007b, Schneider and Pedroni 1995, Paans and Schippers 1993, Lu 2008). One of these techniques consists in the use of PET imaging to measure the β^+ isotopes produced by the proton beam through inelastic collisions inside the patient. Dose is mainly produced by atomic interactions, while β^+ isotopes are produced through nuclear interactions. Therefore, the measured activity signal is correlated but not directly proportional to the spatial pattern of the delivered dose. Two methods for proton range verification have been proposed. The first one proposes verification by comparison of the distal falloff regions of measured and predicted PET images (Pönisch et al 2004, Parodi and Enghardt 2000). The second method proposes a convolution of the PET signal with

precalculated filter functions (Parodi and Bortfeld 2006). In this case the shape and integral activity of the entire PET signal translates into the shape and integral dose after the convolution process.

PET imaging for range verification has been already used clinically in ion beam therapy (Enghardt *et al* 2004) and promising results were obtained in proton therapy (Parodi *et al* 2007a, Knopf *et al* 2009). However, the accuracy of this method has to be understood in detail before this technique can be widely used in the clinic. One of the factors limiting the prediction accuracy are the measured cross sections for the relevant nuclear reaction channels. The prediction of proton-induced PET images relies on the proton fluence and energy distribution in a given volume, i.e. at each voxel. This in turn depends on the tissue density and elemental composition as well as the nuclear reaction cross sections. The importance of having accurate cross section values to make PET images suitable for proton range monitoring has been pointed out previously (Oelfke *et al* 1996, Litzenberg *et al* 1999, Beebe-Wang *et al* 2003, Parodi *et al* 2005). An extensive comparison of various different cross section values for use with a high resolution PET scanner have been reported by other groups (Beebe-Wang *et al* 2003, Parodi *et al* 2005). A variety of experimental values for cross sections of the different reaction channels can be found in the EXFOR library (EXFOR). Furthermore, theoretical values can be obtained in the ICRU report 63 (ICRU 2000). There are significant discrepancies between different data sets.

The purpose of this work was to study which combination of the nuclear reaction cross section values available in the literature describes best the experimentally determined proton-induced PET images. We separated the contribution of the main nuclear reaction channels by the proper selection of materials and acquisition protocols and used a high resolution PET scanner to compare the measured images with different predictions.

2. Materials and Methods

2.1. Experimental setup

A mobile PET scanner, NeuroPET, is available at the Radiology Department of Massachusetts General Hospital (MGH), Boston. NeuroPET was developed by the PhotoDiagnostic Systems, Inc. for brain PET imaging, and has received clearance from the US Food and Drug Administration (FDA). It uses CsI crystals covering an open bore diameter of 31cm and an axial FOV of 24cm. The scanner uses wavelength-shifting fiber technology to improve sensitivity and spatial resolution. Its compact components make it easy to move it quickly in and out of the proton therapy treatment room at the proton therapy center at MGH. The PET images can be acquired in list mode allowing the time-frames arrangement to be modified afterwards. The 3D-OSEM reconstruction software is provided with the scanner. To study the accuracy of the absolute activity concentration values obtained from measured PET images, we performed several calibration acquisitions with phantoms with different sizes and activity concentrations. The overall error obtained from this calibration was 4 %.

During proton therapy, different β^+ isotopes are produced by nuclear inelastic interactions of protons with the target elements that compose human tissues. Several nuclear reaction channels contribute to the production as shown in table 1. It has been observed (España *et al* 2010, Zhu *et al* 2010) that up to 95% of the β^+ isotopes produced in the patient are produced by three nuclear reaction channels: $^{16}\text{O}(p,pn)^{15}\text{O}$, $^{12}\text{C}(p,pn)^{11}\text{C}$ and $^{16}\text{O}(p,3p3n)^{11}\text{C}$. Consequently, we focused our study on those channels.

A phantom where these main reaction channels could be studied independently was built (see figure 1). The phantom contains three different materials: high-density polyethylene

(HDPE), gelatinous water (gel-water) and tissue equivalent gel (gel-tissue) with similar oxygen/carbon weight fraction ratio as in soft tissue (White *et al* 1987, Woodard and White 1986) (see figure 2). The dimensions are $12 \times 12 \times 6 \text{ cm}^3$ for HDPE, and $12 \times 6 \times 6 \text{ cm}^3$ for gel-water and gel-tissue. The elemental composition and densities for these three materials are given in table 2. The use of HDPE material allowed us to separate the contribution from the carbon channels as it lacks oxygen and nitrogen. In the gel-water material the very low contribution of carbon and nitrogen allows to study the oxygen channels separately. Finally, the gel-tissue material allows to study the accuracy of the cross section values in a tissue-equivalent material.

A monoenergetic proton field with 10 cm range ($\sim 116 \text{ MeV}$) and a spread-out Bragg-peak (SOBP) field with 10 cm range and 6 cm modulation (see figure 1) were delivered to the phantom at one of the gantry rooms of the Francis H. Burr Proton Therapy Center (MGH, Boston). The monoenergetic field was used in order to minimize the spread of the energy spectrum of proton contributing at different depths of the phantom, while the SOBP field was used to analyze a realistic case scenario. A $7 \times 7 \text{ cm}^2$ square aperture and no compensator were used in both cases and the beams were directed perpendicular to one of the bases of the phantom and centered with the interfaces of the different materials (see figure 1). Thus, all materials are irradiated at the same time allowing simultaneous analysis of the measured data. The entrance dose delivered with the monoenergetic field was calculated in order to produce similar activity level than the one achieved when 2 Gy are delivered at the flat region of the SOBP field (see figure 1). The time between the two irradiations was 2 hours, which corresponds to 6 half-lives of the produced β^+ isotope with longer half-life (^{11}C , $T_{1/2} = 20.33 \text{ min}$). After each irradiation the phantom was taken manually from the treatment couch, placed inside the NeuroPET scanner's field of view (FOV) and acquired in list mode for 45 min. The phantom contained fiducial markers to guide the co-registration with the pre-acquired CT images, achieving co-registration accuracy below 1 mm. Good co-registration accuracy is needed for the attenuation correction and the comparison with Monte Carlo results. The parameters for the experimental procedure are provided in table 3. A much longer irradiation time was needed in the monoenergetic case compared to the SOBP one due to a different beam current used. For a better separation of ^{15}O and ^{11}C isotopes a shorter irradiation time is desirable. However, we deduced from simulations that the differences of the $^{15}\text{O}/^{11}\text{C}$ concentration ratio at the beginning of the PET scan is below 10% when comparing irradiation times of 372 s and 40 s.

2.2. Simulation setup

Based on the beam parameters from the treatment plan achieved using the CT image of the phantom, the PET images were calculated using a Monte Carlo system. The code used for this study was developed by Paganetti *et al* (2008), which is based on Geant4 (Agostinelli 2003). This code was applied to simulate the whole path of the proton beam and secondary particles beginning at the entrance of the treatment head and ending in the patient. The density and elemental composition of each material was introduced according to known values shown on table 2. Treatment planning was performed with the XiO (Computerized Medical Systems, Inc.) treatment planning system and all treatment parameters were transferred from the treatment planning system into the Monte Carlo, including the gantry, couch and treatment head configuration as well as the phantom geometries and CT images.

Different cross section data sets for the main reaction channels producing PET isotopes were imported into the Monte Carlo code and convolved during the simulation with the proton fluence at the voxel surface to obtain the distribution of each isotope (Parodi *et al* 2007c, España and Paganetti 2010). Subsequently, after the simulations, the parameters of the irradiation and scan protocols, i.e. irradiation time, delay between irradiation and scan and

scan duration, are considered for generating the simulated PET images (Parodi *et al* 2007a). A three-dimensional Gaussian convolution kernel with 7 mm FWHM was used to model the spatial resolution of the PET scanner.

Protons with kinetic energies up to 250 MeV are currently being used for therapy. However, for range verification purposes we should pay special attention to cross section values for energies below 50 MeV, which corresponds roughly to the final 2 cm of the proton path. The different experimental cross section data available at the EXFOR library for the reaction channels that were studied in this work are shown in the left column of figure 3. Different published studies focused on different proton energy ranges. Therefore, several experimental data must be combined in order to gather a complete set for the entire range of energies needed for this study. The considerable differences among experimental results from different publications show the need of studying their prediction of proton-induced PET images. In addition, theoretical cross section values as given in the ICRU report 63 differ substantially from the experimental values.

Different combinations of experimental and theoretical cross section values were tested (see the right column of figure 3). Four different sets of cross section values for the $^{16}\text{O}(\text{p,pn})^{15}\text{O}$ reaction channel were explored. Experimental cross sections *EXFOR 1* and *EXFOR 2* differ only in the lower energy region and are identical for energies above 45 MeV. In addition, a combination of ICRU cross section values for energies up to 50 MeV and the *EXFOR 1* cross sections for higher energies were explored. Three different sets of cross section data were also evaluated for the $^{12}\text{C}(\text{p,pn})^{11}\text{C}$ reaction channel. In this case, experimental cross sections *EXFOR 1* and *EXFOR 2* have the same production threshold but there are differences of up to 30% in absolute value for higher energies. The ICRU data set has a higher production threshold and lower absolute values. Two different sets of cross section values were also evaluated for the $^{16}\text{O}(\text{p},3\text{p}3\text{n})^{11}\text{C}$ reaction channel. Experimental and ICRU cross section values differs up to 50% in absolute value. Table 4 summarizes the procedure followed to study each reaction channel.

Each simulation was accomplished using the complete set of reaction channels. For each case, the specific channel under analysis was varied as shown in figure 3 while the cross sections presented by Parodi et al (2007c) were used for the remaining nuclear reaction channels.

2.3. Analysis

The three main reaction channels were studied independently using the combination of different materials and acquisition protocols. Measured and simulated depth activity profiles were compared for each case. The comparison of the depth profiles for each material was done using average areas perpendicular to the profile direction as shown in figure 1.

The $^{16}\text{O}(\text{p,pn})^{15}\text{O}$ channel was analyzed using the gel-water material and a 5 min scan, i.e. only the first 5 min of the acquisition were included in the reconstruction of the measured PET image ('5 min protocol'). The high oxygen concentration causes only a minor contribution from the $^{12}\text{C}(\text{p,pn})^{11}\text{C}$ channel. Furthermore, the acquisition protocol allows to maximize the ^{15}O signal due to its shorter half-life compared to other isotopes produced from oxygen as $^{16}\text{O}(\text{p},3\text{p}3\text{n})^{11}\text{C}$ and $^{16}\text{O}(\text{p},2\text{p}2\text{n})^{13}\text{N}$. The contribution from each isotope was estimated as 15% ^{11}C , 5% ^{13}N and 80% ^{15}O .

The $^{12}\text{C}(\text{p,pn})^{11}\text{C}$ channel was analyzed using the polyethylene material and a 30 min scan with additional delay protocol, i.e. skipping the first 15 min of the acquisition and using the following 30 min for the image reconstruction ('30 min protocol'). The very high carbon concentration ensures that the main contribution is from carbon channels and the protocol

minimizes the influence of the $^{12}\text{C}(\text{p},\text{p}2\text{n})^{10}\text{C}$ (^{10}C , $T_{1/2} = 19.29$ s) channel in the very first minutes of acquisition.

The $^{16}\text{O}(\text{p},3\text{p}3\text{n})^{11}\text{C}$ channel was analyzed using the gel-water material and a 30 min protocol. The very high oxygen concentration minimizes the contribution from channels with other target elements. Furthermore, the protocol minimizes the contribution of the $^{16}\text{O}(\text{p},\text{pn})^{15}\text{O}$ channel although some contribution of the $^{16}\text{O}(\text{p},2\text{p}2\text{n})^{13}\text{N}$ channel will remain. Many measurements of the cross section values for the $^{16}\text{O}(\text{p},2\text{p}2\text{n})^{13}\text{N}$ channel are in good agreement (Takács et al 2003). We therefore decided not to vary this cross section, i.e. the only uncertainty in this part of the study will be produced by the $^{16}\text{O}(\text{p},3\text{p}3\text{n})^{11}\text{C}$ channel. The contribution from each isotope was estimated as 87% ^{11}C , 12% ^{13}N and 1% ^{15}O .

3. Results and discussion

Measured and simulated depth activity profiles are compared in figure 4. The profiles obtained for the gel-water material using a 5 min protocol are compared in order to study the $^{16}\text{O}(\text{p},\text{pn})^{15}\text{O}$ reaction channel. Simulated profiles using the combination of ICRU and experimental cross section values produce the best overall agreement with the measurement. The ICRU values reproduce very accurately the falloff region but there is a complete mismatch for the rest of the profile. Next, the $^{12}\text{C}(\text{p},\text{pn})^{11}\text{C}$ reaction channel was studied in the HDPE material using a 30 min protocol. Simulated profiles using *EXFOR 1* cross section values produce the best overall agreement with measurement in this case. However, few percent differences in the slope of the profiles can be observed. Finally, we compared the profiles obtained for the gel-water material using a 30 min protocol in order to study the $^{16}\text{O}(\text{p},3\text{p}3\text{n})^{11}\text{C}$ reaction channel. The distal part for the simulated profiles obtained when using *EXFOR 1* cross section data shows a double falloff due to the combination of $^{16}\text{O}(\text{p},3\text{p}3\text{n})^{11}\text{C}$ and $^{16}\text{O}(\text{p},2\text{p}2\text{n})^{13}\text{N}$ reaction channels with very different production threshold (about 30 MeV and 7 MeV respectively), which differs from the shape obtained from the measurements. The overall agreement is improved when using the ICRU cross section values but a range difference at 50% of the maximum remains at ~4 mm. The long tail obtained at the distal part of the measured profiles is produced by the background noise, which is a consequence of typical random, attenuation and scatter corrections. Therefore, a 50% threshold is more reliable than lower thresholds (Knopf et al 2008). It is important to notice that good agreement of the distal falloff region when using monoenergetic fields does not translate into the same agreement in a SOBP field, where a spread energy spectrum of protons contribute to the activity distal falloff (see ICRU results on figure 4).

The cross section values that produced the best agreement between simulations and measurements for each reaction channel were combined and used for an additional simulation. The overall agreement obtained in the gel-tissue material was then evaluated for both irradiations and acquisition protocols (see figure 5). A range difference between measured and Monte Carlo profiles at the 50% of the maximum at the distal falloff region of 0.2 ± 0.5 mm and 0.8 ± 0.5 mm was obtained for the monoenergetic beam and SOBP irradiation respectively using a 5 min protocol. However, further improvement of the $^{16}\text{O}(\text{p},3\text{p}3\text{n})^{11}\text{C}$ reaction channel is needed to get acceptable agreement when using a 30 min protocol, where range differences of 2.1 ± 0.5 mm and 4.4 ± 0.5 mm were obtained. In addition, the decay curves for the three materials of the phantom after the monoenergetic beam irradiation was obtained from the multi-frame reconstruction images (see figure 6). Differences between simulation and measurement below 4 % were obtained, which is within the absolute activity calibration factor uncertainty.

The areas under each activity profile shown in figure 4 were calculated and are shown in table 5. This would be a sensitive parameter when using the convolution method to reconstruct the entire dose distribution using a filtering approach (Parodi and Bortfeld 2006) because the spatial integral of the activity (for a given PET protocol) is approximately proportional to the dose integral.

The cross sections described above only take into account isotope production from protons. There are also neutrons generated in proton-nuclear interactions that might contribute. Consequently, we also studied the possible influence of β^+ isotopes produced by secondary neutrons produced in the patient and in the treatment head. Experimental (EXFOR database) and theoretical (ICRU 2000) cross section values for the $^{16}\text{O}(n,2n)^{15}\text{O}$ and $^{12}\text{C}(n,2n)^{11}\text{C}$ nuclear reaction channels were included in the simulation obtaining a contribution of only 0.6 % to the total activity.

4. Conclusions

We have explored different cross section values available in the literature for the main reaction channels ($^{16}\text{O}(p,pn)^{15}\text{O}$, $^{12}\text{C}(p,pn)^{11}\text{C}$ and $^{16}\text{O}(p,3p3n)^{11}\text{C}$) contributing to the production of β^+ isotopes by proton beams in patients. Although other groups have reported the comparison of PET images using different cross section values (Beebe-Wang et al 2003, Parodi et al 2005), this is the first time that an extensive evaluation of all available experimental and theoretical values has been implemented in the simulation and compared with measured PET images obtained with a high-resolution PET scanner and where each reaction channel was studied independently.

The cross section values chosen were tested using a tissue-equivalent material leading to range differences below 1 mm when the 5 min protocol was employed and close to 5 mm differences for the 30 min scan time. The results presented here emphasize the need of more accurate measurement of the cross section values of the reaction channels contributing to the production of PET isotopes by proton beams.

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References

- Agostinelli S, et al. Geant4 - a simulation toolkit. Nucl Instrum Methods Phys Res A. 2003; 506:250–303.
- Beebe-Wang J, Vaska P, Dilmanian FA, Peggs SG, Schlyer DJ. Simulation of proton therapy treatment verification via PET imaging of induced positron-emitters. IEEE Nuclear Science Symposium and Medical Imaging Conference Record (Portland, OR). 2003; 4:2496–2500.
- Enghardt W, Crespo P, Fiedler F, Hinz R, Parodi K, Pawelke J, Ponisch F. Charged hadron tumour therapy monitoring by means of PET. Nucl Instr Meth A. 2004; 525:284–8.
- España S, Zhu X, Daartz J, Liebsch N, El Fakhri G, Bortfeld T, Paganetti H. Feasibility of In-Room PET Imaging for in Vivo Proton Beam Range Verification. Med Phys. 2010; 37:3180.
- España S, Paganetti H. The impact of uncertainties in the CT conversion algorithm when predicting proton beam ranges in patients from dose and PET-activity distributions. Phys Med Biol. 2010; 55:7557–72. [PubMed: 21098912]
- EXFOR. Experimental Nuclear Reaction Data File. Energy Sciences and Technology Dept, BNL. <http://www.nndc.bnl.gov/nndc/exfor/>

- ICRU. Nuclear Data for Neutron and Proton Radiotherapy and for Radiation Protection Report No 63. Bethesda, MD: ICRU; 2000.
- Knopf A, Parodi K, Paganetti H, Cascio E, Bonab A, Bortfeld T. Quantitative assessment of the physical potential of proton beam range verification with PET/CT. *Phys Med Biol*. 2008; 53:4137–51. [PubMed: 18635897]
- Knopf A, Parodi K, Bortfeld T, Shih HA, Paganetti H. Systematic analysis of biological and physical limitations of proton beam range verification with offline PET/CT scans. *Phys Med Biol*. 2009; 54:4477–95. [PubMed: 19556685]
- Litzenberg DW, Roberts DA, Lee MY, Pham K, Vander Molen AM, Ronningen R, Bechetti D. On-line monitoring of radiotherapy beams: experimental results with proton beams. *Med Phys*. 1999; 26:992–1006. [PubMed: 10436901]
- Lu HM. A potential method for in vivo range verification in proton therapy treatment. *Phys Med Biol*. 2008; 53:1413–24. [PubMed: 18296770]
- Oelfke U, Lam GKY, Atkins MS. Proton dose monitoring with PET: quantitative studies in Lucite. *Phys Med Biol*. 1996; 41:177–196. [PubMed: 8685254]
- Paganetti H, Jiang H, Parodi K, Slopsema R, Engelsman M. Clinical implementation of full Monte Carlo dose calculation in proton beam therapy. *Phys Med Biol*. 2008; 53:4825–53. [PubMed: 18701772]
- Paans AMJ, Schippers JM. Proton therapy in combination with PET as monitor: a feasibility study. *IEEE Transact on Nucl Science*. 1993; 40:1041–44.
- Parodi K, Enghardt W. Potential application of PET in quality assurance of proton therapy. *Phys Med Biol*. 2000; 45:N151–6. [PubMed: 11098922]
- Parodi K, Pönisch F, Enghardt W. Experimental study on the feasibility of In-Beam PET for accurate monitoring of Proton Therapy. *IEEE Trans Nucl Sci*. 2005; 52:778–86.
- Parodi K, Bortfeld T. A filtering approach based on Gaussian–powerlaw convolutions for local PET verification of proton radiotherapy. *Phys Med Biol*. 2006; 51:1991–2009. [PubMed: 16585841]
- Parodi K, et al. Patient study on in-vivo verification of beam delivery and range using positron emission tomography and computed tomography imaging after proton therapy. *Int J Radiat Oncol Biol Phys*. 2007a; 68:920–34. [PubMed: 17544003]
- Parodi K, Paganetti H, Cascio E, Flanz JB, Bonab A, Alpert NM, Lohmann K, Bortfeld T. PET/CT imaging for treatment verification after proton therapy: a study with plastic phantoms and metallic implants. *Med Phys*. 2007b; 34:419–35. [PubMed: 17388158]
- Parodi K, Ferrari A, Sommerer F, Paganetti H. Clinical CT-based calculations of dose and positron emitter distributions in proton therapy using the FLUKA Monte Carlo code. *Phys Med Biol*. 2007c; 52:3369–87. [PubMed: 17664549]
- Pönisch F, Parodi K, Hasch BG, Enghardt W. The description of positron emitter production and PET imaging during carbon ion therapy. *Phys Med Biol*. 2004; 49:5217–32. [PubMed: 15656273]
- Schneider U, Pedroni E. Proton radiography as a tool for quality control in proton therapy. *Med Phys*. 1995; 22:353–63. [PubMed: 7609715]
- Takács S, Tárkányi F, Hermanne A, Paviotti de Corcuera R. Validation and upgrading of the recommended cross section data of charged particle reactions used for production of PET radioisotopes. *Nucl Instrum Meth B*. 2003; 211:169–89.
- White DR, Woodard HQ, Hammond SM. Average soft-tissue and bone models for use in radiation dosimetry. *Br J Radiol*. 1987; 60:907–13. [PubMed: 3664185]
- Woodard HQ, White DR. The composition of body tissues. *Br J Radiol*. 1986; 59:1209–19. [PubMed: 3801800]
- Zhu X, España S, Paganetti H, Bortfeld T, Liebsch N, Shih H, El Fakhri G. First in-room PET studies for range verification of proton therapy. *J Nucl Med*. 2010; 51:519.

Figure 1.
Left: Heterogeneous phantom used for this experiment. Right: dose distributions used to irradiate the phantom.

Figure 2. Oxygen/Carbon (O/C) weight fraction ratio for several human tissues (adipose, soft and bone) (White *et al* 1987, Woodard and White 1986) and the one corresponding to the gel-tissue material in the phantom.

Figure 3. Cross section values for the $^{16}\text{O}(p,pn)^{15}\text{O}$ (top), $^{12}\text{C}(p,pn)^{11}\text{C}$ (middle) and $^{16}\text{O}(p,3p3n)^{11}\text{C}$ (bottom) nuclear reaction channels. The left column shows the experimental values that can be found at the EXFOR library and the right column shows those considered within the Monte Carlo code.

Figure 4. Measured and simulated (MC) depth activity profiles obtained for the gel-water material using a 5 min acquisition time (top), the HDPE material using a 30 min protocol (middle) and the gel-water material using a 30 min protocol (bottom). Results obtained for the monoenergetic beam (left) and SOBP (right) irradiations are shown. Simulation were performed using EXFOR 1, EXFOR 2, ICRU and ICRU-EXFOR combination cross sections as presented in figure 3.

Figure 5.

Measured and simulated (MC best) depth activity profiles obtained for the gel-tissue material using 5 min (top) and 30 min (bottom) protocols for both pristine peak (left) and SOBP (right) irradiations. Simulations were performed with the combination of cross section values that showed the best agreement in figure 4. Range differences (Δr) between simulated and measured profiles are superimposed.

Figure 6. Time variability of the average activity concentration on each of the three materials of the phantom after the monoenergetic beam irradiation. Measured (meas) and simulated (MC) values are shown. Simulations were performed with the combination of cross section values that gave the agreement in figure 4.

Table 1Proton-nuclear reaction channels and β^+ isotopes produced in human tissues.

target	nuclear reaction channels	β^+ isotopes	half-life
C	$^{12}\text{C}(\text{p,pn})^{11}\text{C}$, $^{12}\text{C}(\text{p,p2n})^{10}\text{C}$	^{10}C , ^{11}C	19.29 s, 20.33 m
N	$^{14}\text{N}(\text{p,p2n})^{11}\text{C}$, $^{14}\text{N}(\text{p,pn})^{13}\text{N}$, $^{14}\text{N}(\text{p,n})^{14}\text{O}$,	^{13}N	9.96 m
O	$^{16}\text{O}(\text{p,pn})^{15}\text{O}$, $^{16}\text{O}(\text{p,p3n})^{11}\text{C}$, $^{16}\text{O}(\text{p,p2n})^{13}\text{N}$, $^{16}\text{O}(\text{p,p2n})^{14}\text{O}$, $^{16}\text{O}(\text{p,p4n})^{10}\text{C}$	^{14}O , ^{15}O	70.61 s, 122.24 s
P	$^{31}\text{P}(\text{p,pn})^{30}\text{P}$	^{30}P	2.50 m
Ca	$^{40}\text{Ca}(\text{p,p2n})^{38}\text{K}$	^{38}K	7.64 m

Table 2

Density and elemental composition for the three materials included in the phantom.

material	H (%)	C (%)	N (%)	O (%)	density (g/cm³)
HDPE	14.3	85.7	0.0	0.0	0.95
gel-tissue	9.6	14.9	1.46	73.8	1.13
gel-water	11.03	1.04	0.32	87.6	1.01

Table 3

Irradiation and PET acquisition parameters.

	monoenergetic	SOBP
dose (Gy)	1.6 @ entrance	2
irradiation time (s)	372	40
delay (s)	47	43
acquisition time (min)	45	45
delay between irradiations (hours)		2
air gap (cm)		8.5

Table 4

Material and protocol used to study each reaction channel and the cross section data evaluated for each one.

reaction channel	material/protocol	cross sections
$^{16}\text{O}(\text{p,pn})^{15}\text{O}$	gel-water / 5 min	EXFOR 1
		EXFOR 2
		ICRU
		ICRU-EXFOR
$^{12}\text{C}(\text{p,pn})^{11}\text{C}$	HDPE / 30 min	EXFOR 1
		EXFOR 2
		ICRU
$^{16}\text{O}(\text{p},3\text{p}3\text{n})^{11}\text{C}$	gel-water / 30 min	EXFOR 1
		ICRU

Table 5

Integral area of the PET activity profiles normalized to the measured value for all cross section cases under study.

material & protocol	cross section	monoenergetic	SOBP
gel-water 5 min	MC EXFOR 1	0.91	0.88
	MC EXFOR 2	0.97	0.93
	MC ICRU	0.78	0.80
	MC ICRU-EXFOR	1.01	0.98
HDPE 30 min	MC EXFOR 1	1.02	0.94
	MC EXFOR 2	1.15	1.06
	MC ICRU	0.80	0.75
gel-water 30 min	MC EXFOR 1	0.73	0.70
	MC ICRU	0.87	0.85
gel-tissue 5 min	Best	1.03	0.99
gel-tissue 30 min		1.03	0.96