Feasibility of quantitative PET/CT dosimetry for proton therapy using polymer gels

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Abstract. A feasibility study of proton beam PET/CT off-line quantitative dosimetry using polymer gels is presented. A newly developed proton-sensitive polymer gel dosimeter (BANG®3-Pro2) is used as a dosimeter and a tissue-equivalent phantom medium for this study. We explore a new approach to correlating measured proton 3-dimensional (3D) dose distributions directly to measured positron emission from in the gel medium using PET/CT imaging. A large cylindrical volume (2.2 Litres) of the gel was irradiated with a clinical modulated proton beam using irregular-shaped aperture geometry. The gel was imaged in a nearby PET/CT unit immediately (<3 min) after irradiation. Dose distribution in the gel was generated using an optical tomography scanning system. Direct 3D spatial comparison of dose and positron emission distributions was then performed. Profiles along the beam path show that the distal fall-off of the dose is nearly 2 cm deeper than the activity profile which is comparable to previous studies with plastic phantoms and Monte Carlo simulations of activity distributions. Planar PET and dose distributions at depth and perpendicular to beam axis show a strong one-to-one spatial correlation. This phantom study demonstrates that the gel medium could be potentially useful for quantifying various physical factors that can influence the PET activity range verification method in patients.

1. Introduction

Several studies have demonstrated that off-line PET imaging of proton beams in phantoms may potentially be a useful technique for proton therapy dosimetry [1]. Widespread clinical implementation of this technique is still challenging due to underlying physical factors that significantly affect the accuracy of this method [2]. Some of these factors include patient intra-fraction motions, variations of tissue compositions, blood perfusion, and setup uncertainties. In order to quantify PET and dose distributions in tissue-equivalent materials, direct measurement of dose and PET activity in the same phantom medium is needed. We have recently shown that a proton-sensitive formulation of the BANG3 polymer gels, BANG3-Pro2, is capable of reproducing ion chamber dose profiles in water with little or no observed quenching in the Bragg peak [3]. The gel dosimeter has very similar elemental composition by weight to that of human tissue. Therefore, the BANG3-Pro2 dosimeter is an ideal medium for systematic studies of PET and dose spatial correlations for proton beam dose and
range verifications. This off-line dosimetry technique has some distinct advantages compared to previous off-line phantom verification studies. First, the homogenous gel medium acts as both a tissue-equivalent phantom and a dosimeter. Second, the gel medium provides a large-volume dosimeter which allows for accurate and direct correlation of PET activity and dose in 3D for a wide range of beam configurations. In this study we describe our experimental approach for this unique verification method using a clinical spread-out Bragg peak (SOBP) beam and present a quantitative description of the correlation between measured PET emissions and dose distributions in 3D.

2. Materials and Methods

A large volume (2.2 Liters) of the BANG3-Pro2 gel was used for this work. The gel medium is tissue equivalent and has a physical density of 1.08 g/cm³. The dosimetry system is composed of the gel dosimeter and a laser-based optical computed tomography scanner, OCTOPUS™-IQ, (MGS Research, Inc) with sub-millimeter scanning resolution capability. The proton-sensitive gel is provided by the manufacturer (MGS Research, Inc) in a clear plastic cylindrical container, measuring approximately 12.7 cm in diameter and 17.5 cm in height.

The gel dosimeter was irradiated at the University of Florida Proton Therapy Institute (UFPTI, Jacksonville, FL) using a modulated clinical proton beam with passive double-scattering technique. The gels were immersed under water in a Wellhofer scanning tank (IBA Dosimetry America) with the long axis of the gel cylinder coinciding with the beam axis. The water depth above the gel was adjusted so as to capture most of the 15.1 cm range modulated (5.0 cm) beam profile including the distal end. An irregular-shaped aperture was chosen for this study to evaluate 3D PET activity in the gel from complex beam aperture geometries. An overview of the experimental setup is shown in figure 1. The gel was irradiated for a total of 3.37 min (beam on time) to a maximum dose of 600 cGy. The dose delivered to the gel was chosen so as to maximize the induced PET activity while maintaining the ability to read the dose within the linear region of the dose response curve of the dosimeter system.

Fig 1 (Left) The brass aperture used in this study. Experimental setup for gel proton beam irradiation using the Wellhofer water tank (Right). The gel is aligned vertically along the beam axis in a special mount that allows the gel to be immersed at variable water depths.

Immediately post exposure, the gel dosimeter was quickly transferred to a nearby PET/CT unit for image acquisition. The time between beam off and start of PET acquisition was 2.57 minutes. The PET/CT imaging was performed using the Philips Gemini PET/CT located on-site at UFPTI. The CT scans were obtained with 1.0 mm slice thickness and 1.172×1.172 mm² pixel spacing and a field of view of 60 cm. This CT study was then later used to perform CT-based phantom attenuation correction (CTAC) of the proton-irradiated gel. The PET imaging following the CT scan was then performed for 60 minutes. This acquisition time was sufficient to collect most of the induced activity within the gel volume since the total decay event counts drop by at least two orders of magnitude over this time period [4].
At the elemental level, the gel is composed mainly of Oxygen (\(^{16}\text{O}\)), Carbon (\(^{12}\text{C}\)), Hydrogen (\(^{1}\text{H}\)), and Nitrogen (\(^{14}\text{N}\)) with w/w fractions of 0.730, 0.144, 0.101, and 0.024, respectively. Both \(^{16}\text{O}\) and \(^{12}\text{C}\) have comparable \(\beta^+\) reactions cross sections over therapeutic proton beam energies [4]. The half life of \(^{15}\text{O}\) isotope is 2 minutes, while the half life for \(^{11}\text{C}\) isotope is about 20.3 minutes. Therefore, in order to maximize the PET signal statistics from \(^{15}\text{O}\), the time between beam off and start of PET image acquisition needs to be minimized to be within 10 minutes after irradiation. Axial, sagittal, and coronal images if the gel’s CTAC PET image are shown in **figure 2**. The PET-defined beam path is shown clearly in the coronal and axial planes, while the sagittal plane reflects the aperture geometry of the incident proton beam. The PET emission distributions from the co-registered PET/CT volume image data set was visualized and analyzed in the Eclipse™ (Varian Medical Systems) treatment planning system. The geometrical correlation between the PET and gel dose data was possible using the geometrical landmarks of the gel container external dimensions and the locations fiducial BBs on the container surface.

**3. Results and Discussion**

A comparison of a 2D dose distribution from gel and the corresponding PET signal distribution is shown in **figure 3**. The PET 2D distribution reflects the raw positron emission counts captured by the PET scanner. The activity map reflects the geometrical shape of the aperture shown in **figure 1** and coincides with dose distribution measured in the gel as shown in **figure 3** (left). The two maps are overlaid onto a 1.0 cm voxel grid to facilitate 2D spatial comparison. The 50% isodose line and the 50% isoemission contour were found to coincide everywhere on the grid to better than half a voxel or 2.5 mm. This is one of the unique aspects of the gel as a volumetric dosimeter. Unlike other types of dosimeters, the gel medium offers the capability to perform direct and accurate spatial correlations between PET and dose distributions within the volume of the gel itself.

The most dosimetrically relevant result from this study is the ability to perform relatively accurate spatial correlation between the distal end fall-off of the PET depth activity profile and the SOBP distal end fall off to the modulated beam along the beam axis as shown in **figure 4**. This range verification method is the most clinically relevant feature of this dosimetry technique. In-vivo dose verification plays an important role in treatment QA as beam distal end variations at depth could result in an ‘overshoot’ or ‘undershoot’ of the distal portion of the target volume [2]. Both profiles were normalized to their maximum raw values to yield the relative profiles in **figure 4**. The gel data was not acquired over the entire physical size of the gel cylinder due to the nature of the mechanical setup of
the gel in the optical scanner scanning tank. However, the collected PET activity extends over the entire volume of the gel dosimeter, and hence, the reported activity extends beyond the dose level at which the gel dose is reported as shown in figure 4. An examination of the profile shapes with depth shows that the induced activity profile shape does not necessarily follow the shape of the dose profile with depth. Other studies report similar observations for both clinical modulated and pristine beams [1]. The depth trend in the positron emission profile is mainly due to cross-section energy dependence of various isotope activation reactions which yield the range of induced activity to be always smaller than the maximal penetration depth of the proton dose profile. We found that the distal 50% end of the proton dose profile to be approximately 20 mm deeper than the 50% distal end of the activity profile. This spatial offset is comparable to other studies done in other materials with similar elemental compositions and similar beam energies for SOBP beams [1]. It should be emphasized that the accuracy of the reported lateral and depth localizations of the PET and dose distributions as reported in this study are primarily limited by the spatial resolution of the PET scanner.

Fig 3 A 2D comparison of dose (left) and PET activity (right) at the same depth in gel. The color bars represent dose range (cGy) on the dose map and raw count range on the PET map. The distribution is generated at a depth of 13 cm in the gel (center of the SOBP plateau).

Future in vivo measurements can be performed to quantify the effect of the physical factors that may influence the correlation between PET activity distributions and dose using the methodology outlined in this paper. There are several attractions about using the gel system for in-depth quantitative phantom studies on PET in vivo dosimetry. First, the gel dosimeter can be available in a variety of volumes (smaller or larger than the size used in this study which allows for verification studies over a wide range of beam configurations. Second, the gel dosimeter can be implanted with various types of heterogeneous objects in the beam path or upstream. This allows for evaluating the effect of dose perturbations downstream on PET activity distributions. Third, the gel dosimeter can be coupled with motion phantoms to study motion dosimetry and its effects on PET emissions from clinical proton beam. This feasibility has already been demonstrated using the BANG3 gel with photon beams. Understanding and quantifying these physical factors using the methodology outlined in this work may potentially increase our confidence and understanding of PET/CT in vivo dosimetry, its advantages and limitations for patient site-specific treatment QA.
**Fig 4** Overlay of depth profiles for PET activity and depth dose in gel. The distance between the 50% distal end of the PET distribution to the 50% distal dose profile is nearly 20 mm.

4. Conclusions

In this work we demonstrate a unique approach to off-line proton dosimetry and depth range verification by direct comparison of measured proton dose distributions in the gel dosimeter volume to the proton-activated positron distributions in the gel. Three-dimensional spatial correlation was possible using PET/CT imaging of the positron activated gel volume immediately post proton beam irradiation. Our results for a clinical SOBP agree well with similar studies on the distal end location of the PET emission profile with respect to the distal end location of the dose depth profile. Using this novel direct comparison methodology, correlations of distal edge doses based on PET activity distributions from clinical proton beams can potentially be quantified under various delivery conditions. This study demonstrates that polymer gels could potentially be useful in assessing various physical factors that could affect PET activity range verification method and its use as a viable patient treatment QA tool.

References

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