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Investigation of optimized prompt gamma detection strategy for real-time Bragg Peak tracking in proton radiation therapy

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Abstract

Prompt gamma (PG) ray signal from proton radiation has been proposed for *in vivo* beam range verification to provide unique real-time tracking of the Bragg Peak (BP) during proton therapy (PT) delivery. In this study, we investigate possible strategies to optimize PG detection for BP tracking in proton radiation therapy. Extensive Geant4 Monte Carlo (MC) simulations have been used to study the energy spectral, spatial and timing characteristics of PG emission signal from 200 MeV proton pencil beam irradiations with water and PMMA phantoms. These include their relationship with the position of the BP and the background of the neutron field originated by the proton beams. Then the optimal energy window, angular window and timing window for PG imaging detection can be determined. Our results show that there could exist an optimal energy window for PG detection around 4.44 MeV. PG emissions show a backward angular preference while neutron emissions have a forward angular preference. Furthermore, employing a timing window could further improve the PG signal detection from strong background interferences of neutrons. Both energy and time resolved PG detection is a promising solution. These results indicate that there could exist an optimized strategy for PG signal detection. Utilizing appropriate energy window, angular window and timing window, PG image formation could be significantly improved for BP tracking.

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Investigation of Optimized Prompt Gamma Detection Strategy for Real-time Bragg Peak Tracking in Proton Radiation Therapy

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Abstract—Prompt gamma (PG) ray signal from proton radiation has been proposed for *in vivo* beam range verification to provide unique real-time tracking of the Bragg Peak (BP) during proton therapy (PT) delivery. In this study, we investigate possible strategies to optimize PG detection for BP tracking in proton radiation therapy. Extensive Geant4 Monte Carlo (MC) simulations have been used to study the energy spectral, spatial and timing characteristics of PG emission signal from 200 MeV proton pencil beam irradiations with water and PMMA phantoms. These include their relationship with the position of the BP and the background of the neutron field originated by the proton beams. Then the optimal energy window, angular window and timing window for PG imaging detection can be determined. Our results show that there could exist an optimal energy window for PG detection around 4.44 MeV. PG emissions show a backward angular preference while neutron emissions have a forward angular preference. Furthermore, employing a timing window could further improve the PG signal detection from strong background interferences of neutrons. Both energy and time resolved PG detection is a promising solution. These results indicate that there could exist an optimized strategy for PG signal detection. Utilizing appropriate energy window, angular window and timing window, PG image formation could be significantly improved for BP tracking.

I. INTRODUCTION

The main advantage of proton therapy (PT) is attributed to its well-defined beam range and favourable depth dose characteristics with a lower entrance dose and the steep dose gradient at the distal edge of the Bragg Peak (BP) [1]. However, to fully exploit this advantage, the location of the sharp dose distal gradient in the patient must be precisely controlled. The uncertainty in determination of the beam range can have a profound impact on the PT treatment quality due to employment of adequate safety margins. To reduce necessary margins and to fully benefit from the advantages of PT, a means of *in vivo* dose monitoring during the irradiation is needed to verify the dose distribution in and around the target volume. Beam range verification has been one of the major

issues in PT to ensure safe and accurate treatment delivery to the targeted region while sparing critical organs-at-risk in the treatments. Over the last decade, many different approaches for *in vivo* beam range verification have been proposed and investigated [2]. Yet there are still great challenges in the development of clinically suitable and reliable *in vivo* beam range verification techniques.

Non-invasive *in vivo* treatment monitoring can be performed by detecting secondary radiation produced as a result of nuclear interactions of the incident proton beam with patient tissue, such as the secondary gamma photons. There are two main indirect approaches for non-invasive *in vivo* beam range verification. One is based on positron emission tomography (PET), which relies on the creation of some short-lived nuclei (^{11}C , ^{13}N , ^{15}O , etc) that decay via positron emission. The emitted positrons annihilate with electrons of the tissue to produce pairs of coincident 511 keV gamma photons [3]-[4]. Another is called prompt gamma (PG) imaging [5]-[7], which relies on the measurement of single gamma photons promptly emitted from some excited tissue nuclei following their decays from the excited states to their ground states. The PET-based range verification technique has been adopted for the post-treatment quality control [8], but it still has some limitations. These include that it cannot offer real-time monitoring because of the delayed decay of the positron emitters and a relatively low rate of positron emissions, which limit the conventional PET for in-beam imaging in real-time. The positron range effect and biological washout or movements also affect the quantitative accuracy for quality control [9].

PG imaging is an emerging *in vivo* imaging technique that has an important potential to overcome the limitations of *in vivo* PET [10]. PG activity signal can offer a real-time monitoring potential because PG is produced immediately when irradiating a target. The affecting issues with biological washout or movement are absent. Moreover, the yields of PG produced are much larger than the annihilation gamma rays. These make PG imaging a very attractive solution for *in vivo* proton beam range verification to track and monitor the BP position in real-time with the beam dose delivery.

However, PG detection also presents great challenges since PGs are produced from different nuclear reaction channels, whose energies depend on the elements of the tissue composite involved. Each element emits PGs with a unique energy spectral line. So overall PGs could have a broad energy spectrum spanning from 2 to 15 MeV [11] with strong interference background from neutrons and stray gamma rays [12]. Traditional gamma camera technology used in nuclear

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medicine is not suitable for the high-energy PG imaging, especially when in the presence of such neutron/gamma background. Significant innovations are required. Previous studies from other research groups are mainly focused on the feasibility of PG imaging [5], [13], [14]. Further investigations of optimized PG detection are important to aid the PG imaging system design for the desired performance.

In this study, we investigate possible strategies to optimize PG detection for BP tracking in a high-energy proton radiation field. Extensive Geant4 Monte Carlo simulations have been used to study the PG field characteristics (1) when originated in phantoms typically used for Quality Assurance studies in PT and (2) at a distance of 50 cm from the centre of the phantom where the gamma camera can be located. The physical quantities under investigation include the yield and the relative ratio of PG with respect to neutrons, energy spectral, spatial and timing characteristics of the PG emission signal produced by a 200 MeV proton beam. These quantities have been studied with respect to the position of the BP. This study should aid in the determination of the optimal energy window, angular window and timing window for PG imaging detection.

II. METHODOLOGY

Geant4 [15],[16], version 10.00 was adopted to characterise the PG emission from a 200 MeV proton pencil beam, with two alternative homogeneous phantoms with the same shape and size but different materials: a water phantom (H_2O , density of 1 g/cm^3) and a standard PMMA phantom (Polymethyl Methacrylate, $\text{C}_5\text{O}_2\text{H}_8$, density of 1.19 g/cm^3) of human tissue equivalence. These two materials are commonly used for Quality Assurance in PT. So we have selected them in this study to investigate the effect of different composition on the PG emission.

The cylindrical phantom has a diameter of 30 cm and height 50 cm. The geometrical setup of the simulations is shown in Fig. 1. The proton pencil beam is incident normally on the surface of the phantom, along the cylinder axis (z-axis).

The Geant4 physics list includes both electromagnetic (Livermore Low Energy Package) and hadronic physics (QGSP_BIC_HP for protons, neutrons and pions, Binary Ion Cascade model for ions). The production threshold of secondary particles was fixed to 1 mm.

As shown in Fig. 1, a dummy sphere (called *detection sphere*) with radius 50 cm is modelled with its centre in coincidence with the centre of the phantom and with the centre of coordinates of the Geant4 simulation setup.

The output of the simulation consists of:

- the energy and location of the secondary neutrons and photons when reaching the detection sphere's surface at a position P. The angles θ and φ (see Fig. 1) identifying the position P are also retrieved. φ represents the axial angle of the gamma/neutron with respect to the z-axis, while θ represents the azimuthal angle of the gamma/neutron with respect to the x-axis.
- the time interval from the entrance of the proton beam into the phantom until the gamma photon or neutron has

reached the detection sphere. So the registered time information contains the proton beam's transit time in the phantom.

Then the main characteristics of PG emission and detection in terms of the energy window dependence, spatial dependence and timing property can be determined. The correlation between the PG distribution and the Bragg curve is quantified within the defined energy windows.

Fig. 1. Geometrical setup of the Geant4 simulation. Phi (φ) represents the axial angle from the z-axis, while theta (θ) represents the azimuthal angle from the x-axis.

III. RESULTS

A. PG Emission Characteristics in Phantoms

It was found that the beam ranges of the 200 MeV proton pencil beam in the water and PMMA phantoms are approximately 26 cm and 22 cm, respectively. The range difference is as expected due to the different material composites between these two phantoms. The beam range here is taken as the 50% BP distal fall-off position.

The energy spectra of gamma emissions in the water and PMMA phantoms showed some distinguishable emission lines that are produced from major constituent elements such as oxygen and carbon, revealing a characteristic spectrum for each phantom, as shown in Fig. 2. These characteristic spectral lines include a positron annihilation gamma peak at 0.511 MeV (^{15}O), a 2.22 MeV gamma peak from the capture of secondary thermal neutrons by Hydrogen, and three prominent PG lines of 4.44, 5.21 and 6.13 MeV. The 4.44 MeV PG emission line is the most prominent one in both phantoms as it originates from the de-excitations of $^{12}\text{C}^*$. The 5.21 MeV PG emission line is from $^{15}\text{O}^*$ de-excitations, and the 6.13 MeV PG line is from $^{16}\text{O}^*$ de-excitations. Then the characteristics of the individual PG lines are further investigated by employing three equal-width energy windows of 4.2-4.6 MeV, 5.0-5.4 MeV, and 5.9-6.3 MeV. An additional larger energy window of 4.2-6.3 MeV is also used to look into the overall effect from all three PG lines. The PG yield and correlation with BP in each energy window are quantified.

Fig. 2. Gamma energy spectra generated in the cylindrical water (left) and PMMA (right) phantoms from 200 MeV proton pencil beam irradiation. The embedded plots show a zoom between 0 and 7 MeV. The gamma emission lines are characteristic to the major constituent elements of the phantom materials, as expected.

The yields and corresponding ratio of PG and neutrons within the defined gamma energy windows are listed in Table I. The most abundant PG emission line is found in the energy window of 4.2-4.6 MeV with about 3% of PGs per incident proton. The signal-to-noise ratio (in terms of gamma-to-neutron yield ratio) in this window is approximately 0.1, which is low. If we consider, instead, a larger energy window, e.g. 4.2-6.3 MeV, the PG yields are significantly increased to $\sim 5\text{-}6\%$. Hence this window yields a higher gamma-to-neutron ratio with $N_\gamma/N_n \cong 0.30$ in water, and $N_\gamma/N_n \cong 0.21$ in PMMA.

TABLE I. SECONDARY RADIATIONS OF PG AND NEUTRON YIELDS IN CYLINDER PHANTOMS FROM 200 MEV PROTON PENCIL BEAM IRRADIATION.

Phantom	PG energy window (MeV)	Number of gammas per incident proton N_γ (%)	Number of neutrons per incident proton N_n (%)	Ratio (N_γ/N_n)
Water	No window	43.42	21.00	2.07
	4.2-4.6	2.53		0.12
	5.0-5.4	1.72		0.08
	5.9-6.3	1.11		0.05
	4.2-6.3	6.31		0.30
PMMA	No window	41.44	24.37	1.70
	4.2-4.6	2.75		0.11
	5.0-5.4	0.76		0.03
	5.9-6.3	0.58		0.02
	4.2-6.3	5.03		0.21

The strong longitudinal distribution correlations between PG emission and the Bragg curve are observed and shown in Fig. 3. These correlations show a considerable dependence on the PG energy, which could make a large contribution to the uncertainty in the actual BP tracking. The quantitative comparisons in peak position and fall-off position are listed in Table II. In the water phantom, the PGs in the energy window of 5.9-6.3 MeV exhibit the closest peak and fall-off correlation with the BP. However, the PG yield in this energy window is too low. In both materials, the 4.2-4.6 MeV window exhibits the most similar distribution shape and correlation between PG and the Bragg curve. This window presents a ~ 4 mm fall-off difference in water, and ~ 1 mm fall-off difference in PMMA. The overall PG window of 4.2-6.3 MeV also offers good PG fall-off correlation with the BP fall-off but with the benefit of a higher PG yields. This window presents a fall-off

difference of ~ 4 mm in water and ~ 2 mm in PMMA. Due to the bin width of the histograms, the uncertainty of these position values is about 1 mm. These results indicate that the 4.44 MeV PG emission is the best suitable for BP tracking.

Water Phantom

PMMA Phantom

Fig. 3. Longitudinal PG distribution correlation with the Bragg curve in water and PMMA cylindrical phantoms from different gamma energy windows. Black curve: number of photons originated along the Bragg peak, in the phantom, within a specific energy window. Blue curve: Bragg Peak. The scale on the y-axis is arbitrary for the Bragg Peak. The 4.2-4.6 MeV energy window reveals the greatest PG distribution correlation with the Bragg curve with close distal fall-off position.

TABLE II. CORRELATION COMPARISON OF PEAK POSITION AND FALL-OFF POSITION BETWEEN PG AND BP.

Phantom	Energy window (MeV)	Peak position (mm)			50% fall-off position (mm)		
		PG	BP	Difference	PG	BP	Difference
Water	4.2-4.6	249	254	5	254	258	4
	5.0-5.4	246		8	251		7
	5.9-6.3	254		0	258		0
	4.2-6.3	249		5	254		4
PMMA	4.2-4.6	217	219	2	222	223	1
	4.2-6.3	215		4	221		2

B. PG Detection Characteristics at a Typical Detector Distance with an Ideal Detection Sphere

The yields of PGs produced in the cylindrical phantom and reaching the detection sphere are listed in Table III. As compared to the data in Table I, we can see that the number of gamma rays and neutrons per incident proton reaching the detection sphere has decreased, as expected. But the ratio of gamma-to-neutron in each energy window almost remains unchanged. The 4.2-6.3 MeV energy window offers the

highest signal-to-noise ratio compared to the other energy windows since a greater number of PG photons are detected; this is important for good image formation.

TABLE III. PG AND NEUTRON DETECTION YIELDS ON THE DETECTION SPHERE FROM THE CYLINDER PHANTOMS.

Phantom	PG energy window (MeV)	Number of gammas per incident proton N_γ (%)	Number of neutrons per incident proton N_n (%)	Ratio (N_γ/N_n)
Water	No window	35.10	13.33	2.63
	4.2-4.6	1.56		0.12
	5.0-5.4	1.08		0.08
	5.9-6.3	0.73		0.05
	4.2-6.3	4.05		0.30
PMMA	No window	33.11	14.76	2.24
	4.2-4.6	1.58		0.11
	4.2-6.3	3.01		0.20

The PG emissions from both water and PMMA phantoms show similar spatial characteristics with isotropic azimuthal distribution, as expected, but non-isotropic axial distribution. Fig. 4 shows a typical axial angular distribution of PGs and neutrons in the 4.2-6.3 MeV energy window from the cylinder phantoms. PG emissions show a backward preference ($\phi > 90^\circ$) while neutron emissions have a forward preference ($\phi < 90^\circ$) with respect to the centre of the global coordinate system of the simulation geometry setup. With respect to the BP position, this angular preference corresponds to a slightly larger backward direction in the water phantom than in the PMMA phantom. Quantitative comparisons of the angular preference are listed in Table IV. The angular preference doesn't show much dependence on the energy windows.

Fig. 4. Axial angular distribution of PGs and neutrons reaching the detection sphere from the cylindrical water (left) and PMMA (right) phantoms, with the PG energy window 4.2-6.3 MeV. PG emission shows a maximum at $\phi \sim 110^\circ$ in both materials, with respect to the coordinate system centre.

However, the angular information of PG emission is more complicated. The axial PG curves in Fig. 4 contain an integral of all PGs along the Bragg curve. They represent what an uncollimated detector would detect at the specific position on the detection sphere. The position of the peak of the curve reflects a combination of the distribution of emission rates along the Bragg curve and the angle of emission relative to the point on the sphere.

TABLE IV. PG AND NEUTRON ANGULAR PREFERENCE ON THE DETECTION SPHERE FROM THE CYLINDER PHANTOMS.

Phantom	PG energy window (MeV)	Angular preference, ϕ (degree)	Gamma backward angle with respect to BP (degree)
Water	No window	107	60
	4.2-4.6	108	
	5.0-5.4	110	
	5.9-6.3	110	
	4.2-6.3	110	
PMMA	No window	107	70
	4.2-4.6	110	
	4.2-6.3	110	

Investigating the timing properties of gamma and neutron emission showed that most gamma rays were emitted at ~ 3 ns while neutrons can be differentiated as they were emitted after ~ 4 ns. Applying then the 4.2-6.3 MeV energy window, the timing properties of PG detection show a narrow timing window at around 3 ns in both water and PMMA, shown in Fig. 5. This indicates that gamma rays and neutrons can be well differentiated, and that a time-of-flight technique can be utilized to improve the signal-to-noise ratio of PG detection. Both energy and time resolved PG detection is a promising solution. The feasibility of this method has recently been proposed by Verburg *et al* 2013 [17].

Fig. 5. Timing distribution of PGs and neutrons reaching the detection sphere from the cylindrical water (left) and PMMA (right) phantoms, with the PG energy window 4.2-6.3 MeV.

IV. CONCLUSION

The emission and detection characteristics of PGs and neutrons in water and PMMA phantoms from 200 MeV proton irradiations have been investigated in this study. Our results show that there could exist an optimal energy window for PG detection around 4.44 MeV. PG emissions show a backward angular preference ($\phi > 90^\circ$) while neutron emissions have a forward angular preference ($\phi < 90^\circ$). Furthermore, employing a timing window could further improve the PG signal detection from strong background interferences of neutrons. Both energy and time resolved PG detection is a promising solution. These results indicate that there exists an optimized strategy for PG signal detection. Utilizing appropriate energy window, angular window and timing window, PG image formation could be significantly improved for BP tracking. Further investigation for development of an energy and time resolved PG imaging detector is under study.

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