A Geant4 Simulation Study for *in-vivo* Range Verification in Proton Therapy

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Hadron Therapy

• The advantage of hadron therapy (protons, carbon, helium ions) compared to conventional X-ray radiotherapy is the localised energy deposition in the **Bragg Peak (BP)**.

• But due to the sharp BP distal fall-off, tumour targeting must be precise, to avoid irradiation of normal tissue.

• High precision hadron therapy requires *in-vivo* **beam range verification** techniques to verify dose delivery while assuring safety margins during the treatment process.

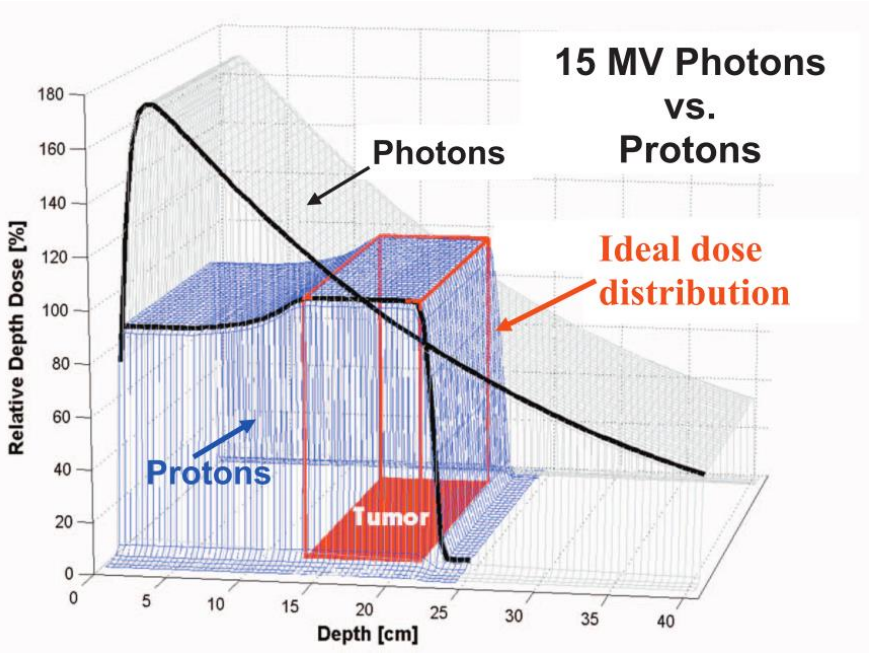

Figure showing comparison between photon and proton beams. Smith AR 2009.

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Beam Range Verification: Prompt Gamma

• There are various beam monitoring techniques, PET is used to detect delayed gammas from β^+ emitting radioisotopes (^{11}C, ^{13}N, ^{15}O).

– Does not offer real-time monitoring, biological washout for soft tissue, organ motion, difficulties in image co-registration

• Prompt gamma (PG) imaging is a novel technique which can provide a real-time signal for beam range verification, but this technology is still unavailable for clinical applications.

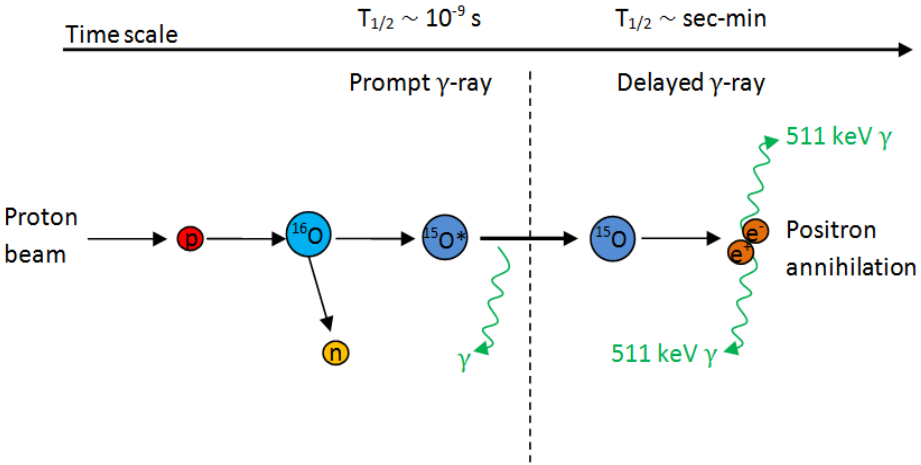
• PG is emitted in the decay process from an excited nucleus following proton-nuclear interaction.

•PG technique unique advantages:

– Enable on-line treatment monitoring in real time

– Provide high accuracy of range verification (~1mm), with close correlation between proton range and PG production position

– Discrete spectral lines in PG emission contain information of tissue composition



Literature Review

Characteristics and feasibility of prompt gamma

• **Studied PG characteristics** and **feasibility** as range verification technique (Min *et al* 2006, Polf *et al* 2009a, Peterson *et al* 2010, Frandes *et al* 2010). Use emitted spectrum to determine **elemental composition** of irradiated tissue (Polf *et al* 2009b, Polf *et al* 2013).

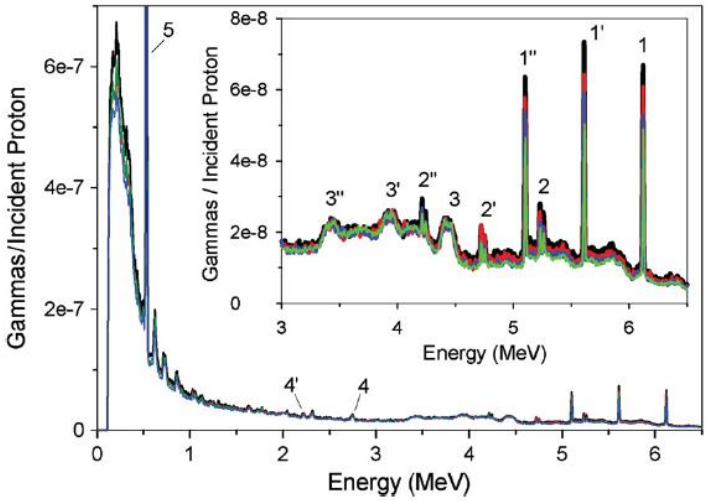


Figure 4. Measured prompt gamma spectra per incident proton emitted from the irradiated water (black line), and the 25 g (red line), 75 g (blue line), and 130 g (green line) sucrose solutions. The spectra show the prompt gamma, single escape, and double escape emission peaks for ^{16}O (1, 1′, 1″, 4, 4′), ^{15}O (2, 2′, 2″), and ^{12}C (3, 3′, 3″), as well as the positron annihilation gamma peak (5).

< Polf et al, *Measurement of characteristic prompt gamma rays emitted from oxygen and carbon in tissue-equivalent samples during proton beam irradiation*, 2013.

Verburg et al, *Energy- and time-resolved detection of prompt gamma-rays for proton range verification*, 2013. >

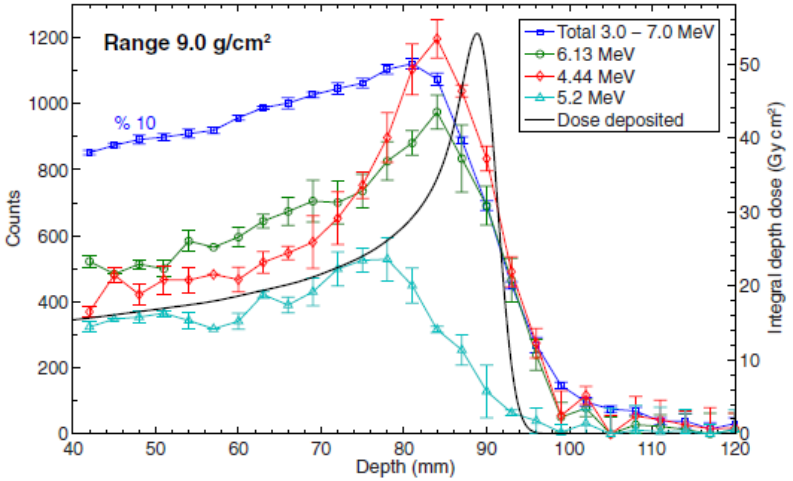


Figure 7. Energy-integrated (□) and discrete (○, ◇, Δ) prompt gamma-ray emissions along the path of proton pencil-beams in water. For proton ranges of 9.0, 16.0 and 23.0 g cm^{-2}, shown is the mean and $\pm 1\sigma$ statistical uncertainty of five measurements with 10^{10} incident protons per measurement point. The lines connecting the points serve to guide the eye. The dose deposited by 10^{10} protons is shown for reference, which is based on the clinically commissioned depth-dose curve.

Literature Review

Detector designs for PG imaging

- **Passive (mechanical) collimation**: collimated PG camera (Min *et al* 2006, Testa *et al* 2010), pinhole, knife-edge shaped slit placed perpendicular to beam direction (Bom *et al* 2012, Smeets *et al* 2012).
- **Active (electronic) collimation**: Compton cameras (Kormoll *et al* 2011), double-scattering cameras (Peterson *et al* 2010, Richard *et al* 2011) use Compton kinematics to trace gamma source.

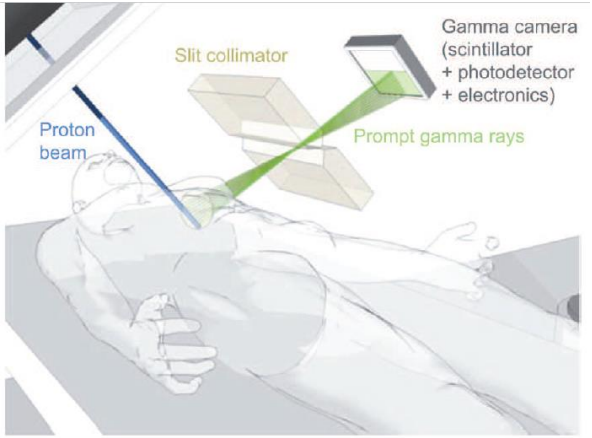


Figure 1. The slit camera concept: a slit collimation gives a 1D projection of prompt gamma emissions along the beam path on a scintillation detector.

Perali et al, *Prompt gamma imaging of proton pencil beams at clinical dose rate*, 2014.

cf. **Figure 4** for the two-plane camera. The Compton equation (41) relates the scattering angle θ to the initial (E_γ) and final (E_γ') photon energies:

$$\begin{aligned} E_\gamma &= L_s + L_a \\ E_\gamma' &= L_a \\ \cos\theta &= 1 - m_e c^2 \left(1/E_\gamma' - 1/E_\gamma\right) \end{aligned} \qquad (1)$$

where L_s and L_a are the energies released in scatterer and absorber, respectively, and $m_e c^2 = 511$-keV is the electron rest energy. In contrast to a slit camera, no collimation is needed

Gonzalez et al, *Compton camera and prompt gamma ray timing: two methods for in vivo range assessment in proton therapy*, 2016.

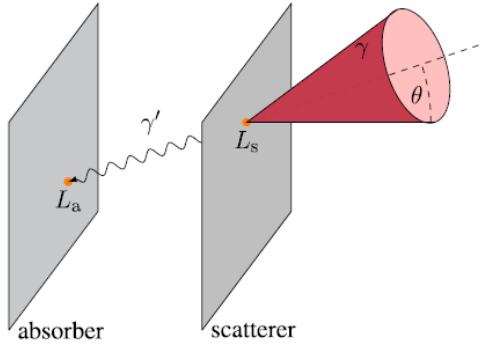


FIGURE 4 | Incoherent scattering event in a two-plane Compton camera. The cone surface contains the possible incidence directions (any generatrix) of the initial photon (γ). It interacts with the scatterer plane and deposits an energy L_s. The scattered photon (γ') releases the rest of the energy L_a in the absorber. The line connecting both interaction points (in orange) is the propagation direction of γ'. This defines the axis (directrix) of the aforementioned cone, with half-opening (scattering) angle θ and vertex at the scatter point.

Literature Review

Other beam monitoring techniques

• **Prompt gamma spectroscopy (PGS)**: Discrete excited states of nuclei to monitor beam range and assess elemental composition of irradiated tissue (Verburg *et al* 2014).

• **Prompt gamma timing (PGT)**: TOF distributions encode information about spatial emission point (Golnik *et al* 2014). TOF also for reducing neutron background (Testa *et al* 2008, Biegun *et al* 2012).

• **Prompt gamma peak integration (PGPI):** Integral and mean of TOF peak used to detect deviations from the prescribed treatment (Krimmer *et al* 2017).

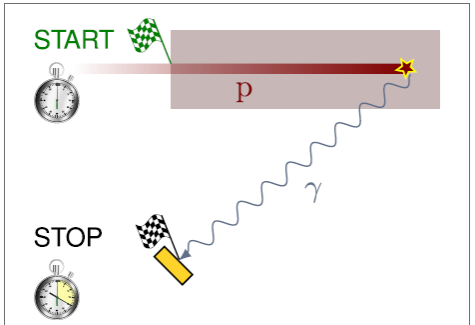
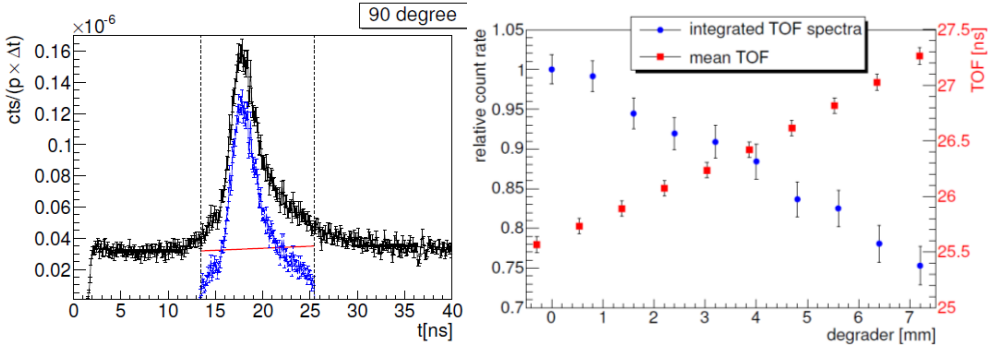


FIGURE 5 | Illustrative sketch of the PGT method. The therapeutic proton p (the projectile) slows down as it penetrates the target and interacts with a nucleus, which emits a prompt gamma ray. The time between the entrance of the proton to the target (the start flag) and the arrival of the gamma ray to the detector (the stop flag at the yellow rectangle) encodes the proton transit time and gamma time of flight, which can be correlated to the depth of interaction of the proton (gamma emission point).

Gonzalez et al, 2016.

Golnik et al, *Range assessment in particle therapy based on prompt gamma-ray timing measurements*, 2014.



Krimmer et al, *A cost-effective monitoring technique in particle therapy via uncollimated prompt gamma peak integration*, 2017.

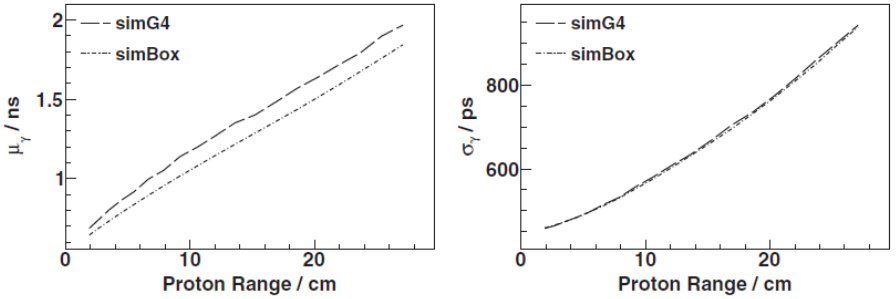


Figure 12. Range-dependent mean value μ_γ (left) and standard deviation σ_γ (right) of modeled prompt γ-ray PGT spectra. The target material is PMMA. The proton energies are in the range of 50 MeV up to 230 MeV, corresponding to proton ranges from 2 cm up to 27 cm. The assumed system time resolution σ_Σ is 450 ps.

Research Goal

• Main challenges of PG imaging are the absence of optimised PG detection methodology and technology.

- Capable of measuring **high-energy** gamma rays, high count rates, with suitable efficiency and precision.
- Technique to reduce background for **improving signal-to-noise** ratio.
- Technology for **fast timing** of gamma detection and electronics.

• **Goal**: investigate and develop a novel *in-vivo* dose verification technique using PG signals to enable on-line treatment monitoring in particle therapy.

1. Monte Carlo simulations to (1) investigate PG **emission and detection characteristics** and (2) determine optimal system for **uncollimated PG detection** using TOF information for BP tracking.
2. Develop detector/s, optimise system. Main requirement is good **energy and timing resolution**.
3. Test/verification.

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Conclusion

• The **energy spectra** of gamma emission is characteristic to the elemental composition of the phantom material. Prominent PG emission lines are 4.44, 5.21, 6.13 MeV from ^{12}C, ^{15}O and ^{16}O, respectively.

• **PG rays** offer improved correlation to the BP distal fall-off compared to total gamma emission.

• The **preferential position** for PG detection is slightly backward peaked, for proton beam, and normally, for ^{12}C beam, relative to the BP position.

• PG **TOF spectra** changes with beam energy, the peak mean and integral increase with higher beam energy – the potential for a simple, uncollimated means of BP tracking.

• **Next stage of simulations:**

- Different phantom shapes (e.g. cylinder) and materials (e.g. plastic, tissue-equivalent).
- Model PG energy and TOF response of realistic scintillation detectors positioned around the phantom.

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Thank you

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Acknowledgements

• We would like to thank the University of Wollongong Information Management & Technology Services (IMTS) for computing time on the UOW High Performance Computing Cluster.

• This research has been conducted with the support of the Australian Government Research Training Program Scholarship.

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References

Smith AR, *Vision 20/20: Proton therapy*, Med. Phys. 2009, 36: pp 556-568
Min CH *et al*, *Prompt gamma measurements for locating the dose fall-off region in proton therapy*, Appl. Phys. Lett. 2006, 89: pp 183517
Polf JC *et al*, *Prompt gamma-ray emission from biological tissues during proton irradiation: a preliminary study*, Phys. Med. Biol. 2009a, 54: pp 731-743
Peterson SW *et al*, *Optimizing a three-stage Compton camera for measuring prompt gamma rays emitted during proton radiotherapy*, Phys. Med. Biol. 2010, 55: pp 6841-6856
Frandes M *et al*, *A tracking Compton-scattering imaging system for hadron therapy monitoring*, IEEE Trans. Nucl. Sci. 2010, 57: pp 144-150
Polf JC *et al*, *Measurement and calculation of characteristic prompt gamma ray spectra emitted during proton irradiation*, Phys. Med. Biol. 2009b, 54: pp 519-527
Polf JC *et al*, *Measurement of characteristic prompt gamma rays emitted from oxygen and carbon in tissue-equivalent samples during proton beam irradiation*, Phys. Med. Biol. 2013, 58: pp 5821-5831
Verburg JM et *al,* E*nergy- and time-resolved detection of prompt gamma-rays for proton range verification,* Phys. Med. Biol. 2013, 58: pp L37-L49
Verburg JM *et al*, *Proton range verification through prompt gamma-ray spectroscopy*, Phys. Med. Biol. 2014, 59: pp 7089-7106
Testa M *et al*, *Monitoring the Bragg peak location of 73 MeV/u carbon ions by means of prompt g-ray measurements*, Appl. Phys. Lett. 2008, 93: 093506
Bom V et *al,* R*eal-time prompt gamma monitoring in spot-scanning proton therapy using imaging through a knife-edge shaped slit,* Phys. Med. Biol. 2012, 57: pp 297-308
Smeets J et *al,* P*rompt gamma imaging with a slit camera for real-time range control in proton therapy,* Phys. Med. Biol. 2012, 57: pp 3371-3405
Kormoll T et *al,* A *Compton imager for in-vivo dosimetry of proton beams – A design study,* Nucl. Instrum. Methods Phys. Res. 2011, 626-627: pp 114-119
Richard MH et *al, Design guidelines for a double scattering Compton camera for prompt-γ imaging during ion beam therapy: a Monte Carlo simulation study,* IEEE Trans. Nucl. Sci. 2011, 58: pp 87-94
Perali I et *al, Prompt gamma imaging of proton pencil beams at clinical dose rate,* Phys. Med. Biol. 2014, 59: pp 5849-5871
Gonzalez FH *et al*, *Compton camera and prompt gamma ray timing: two methods for in vivo range assessment in proton therapy*, Front. in Onc. 2016, 6: pp 1-13
Biegun AK *et al*, *Time-of-flight neutron rejection to improve prompt gamma imaging for proton range verification: a simulation study*, Phys. Med. Biol. 2012, 57: pp 6429-6444
Golnik C *et al*, *Range assessment in particle therapy based on prompt gamma-ray timing measurements*, Phys. Med. Biol. 2014, 59: pp 5399-5422
Krimmer J et *al, A cost-effective monitoring technique in particle therapy via uncollimated prompt gamma peak integration*, 2017, DOI: 10.1063/1.4980103