Gadolinium neutron capture agent for charged particle radiotherapy

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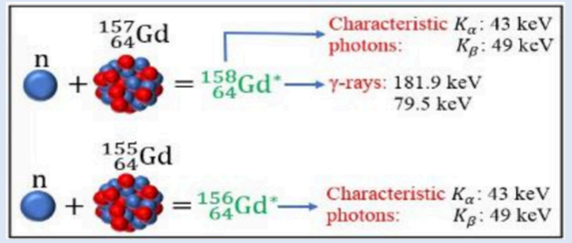
Introduction

Background: Recently, a novel imaging procedure termed proton neutron gamma-x detection (PNGXD) was proposed as a method to take advantage of the secondary neutrons produced from the treatment of proton therapy by capturing them using a pre-administered gadolinium contrast agent (GDCA) located within the tumor volume of interest [1].



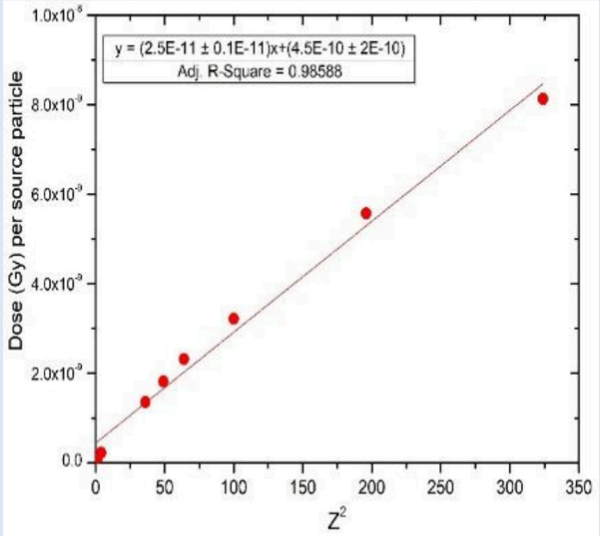
Study Purpose: To investigate the secondary thermal neutron production from ten different charged particles for the application of gadolinium (Gd) based tumor dose enhancement [1] and particle neutron gamma-x detection technique (PNGXD) [2].

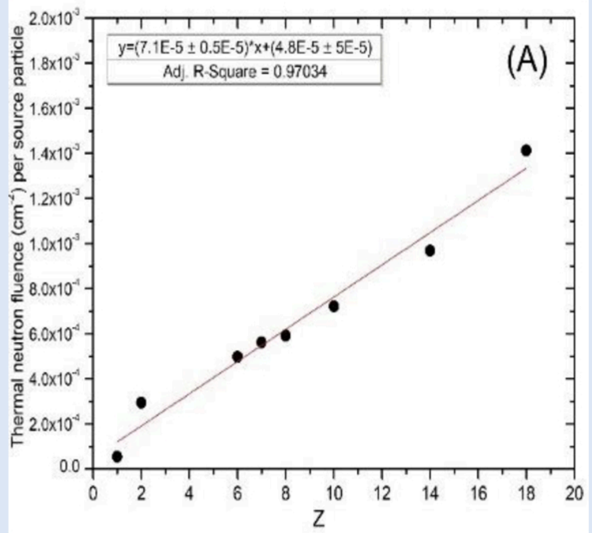
Methods

We simulated a 5-10 cm spread-out Bragg peak (SOBP) using MCNP6 Monte Carlo code for ten different particles on a 30×30×30 cm^3 phantom. The ten charged particles included: protons, He, C, N, O, Ne, Si, Ar, antiprotons and negative pions. A 8 cm^3 Gd solution with a concentration of 3 mg/g was placed central to the SOBP.

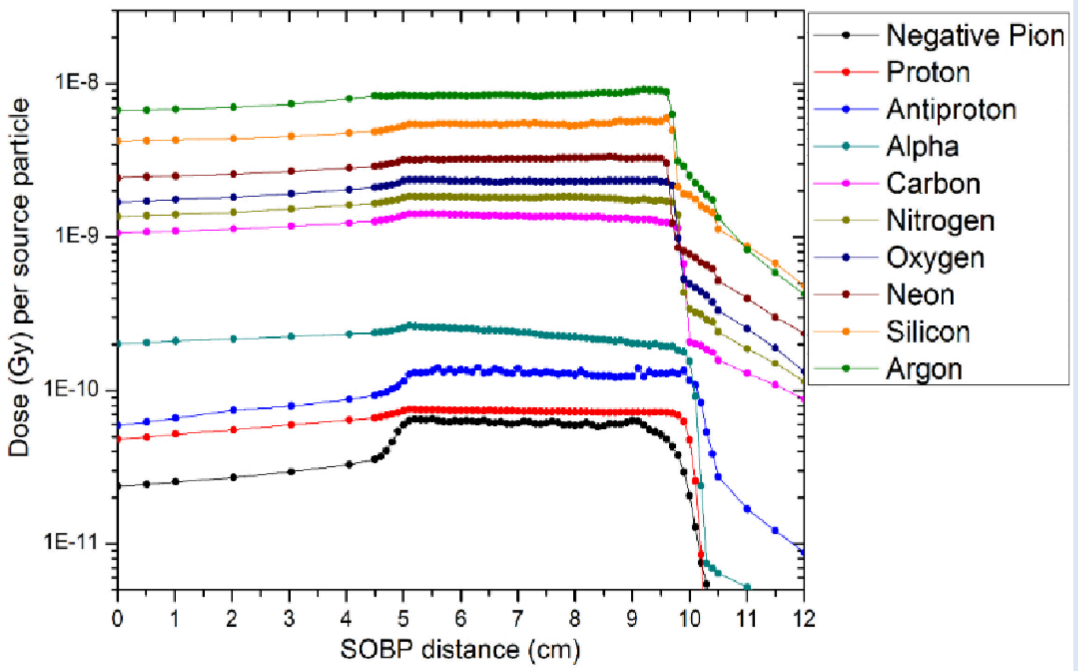
Monte Carlo Simulation Results

(Right): Raw Gd Dose per source particle versus atomic number squared (Z^2). The relationship is linear as expected based on the Z^2 dependence of the Bethe stopping power equation.



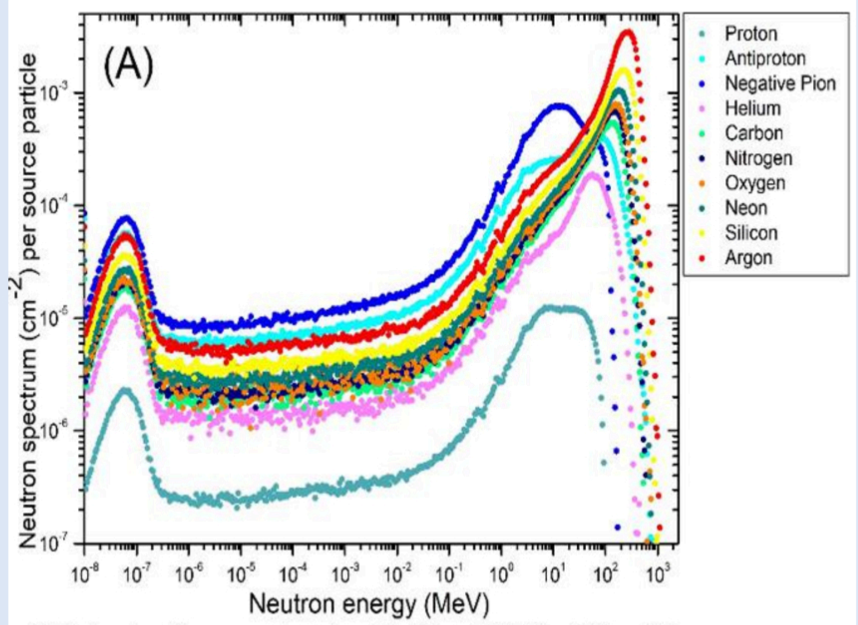


(Left): Raw Gd (A) Thermal neutron production per source particle as a function of atomic number (Z). The thermal neutron fluence was found to scale linearly with the atomic number for all particles except antiprotons, and negative pions.



(Left): SOBPs produced from 10 different particles with MCNP6 administered on a ICRU-4 soft tissue phantom.

(Right): Total neutron fluence (cm^{-2}) from each particle in a 2×2×2 cm^3 centered tumor.



A) Total neutron fluence spectrum for a 5 to 10 cm SOBP for all 10 particles.

Simulated neutron fluence and Gd neutron capture reactions per Gy of absolute dose for the various charged particles investigated in this study. The last column is the Gd neutron capture rate relative to protons.

Particle 5 to 10 cm (SOBP)	Thermal neutron fluence (cm^{-2}/Gy)	Total neutron fluence (cm^{-2}/Gy)	Gd neutron capture reactions (captures/Gy)	Normalized Gd neutron capture reactions (captures/Gy)
Argon	1.7×10^5	1.2×10^7	5.0×10^5	0.24
Silicon	1.7×10^5	9.5×10^6	5.0×10^5	0.24
Neon	2.2×10^5	1.1×10^7	6.5×10^5	0.30
Oxygen	2.6×10^5	1.2×10^7	7.4×10^5	0.34
Nitrogen	3.1×10^5	1.4×10^7	8.9×10^5	0.42
Carbon	3.7×10^5	1.5×10^7	1.1×10^6	0.49
Helium	1.3×10^6	3.3×10^7	3.7×10^6	1.7
Proton	7.4×10^5	1.1×10^7	2.1×10^6	1.0
Antiproton	1.4×10^7	2.8×10^8	3.7×10^7	18
Negative Pion	2.9×10^7	6.9×10^8	8.3×10^7	39
10 to 15 cm (SOBP)				
Carbon	7.1×10^5	2.4×10^7	4.5×10^6	0.56
Helium	2.1×10^6	4.7×10^7	1.1×10^7	1.7
Proton	1.3×10^6	1.4×10^7	5.8×10^6	1.0

Simulated Gd neutron capture reactions normalized to an estimate of RBE weighted dose (RBE×Gy). The last column is RBE weighted captures normalized to protons.

RBE	RBE value reference	Particle 5 to 10 cm (SOBP)	Gd neutron captures reactions per RBE×Gy (captures/GyE)	Normalized RBE weighted Gd neutron capture reactions
4.25	Goldstein *et al.* 38	Argon	1.2×10^5	0.06
3.75	Blakely *et al.* 40	Silicon	1.3×10^5	0.07
3.5	Goldstein *et al.* 38	Neon	1.9×10^5	0.10
3.25	Tran *et al.* 41	Oxygen	2.3×10^5	0.12
3	Tran *et al.* 41	Nitrogen	3.0×10^5	0.15
2.75	Goldstein *et al.* 38	Carbon	3.8×10^5	0.20
1.5	Goldstein *et al.* 38	Helium	2.5×10^6	1.3
1.1	Tepper *et al.* 39	Proton	1.9×10^6	1.0
2	Holzscheiter *et al.* 42	Antiproton	1.9×10^7	10
2.5	Raju *et al.* 27	Negative Pion	3.3×10^7	17
		10 to 15 cm (SOBP)		
2.75	Goldstein *et al.* 38	Carbon	1.6×10^6	0.2
1.5	Goldstein *et al.* 38	Helium	7.2×10^6	1.2
1.1	Tepper *et al.* 39	Proton	5.3×10^6	1.0

Conclusions

- Ten different particles were simulated to study thermal neutron production for the application of Gd neutron capture imaging (PNGXD) and Gd neutron capture therapy.
- Three particles, antiprotons, negative pions, and helium ions, consistently produced more thermal neutron captures than protons.
- For a 5 to 10 cm SOBP, these three particles produced 1.9×10^7, 3.3×10^7, 2.5×10^6 neutron captures per GyE, respectively.

References

1) Van Delinder KW, Crawford D, Zhang T, Khan R, Gräfe JL. Investigating neutron activated contrast agent imaging for tumor localization in proton therapy: a feasibility study for proton neutron gamma-x detection (PNGXD). Physics in Medicine & Biology. 2020 Jan 24; 65(3): 035005 (12pp).

2) Paganetti H, Goitein M, Parodi K. Spread-out antiproton beams deliver poor physical dose distributions for radiation therapy. Radiotherapy and Oncology. 2010 Apr 1;95(1):79-86.

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