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Proton FLASH Therapy-Induced Radioisotopes as a Source of Entangled 511 keV Photons

Uriel Ngwa, BSc.[1]; Wilfred Ngwa, PhD[2]
[1]University of Florida, [2]Global Oncology University

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Abstract

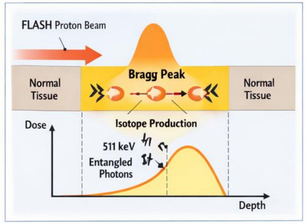
- Ultra-high dose rate (FLASH) proton therapy generates positron-emitting radioisotopes, including C-11, O-15, and F-18, which decay via β^+ emission. Each annihilation produces a pair of 511 keV photons naturally entangled in momentum and polarization.
- We evaluated the entangled photon yield and temporal profile from realistic FLASH pulses and explored their potential as spatially localized reporters of tumor microenvironment (TME) changes and adaptive radiotherapy biomarkers, leveraging the Bragg peak dose localization.
- Results show that Proton FLASH therapy predominantly generate entangled photon pairs after the pulse, with both temporal and spatial profiles determined by isotope half-lives and Bragg peak localization.

Introduction

- Proton FLASH therapy inherently generates positron-emitting isotopes, including C-11, O-15, and F-18, through nuclear interactions within tissue.
- Each positron subsequently annihilates with an electron, producing a pair of 511 keV photons that are naturally entangled in momentum and polarization.
- This phenomenon offers a unique opportunity to leverage entangled photons for real-time dosimetry and monitoring of the tumor microenvironment (TME).
- The spatial localization of isotope production around the Bragg peak ensures that entangled photon emission is concentrated within the high-dose tumor region, minimizing background from surrounding healthy tissue and providing a novel quantum-functional biomarker for adaptive radiotherapy..
- In this study, we evaluated the entangled photon yield and temporal profile from realistic FLASH pulses and explored their potential as spatially localized reporters of tumor microenvironment (TME) changes and adaptive radiotherapy biomarkers, leveraging the Bragg peak dose localization.

Methods and Materials

- A 1 ms proton FLASH pulse containing 10^9protons traversing 1 cm of tissue (atomic density 6×10^{22}atoms/cm³) was modeled.
- Isotope production cross-sections were taken from literature (C-11: 1×10⁻²⁶ cm², O-15: 5×10⁻²⁶ cm², F-18: 1×10⁻²⁷ cm²) with 100% β^+ branching.
- Decay and entangled photon emission were calculated using $N_\gamma(t) = 2\lambda N_0 e^{-\lambda t}$.
- Data was generated as a function of dose.
- The Bragg peak localization of proton dose was considered to estimate spatial concentration of isotope production and photon emission.



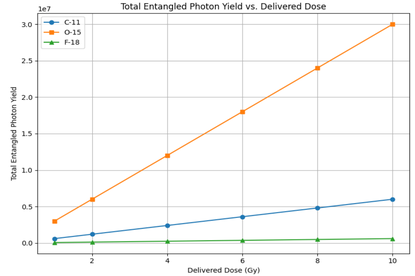


Figure 1. Top: Set-up geometry; Bottom: Yield vs Dose

Results

- The estimated isotope yields per FLASH pulse were 6×10⁵ for C-11, 3×10⁶ for O-15, and 6×10⁴ for F-18.
- Photon emission during the 1 ms pulse itself was negligible due to the short duration relative to isotope half-lives, with 0.35 photons for C-11, 17 for O-15, and 0.006 for F-18.
- Total entangled photons emitted over several half-lives were 1.2×10⁶ for C-11, 6×10⁶ for O-15, and 1.2×10⁵ for F-18.
- The Bragg peak ensures that these photons are concentrated in the tumor region, with O-15 dominating early post-pulse emission and C-11 providing sustained signal over minutes.
- This spatial and temporal distribution supports the feasibility of quantitative, localized FLASH dosimetry and functional assessment of TME changes for guiding adaptive radiotherapy.

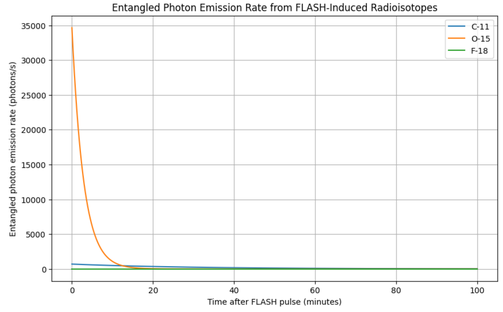


Figure 2. Data to show the entangled photon emission rate vs. time for C-11, O-15, and F-18 after a FLASH pulse: O-15 (blue) peaks quickly and decays over a few minutes, highest immediate entangled photon flux. C-11 (orange) is longer-lived, so its photon emission is slower but lasts much longer. F-18 (green) has a very low rate due to low production and long half-life. This clearly shows that the bulk of entangled photons appear after the pulse, not during the sub-ms FLASH pulse itself.

Isotope	Half-life	Isotopes Produced/ Pulse	Decays During 1 ms Pulse	Total Entangled Photons
C-11	20 min	6×10^5	0.35	1.2×10^6
O-15	2 min	3×10^6	17	6×10^6
F-18	110 min	6×10^4	0.006	1.2×10^5

Discussion

- The generation of entangled photons during FLASH therapy provides a non-invasive, temporally precise measure of dose deposition.
- The early-time photon flux from short-lived isotopes such as O-15 can serve as a sensitive indicator of local radiation delivery, while longer-lived isotopes like C-11 provide sustained emission over minutes, enabling continuous monitoring.
- Beyond dosimetry, variations in entanglement coherence could reflect changes in tissue characteristics such as hypoxia, perfusion, and necrosis, making these photons potential functional reporters of TME changes.
- Together, these properties suggest a pathway for developing quantum-assisted biomarkers that could guide adaptive radiotherapy and longitudinal treatment response measurement
- The Bragg peak concentrates both the dose and the entangled photon production, making these photons a natural, high-resolution reporter of the tumor region. This could allow real-time verification of FLASH dose deposition and non-invasive assessment of TME changes in the tumor, without significant signal from surrounding healthy tissue.

Conclusions

- Proton or particle FLASH generates entangled photon pairs with temporally and spatially resolved distributions that provide a novel pathway for high-precision dosimetry and functional imaging of the tumor microenvironment, establishing a quantum-functional biomarker platform for adaptive radiotherapy.
- This framework establishes a basis for exploiting **quantum-correlated photons** as both a **theranostic tool** and a **novel biomarker platform** leveraging emerging FLASH platforms .

Contact

<your name>
<your organization>
Email:
Website:
Phone:

References

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