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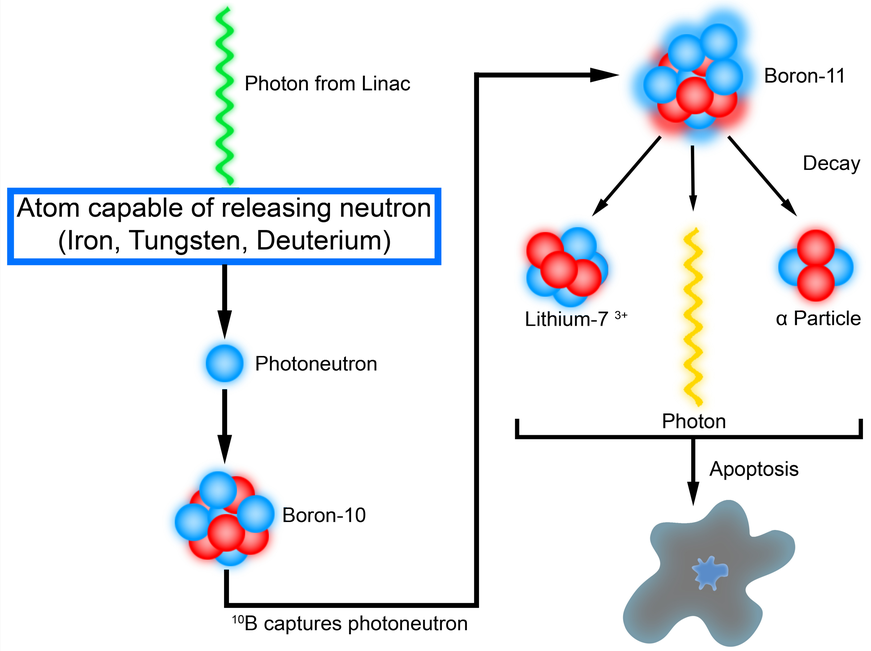
An investigation into Linac intracellular photoneutron generation and its possible use with BNCT

James Y. Lee, Charles A. Maitz, Senthil Kumar

MU College of Veterinary Medicine
International Institute of Nano & Molecular Medicine
University of Missouri, Columbia, MO 65201

Introduction

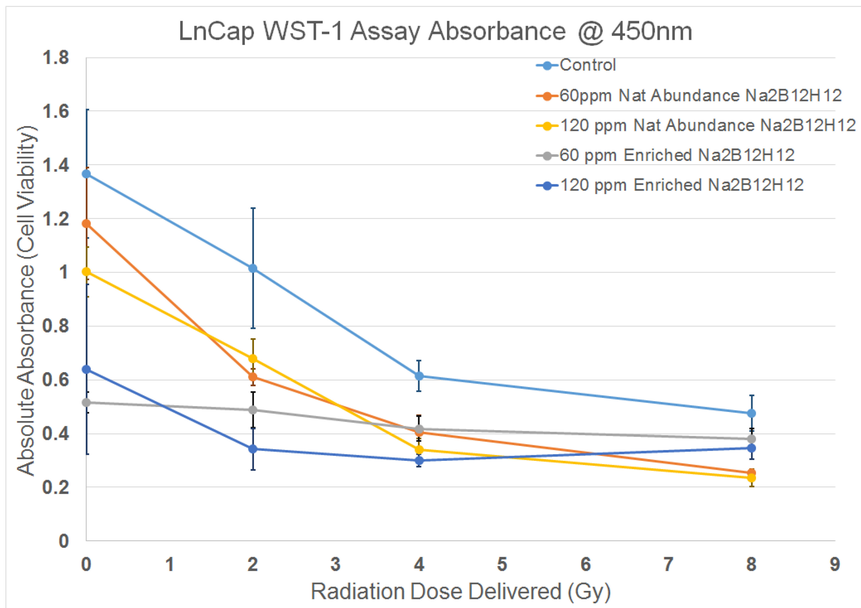


Boron Neutron Capture Therapy (BNCT) is a type of radiation therapy involving the capture of slow-moving neutrons with boron nuclei in compounds. Neutron sources are currently limited to nuclear reactors. Linear accelerators (Linacs), commonly found in many hospitals for radiation therapy, produce photons with sufficient energy to produce neutrons when collided with other materials. These low-energy neutrons generally do not affect living tissue. However, they can be captured by Boron-10 compounds, which then decay into a lithium nucleus and an alpha particle along with gamma rays. Intracellular photoneutrons used with BNCT could be an effective way to augment traditional radiation therapies with little to no change in current equipment or technologies. The purpose of this study is to investigate intracellular photoneutron generation by measuring the killing effect of photon irradiation with boron compounds present. We hypothesize that BNCT would further reduce cell culture viability when compared to cell cultures that received radiation alone.

Methods

LnCap cells were plated in a 96 well plate at 8000 cells per well and incubated for 24 hours. Four plates were designated to receive 0, 2, 4, and 8 Gy of radiation from the Linac using photons with peak energy of 15 MeV. Each plate was further subdivided into rows that would receive no boron compound, natural abundance $Na_2B_{12}H_{12}$, and enriched ^{10}B $Na_2B_{12}H_{12}$ at 60 and 120 ppm each. Plates were incubated for 2 hours then irradiated. The plates were again incubated for 48 hours, and a WST-1 (cell viability) assay was performed.

Data



% Change	Control	60 ppm Nat Abundance	120 ppm Nat Abundance	60 ppm Enriched	120 ppm Enriched
0 vs 2	-25.6249	-48.4030	-32.1597	-5.3622	-46.4688
0 vs 4	-55.1129	-65.6668	-66.2170	-18.9906	-53.2101
0 vs 8	-65.1548	-78.4155	-76.6102	-26.0690	-45.6663

- 0 Gy -- Compared to Control (N= 8, M= 1.37, SD= 0.24)
  - 60 ppm Natural Abundance (N= 4, M= 1.18, SD= 0.21) -- $t(10)$= 1.19, $p \leq .13$, CI_{95} -0.16, 0.53
  - 120 ppm Natural Abundance (N= 4, M= 1.00, SD= 0.093) -- $t(10)$= 2.68, $p \leq .012$, CI_{95} 0.061, 0.67
  - 60 ppm Enriched (N= 4, M= .52, SD= 0.039) -- $t(8)$= 9.12, $p \leq$ 8.4E-06, CI_{95} 0.64, 1.06
  - 120 ppm Enriched (N= 4, M= .64, SD= 0.32) -- $t(10)$= 4.06, $p \leq .0011$, CI_{95} 0.33, 1.13
- 2 Gy -- Compared to Control (N= 8, M= 1.02, SD= 0.22)
  - 60 ppm Natural Abundance (N= 4, M= .61, SD= 0.31) -- $t(8)$= 4.70, $p \leq .00077$, CI_{95} 0.17, 0.65
  - 120 ppm Natural Abundance (N= 4, M= .68, SD= 0.072) -- $t(10)$= 2.68, $p \leq .012$, CI_{95} 0.056, 0.62
  - 60 ppm Enriched (N= 4, M= .49, SD= 0.066) -- $t(9)$= 5.70, $p \leq .00015$, CI_{95} 0.29, 0.77
  - 120 ppm Enriched (N= 4, M= .34, SD= 0.076) -- $t(10)$= 5.36, $p \leq .00016$, CI_{95} 0.39, 0.95
- 4 Gy -- Compared to Control (N= 8, M= .61, SD= 0.057)
  - 60 ppm Natural Abundance (N= 4, M= .41, SD= 0.061) -- $t(10)$= 5.30, $p \leq .00018$, CI_{95} 0.16, 0.25
  - 120 ppm Natural Abundance (N= 4, M= .34, SD= 0.042) -- $t(10)$= 7.80, $p \leq$ 7.37E-06, CI_{95} 0.21, 0.33
  - 60 ppm Enriched (N= 4, M= .42, SD= 0.046) -- $t(10)$= 5.43, $p \leq .00014$, CI_{95} 0.15, 0.24
  - 120 ppm Enriched (N= 4, M= .30, SD= 0.023) -- $t(10)$= 9.69, $p \leq$ 1.06E-06, CI_{95} 0.24, 0.38
- 8 Gy -- Compared to Control (N= 8, M= .48, SD= 0.067)
  - 60 ppm Natural Abundance (N= 4, M= .26, SD= 0.0076) -- $t(7)$= 8.64, $p \leq$ 2.78E-05, CI_{95} 0.16, 0.25
  - 120 ppm Natural Abundance (N= 4, M= .23, SD= 0.032) -- $t(10)$= 6.27, $p \leq$ 4.64E-05, CI_{95} 0.21, 0.33
  - 60 ppm Enriched (N= 4, M= .38, SD= 0.039) -- $t(10)$= 2.40, $p \leq .00014$, CI_{95} 0.019, 0.24
  - 120 ppm Enriched (N= 4, M= .35, SD= 0.044) -- $t(10)$= 3.21, $p \leq .0047$, CI_{95} 0.24, 0.38

Conclusion and Ongoing Studies

Of the compounds added and their respective concentrations, there was a statistically significant difference in cell viability in wells that received $Na_2B_{12}H_{12}$ synthesized with natural abundance boron at 60 ppm and its respective control groups at 2, 4, and 8 Gy of radiation. No difference was found in the wells that did not receive radiation. However, the wells that received $Na_2B_{12}H_{12}$ synthesized with natural abundance boron at 120 ppm and also $Na_2B_{12}H_{12}$ synthesized with enriched Boron-10 at 60 and 120 ppm were statistically significant when compared to the controls in the plate that did not receive radiation. There should have been no difference in cell viability in the plate that did not receive radiation. The boron compounds may have had an impurity that affected the cells in all wells that contained the compound. Currently, these compounds are being analyzed for purity through mass spectroscopy and high performance liquid chromatography. It is highly unlikely that these compounds are toxic to the cells, but is another possibility. Another explanation for the unexpected results is insufficient photoneutron generation within the target. Future studies will be focused in decreasing the photoneutron production threshold, possibly by deuterating (replacing ^1H with ^2H) the compounds as deuterium has a low photoneutron threshold.

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