Lithium Neutron Capture Therapy: First In Vivo Efficacy in Melanoma Model

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Lithium neutron capture therapy (LiNCT) is proposed as an alternative to boron neutron capture therapy (BNCT). The $^{6}Li(n,\alpha)^{3}H$ reaction releases 100% of its energy within the cell – a key advantage over ^{10}B, despite a four times smaller cross-section but twice higher energy release. The concept of lithium using for NCT was proposed yet in 1936 by Locher, and a renewed interest in LiNCT was sparked by Rendina in 2010 [1, 2]. Our previous study showed effective accumulation of lithium in melanoma cells following the administration of various lithium salts containing the natural lithium, moreover, the study also demonstrated the absence of toxicity after a single administration of high-dose lithium for the LiNCT [3]. This study provides the first in vivo evaluation of LiNCT using an accelerator-based neutron beam suitable for clinical implementation.

B16 melanoma-bearing C57BL/6 mice received ^{6}Li-enriched lithium chloride (450 mg/kg) either orally or intraperitoneally. Lithium biodistribution was measured by ICP-AES at 1–4 h post-administration. Neutron irradiation (2.1 MeV protons, 1.6 mA, ~1.5 h) was performed at the VITA accelerator-based neutron source [4]. Tumor growth and survival were monitored.

Intraperitoneal administration achieved a significantly higher peak tumor lithium concentration (54.1 μg/g at 1 h) compared to oral route (30.2 μg/g at 4 h). Tumor-to-blood ratios (1.4–1.5) and tumor-to-skin ratios (4.7–13.7) were favorable for LiNCT. Intraperitoneal LiNCT significantly increased median survival (34 days vs. 15 days in control, $p<0.0001$, Table 1) and slowed tumor growth 2–4 times during the first three weeks. No significant efficacy was observed with oral administration.

Table 1. The survival median and increase in life span (ILS, %) of B16 melanoma-bearing mice after intraperitoneal lithium administration and LiNCT.

Group	Median	ILS (%)	P-value
Control	15	0	-
Li	10	-33.3	0.11815 vs Control
Neu	20	33.3	0.01688 vs Control; 0.00023 vs Li
LiNCT	34	127	0.000017 vs Control; 0.000015 vs Li; 0.00019 vs Neu

These results demonstrate that LiNCT with intraperitoneal lithium delivery produces a pronounced antitumor effect in a murine melanoma model, opening new opportunities for neutron capture therapy using lithium alone or in combination with boron.

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