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Abstract

Chordoma Treatment with Boron Neutron Capture Therapy (BNCT): Experimental Insights †

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1. Background

Boron Neutron Capture Therapy (BNCT) is a particle beam therapy that enables the precise targeting of tumors at the cellular level. Drawing on the success observed in nuclear reactors, BNCT holds promise as a therapeutic approach for addressing invasive brain tumors, such as malignant gliomas and high-grade meningiomas.

Chordomas are rare bone tumors characterized by locally invasive, frequent recurrence, and relative radioresistance. Recently, treatment modalities, including proton or carbon ions particle irradiation, have been developed; however, conclusive evidence supporting their efficacy is yet to be established. This experimental study aimed to evaluate the effectiveness of BNCT in the treatment of chordoma.

2. Methods

The U-CH1 and JHC7 human chordoma cell lines were employed in this study. In the in vitro experiment, both cell lines were exposed to p-boronophenylalanine (BPA) at a concentration of 10 μg boron/mL for duration of 3, 6, and 24 h. Subsequently, the measurement of cellular boron uptake was conducted using Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES). After 24 h of exposure, the medium was replaced with a boron-free medium, and the subsequent investigation was focused on boron clearance. Neutron irradiation was then applied to these two cell lines, BNCT with BPA (10 μg Boron/mL for a 24-h exposure before irradiation) (BNCT group), and neutron irradiation without BPA (hot control group), for 0 to 30 min. Assessment of the cell-killing effect was carried out using a colony forming assay. In the in vivo experiment, subcutaneous tumor-bearing mice were intravenously administered BPA (250 mg/mouse body weight). After 1 h, the mice were sacrificed, and the boron concentrations in both the tumor and each organ were measured using ICP-AES.

3. Results

In the in vitro BPA exposure experiment, U-CH1 exhibited an increase in cellular boron uptake with prolonged BPA exposure time, whereas JHC7 demonstrated a consistent uptake

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unaffected by exposure time. Both cell lines showed a rapid decrease in cellular boron concentration after incubation with boron-free medium. Neutron irradiation revealed that the BNCT group demonstrated a more pronounced cell-killing effect than the hot control group in both cell lines. In the in vivo biodistribution of boron, the tumor accumulation was 5.7 μg B/g with a tumor-to-blood ratio (T/Bl) of 1.3 in U-CH1, while JHC7 showed a tumor accumulation of 9.3 μg B/g, with a T/Bl of 1.5.

4. Conclusions

Despite the relatively low intracellular boron uptake compared to other malignant tumors, these findings suggest that BNCT may represent an effective approach in the management of chordoma. Future efforts will include in vivo neutron irradiation experiments to more fully assess the effects of BNCT on survival and neurological function.

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Conflicts of Interest: The authors declare no conflicts of interest.