Ongoing translational studies of therapeutic efficacy of BNCT/GB-10 and BNCT/GB-10+Electroporation for oral cancer in the RA-1 facility

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Introduction: To explore the therapeutic potential of boron carriers and administration protocols for head and neck cancer in the hamster cheek pouch oral cancer model, we evaluated novel BNCT strategies employing boron compounds approved for their use in humans (eg. Trivillin et al., 2006; Garabalino & Olaiz et al., 2019). Our previous studies in the facility of the RA-1 Nuclear Reactor consisted in BPA/BNCT experiments on non-cancerized Syrian hamsters. RA-1 is of particular interest because it is located in Buenos Aires and has a neutron spectrum that includes a fast neutron component that might contribute to the treatment of Squamous Cell Carcinomas. We also demonstrated the feasibility of treating spontaneous head and neck tumors in domestic felines with BNCT in RA-1 and RA-6 Reactors (eg. Rao et al., 2004; Trivillin et al. 2008). **Aim**: perform experiments to assess the therapeutic efficacy of BNCT and radiotoxicity *in vivo* in an oral cancer model in the hamster cheek pouch using BNCT/GB-10 and the combination of BNCT/GB-10 + Electroporation (EP) at the facility thermal RA-1. **Materials and methods:** Tumors were induced in the right cheek pouch of Syrian hamsters as previously (Garabalino & Olaiz et al., 2019). Once the exophytic tumors developed, i.e. squamous cell carcinomas, the animals were used for pilot BNCT studies: Group 1) BNCT/GB-10 (50 mg ^{10}B/kg, iv) (n=17 tumors) and Group 2) BNCT/GB-10 (50 mg ^{10}B/kg, iv) +EP (10 min. post-administration of GB-10) (n=8 tumors). Electroporation was performed on each tumor employing the standard sequence of pulses for electrochemotherapy (1000 v/cm, 8 pulses of 100 μs). Prior to each *in vivo* BNCT study the volume of each tumor was determined. We arbitrarily defined 2 tumor volume ranges, i.e. small (1 mm^3 >volume >10 mm^3) and medium/large (volume ≥10 mm^3). Irradiations were carried out 3 hours post-administration of GB-10 in the RA-1 facility with 10 minutes exposures and using a ^{6}Li carbonate shielding. Tumor response and mucositis in precancerous tissue surrounding tumors were evaluated 7, 10, 14, 21 and 28 days post-irradiation. All experiments were approved by CICUAL-CNEA. **Results:** No severe radiotoxicity (mucositis) was observed in the BNCT/GB-10 or BNCT/GB-10+EP protocols at any follow-up time. 28 days post-irradiation total tumor response (complete remission + partial remission) was 65% for BNCT/GB-10 and 88%

for BNCT/GB-10+EP. Although these results are preliminary, small tumors´ overall response was increased in BNCT/GB-10+EP vs. BNCT/GB-10 (100% vs 65%, respectively). For the case of medium and large tumors a total tumor response of 67% was obtained for both protocols. **Conclusion:** These preliminary data suggest that BNCT/GB-10-and BNCT/GB-10+EP carried out at the RA-1 facility might be therapeutically useful for the treatment of head and neck tumors without associated apparent radiotoxicity.

Acknowledgments
The authors wish to acknowledge the expert advice and generous support of the RA-1 Reactor team.

References

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