Comparison of RBE doses with the photon iso-effective dose model for predicting the normal tissue complication probability in boron neutron capture therapy (BNCT) for head and neck cancer patients

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The radiation dose in boron neutron capture therapy (BNCT) consists of the high-LET dose from the 10B(n,a)7Li reaction, the nitrogen capture dose, the recoil proton dose, and the photon dose. Traditionally, the biological radiation dose from BNCT is calculated as a sum of the dose components after multiplying each component with a constant relative biological effectiveness (RBE) factor [1]. An alternative biological dose calculation method, the photon iso-effective dose formalism, considers the dose rate, the cumulative dose per fraction, and synergistic interactions between the radiation dose components [2,3].

When head and neck cancer (H&N) is treated with boronophenylalanine (BPA)-mediated BNCT, the highest normal tissue doses often accumulate in the buccal mucosa as the mucosal membranes take up BPA approximately twice as much as what is present in the blood at the time of neutron irradiation. In addition, mucosal membranes are radiosensitive, thus the absorbed dose in the mucosal membranes often becomes the dose-limiting factor.

Our previous study suggested that the photon iso-effective dose model predicts mucosal membrane toxicity from BNCT more reliably than the traditional RBE model or the physical absorbed doses. In this study we investigated the dose and other clinical factors associated with severe oral mucositis in a larger series of patients with H&N cancer. The factors associated with mucosal

toxicity are of special interest as clinical trials are being planned to be started for recurrent H&N cancer patients at our institute with new accelerator-based BNCT in 2019.

Data from 92 patients with recurrent inoperable H&N carcinoma treated with BNCT in Finland from 2003 to 2011 were analyzed. The photon iso-effective dose formalism and the traditional RBE model were used to calculate the biological dose to the mucosal membranes. Since the nitrogen concentration of the oral mucosa is unknown, the dose was calculated using three different nitrogen concentrations 3.4%, 4.2%, and 6.8% as in the muscle, skin, and melanoma tissue, respectively [4, 5]. The maximum mucosal membrane dose was compared with the clinically observed mucositis at 2 to 4 weeks after the date of BNCT. The effects of chemotherapy, tumor site, tumor histology, patient age, and gender on mucositis were assessed using a binary logistic regression analysis.

Severe mucositis (CTCAE grade 3) was observed in 40 (43%) out of the 92 patients. The maximum mucosa RBE doses were 16-43% lower than the corresponding photon iso-effective doses, the median RBE doses remaining below the reported mucosa tolerance dose limit of 15 Gy for a single radiotherapy fraction. All median photon iso-effective mucosa doses were higher than the 15 Gy tolerance dose. The other factors evaluated were not predictive for mucositis.

The results suggest that the photon iso-effective dose model predicts mucosal membrane dose from BNCT more reliably than the traditional RBE model. A dose volume distribution in the oral cavity may be needed to improve the prediction of the mucosal toxicity.

References

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