Prophylactic Administration of Amifostine Protects Vessel Thickness and Luminal Diameter in the Setting of Irradiation

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Introduction: Although often beneficial in the treatment of head and neck cancer (HNC), radiation therapy (XRT) leads to the depletion of vascular supply and circulation. Specifically, previous studies have demonstrated the depletion of vessel volume fraction (VVF) and vessel thickness (VT) associated with XRT. Amifostine (AMF) provides protection from the detrimental effects of radiation damage, allowing for reliable post-irradiation fracture healing in the murine mandible. The purpose of this study is to investigate the prophylactic ability of AMF to protect the vascular network in an irradiated field.

Materials and Methods: Sprague-Dawley rats (n=17) were divided into 3 groups: control (C, n=5), radiated (XRT, n=7), and radiated mandibles treated with Amifostine (AMF XRT, n=5). Both groups receiving radiation underwent a previously established, human equivalent dose of XRT totaling 35 Gray, equally fractionated over 5 days. The AMF XRT group received a weight dependent (0.5mg AMF/5g body weight) subcutaneous injection of AMF 45 minutes prior to XRT. Following a 56-day recovery period, mandibles were perfused, dissected, and imaged with μCT. ANOVA was used for comparisons between groups and $p < 0.05$ was considered statistically significant.

Results: Stereologic analysis demonstrated a significant and quantifiable restoration of VT in AMF treated mandibles as compared to those treated with radiation alone (0.061±.011mm versus 0.042±0.004mm, p=0.027). Interestingly, further analysis demonstrated no significant difference in VT between control mandibles and those treated with AMF (0.067±0.016mm versus 0.061±0.011mm, p=0.633) (Figure 1). AMF treatment also showed an increase in VVF, however those results were not statistically significant from VVF values demonstrated by the XRT group (Figure 2).

Conclusions: Our data support the contention that AMF therapy acts prophylactically to protect vessel thickness, as AMF-treated mandibles demonstrate VT levels that are not statistically different from controls in the setting of irradiation. Based on these findings, we support the continued investigation of this treatment paradigm in its potential translation for the prevention of vascular depletion after radiotherapy.

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