Radiation treatment in pediatric patients is a well-established adjunct to surgical excision for soft tissue sarcomas and may be used as an alternative to surgery for Ewing’s sarcoma of bone. Radiotherapy in the growing child, however, deleteriously affects growth plate function, often resulting in permanent limb shortening and deformity. Fractionation of a 12.5 Gy radiotherapy dose has been previously shown in Sprague-Dawley rats to reduce but not completely eliminate these damaging effects. The radioprotectant free-radical scavenger drug amifostine (S-2-[3-aminopropylamino]-ethylphosphorothioic acid), administered just prior to radiotherapy, has been demonstrated to protect normal cells from ionizing radiation to a greater extent than tumor cells. Much is known regarding its effects on various soft tissues, bone marrow hematopoietic stem cells, and splenic T-lymphocytes, but not previously to our knowledge on growing bone.

**Introduction**: Radiation treatment in pediatric patients is a well-established adjunct to surgical excision for soft tissue sarcomas and may be used as an alternative to surgery for Ewing’s sarcoma of bone. Radiotherapy in the growing child, however, deleteriously affects growth plate function, often resulting in permanent limb shortening and deformity. Fractionation of a 12.5 Gy radiotherapy dose has been previously shown in Sprague-Dawley rats to reduce but not completely eliminate these damaging effects. The radioprotectant free-radical scavenger drug amifostine (S-2-[3-aminopropylamino]-ethylphosphorothioic acid), administered just prior to radiotherapy, has been demonstrated to protect normal cells from ionizing radiation to a greater extent than tumor cells. Much is known regarding its effects on various soft tissues, bone marrow hematopoietic stem cells, and splenic T-lymphocytes, but not previously to our knowledge on growing bone.

**Methods**: Forty-two weanling four week old Sprague-Dawley rats were randomized into six study groups of six animals each and a control group of six animals. In all of the study groups, the distal femur and proximal tibia in the right leg of each animal was exposed to therapeutic x-irradiation (17.5 Gy) with the contralateral left leg as internal control. The radiotherapeutic dose was administered as a single dose or in three or five equal fractions. In three of the treatment groups, the animals received amifostine (AMF) 100 mg/kg intraperitoneally twenty minutes prior to each radiation exposure. Study groups were organized as follows: Group R1: 6 animals 17.5 Gy (1 fraction) 0 mg/kg AMF
Group A1: 6 animals 17.5 Gy (1 fraction) 100 mg/kg AMF
Group R3: 6 animals 17.5 Gy (3 fractions) 0 mg/kg AMF
Group R5: 6 animals 17.5 Gy (5 fractions) 0 mg/kg AMF
Group A3: 6 animals 17.5 Gy (3 fractions) 100 mg/kg AMF
Group A5: 6 animals 17.5 Gy (5 fractions) 100 mg/kg AMF

The control group received neither radiation or amifostine. At six weeks following irradiation, the limbs were harvested and femoral and tibial bone lengths were measured in treated and untreated legs and compared to baseline measurements.

**Results**: Concordant with previous reports in the literature, the single radiation dose of 17.5 Gy reduced net growth in overall limb length by a mean 58.3% (range 52-66%, SD 4.6%) in the treated leg [Group R1]. Statistically significant (p<0.01) reductions were documented compared to the single dose radiation group [Group R1] and to the single dose radiation and amifostine group [Group A1] for groups R3, R5, A3, and A5, but there was no statistically significant difference shown between groups R3, R5, A3, and A5.

**Discussion**: The radioprotectant drug amifostine has a statistically significant independent effect on reducing growth arrest from a single 17.5 Gy radiation dose fraction in the weanling Sprague-Dawley rat. Fractionation of the 17.5 Gy dose into three and five fractions reduces growth arrest to an even greater degree than amifostine alone. However, the question of whether there is an additional added benefit of amifostine to fractionated radiation doses in this model remains unanswered. While small absolute mean improvements in growth lost were observed with the combination of amifostine to fractionated radiotherapy doses, these differences were statistically insignificant compared to the effects of fractionation alone.

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