Evaluation of the Combined Effects of Radiation Therapy and Either Pamidronate or Zoledronate on Canine Osteosarcoma Cells. Katie Hoddinott¹, Michelle L. Oblak¹, Geoff E. Wood², Sarah E. Boston³, Anthony J. Mutsaers¹,⁴.
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Introduction: Canine osteosarcoma (OSA) is a devastating disease, with an overall poor prognosis. Radiation therapy and bisphosphonates are currently used in combination for palliative treatment, despite a paucity of literature to support their combined use. The objectives of this study were to assess the in vitro effects of radiation therapy and bisphosphonates on canine osteosarcoma cells alone and in combination.

Materials and Methods: Canine OSA cell lines D17 and Dharma were treated with radiation, pamidronate (PAM) and zoledronate (ZOL) alone and in combination. The effects of these treatments were assessed using clonogenic survival and cell viability assays. A general linear mixed model (2-way ANOVA) was used to test the fixed effects of PAM or ZOL and RT and their interactions. Effects of the combination of PAM or ZOL and RT were assessed using a combination index method. Only combinations resulting in <50% cell growth inhibition were included for assessment to allow for potentially equal contributions from PAM or ZOL and RT.

Results: Dose dependent decreases in clonogenic survival and cell viability were observed for both radiation and bisphosphonate treatment. Statistically significant differences were only identified during the clonogenic survival experiments. Combination index assays for PAM and ZOL identified antagonism for all dose combinations of PAM or ZOL and RT assessed for both the D17 and Dharma cell lines.

Conclusions: Based on the combination index, there appears to be an antagonistic relationship between bisphosphonates and RT in vitro. Further clinical investigation of this combination for the palliative treatment of canine OSA is warranted.