Introduction: The purpose of this study was to investigate the use of IONP in combination with fractionated ionizing radiation, with and without magnetically induced mild localized hyperthermia, to enhance conventional fractionated radiation. It has been shown that ionizing radiation combined with hyperthermia can result in a greater therapeutic ratio than radiation or hyperthermia alone. Recent work has also shown that iron oxide nanoparticles may have potential as radiation sensitizers. IONP are additionally interesting because when IONP are exposed to an alternating magnetic field (AMF), a localized hyperthermia can be induced. In 1977 Adams et al. published a study which showed enhanced radiation-induced lymphocyte toxicity caused by the iodine (contrast agent) in angiography patients. Since then, the body of materials shown to modify the toxicity of radiation has grown, including not only high-Z materials, but also nanoparticles, which also may be carriers for pharmalogic agents. These materials may be the reverse radiation resistance, enhance sensitivity, or provide radioprotection of normal tissue. Though largely unexplored, a proposed mechanism for radiation sensitization by IONP includes the increase in production of reactive oxygen species (ROS) when ionizing radiation interacts with IONP. Physiologically meaningful changes due to the combination of mild heat and radiation have been demonstrated in numerous cancer studies using a wide variety of heating techniques (microwave, ultrasound, perfusion and regional/whole body). Previous studies, have shown that raising the temperature of tumors with IONP-mediated hyperthermia can potentiate the efficacy of ionizing radiation. However, these studies have not considered the interaction of the IONP themselves with the ionizing radiation or as part of a fractionated treatment plan.

Methods: Murine mammary adenocarcinoma (MTGB) tumors were grown in C3H mice. Six groups were utilized, including two control groups: IONP alone and phosphate buffered saline (PBS) injection alone. Tumors treated with radiation (5 X 3 Gy) were compared to those receiving the same radiation dose with intratumoral injections of IONP (7.5 mg Fe/g tumor). Additional treatment groups included IONP induced hyperthermia (2 X 43°C for 30 minutes) with and without radiation. Treatment outcome was measured by tumor regrowth.

Conclusions: This study indicates that IONP may significantly improve the therapeutic efficacy of fractionated ionizing radiation in a clinical setting as a monotherapy, or in an adjuvant approach with mild AMF-induced hyperthermia. The mechanism of sensitization is not yet determined, but is likely a physical or chemical (ROS) effect, which is improved by the induced mild hyperthermia.

Citations