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# "SYSTEMIC RADIOTHERAPY FOR METASTATIC BREAST CANCER TO BONE WITH Ra-223"

by

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Wednesday, December 30th, 2020
11:00 A.M.

Meeting link:
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Meeting number: 120 173 9299
Password: 5c27dbb2c9

# ABSTRACT

Breast cancer cells disseminate to bone, forming skeletal metastases that greatly lower the life expectancy of patients. Skeletal metastases can be treated with $^{223}RaCl_2$, an alpha particle emitting radiopharmaceutical that localizes to bone surfaces. The efficacy of $^{223}RaCl_2$ has been attributed to direct irradiation of tumor cells and bone osteoblast and osteoclast cells. However, the limited range that the alpha particles can travel (< 100 µm) and the prevalence of tumor cells in the marrow and beyond the range of the alpha particles, suggests that radiation-induced bystander effects may also be responsible for the therapeutic efficacy of $^{223}RaCl_2$. Bystander effects induced by alpha particles have been studied extensively in vitro with limited in vivo experimentation. But it is unknown if radiation-induced bystander effects play a role in the therapeutic efficacy of $^{223}RaCl_2$. Furthermore, osteocytes, the master regulators of bone homeostasis, have an emerging role in bone related diseases, yet the effects of $^{223}Ra$ and alpha particles on bone cell osteocytes are also not well characterized. I therefore hypothesized that $^{223}Ra$ inhibits proliferation of disseminated breast cancer cells in the bone marrow through direct irradiation and radiation-induced bystander effects. This hypothesis was tested in a mouse tumor xenograft model in the tibial marrow. To examine whether bystander effects inhibit proliferation in vivo, $^{223}RaCl_2$ must be administered before human breast cancer cells are inoculated and the inoculation must take place after $^{223}RaCl_2$ clears. Intratibially inoculated human breast cancer cells localized within and beyond the range of alpha particles emitted by $^{223}Ra$ injected mice. Bystander breast cancer cells, in $^{223}Ra$ injected mice, experienced increased DNA damage and apoptosis. The extent of DNA damage showed that bystander breast cancer cells experienced prolonged low and medium type DNA damage compared to the high, clustered damage shown in osteocytes and breast cancer cells within range of the alpha particles. Additional support for the importance of radiation-induced bystander effects was found when the spatial and density properties of inoculated human breast cancer cells were calculated and used to successfully simulate bystander effect dependent growth delays. Future work may examine intercellular communication between osteocytes and breast cancer cells as a mechanism for radiation-induced bystander effects. Given their potential importance for treating disseminated tumor cells, radiation-induced bystander effects may suggest use of systemic radiotherapy with $^{223}Ra$ for some early-stage breast cancer patients.