Released Tumor DNA (rtDNA) as a Biomarker of Radiation-Induced Tumor Killing in Metastatic Spine Disease

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Purpose
Though surgery has been the staple of treatment for spine metastasis, advances in stereotactic radiation mean that many patients are now treated focused radiation as either primary or adjuvant/neoadjuvant therapy. Given this increase in the use of radiation, it is imperative that the treatment team be able to assess the relative radiosensitivity of the patient’s lesion. Currently, the radiosensitivity is judged by primary pathology, yet it has been shown that pathology is only moderately predictive of radiation response. Therefore, it is clear that a better means of assessing tumor radiosensitivity is an unmet medical need in the field of spinal oncology. Ideally, such a test would be non-invasive and would also allow for real-time monitoring of tumor response to radiation. Therefore, we propose to study changes in ctDNA titers as a marker of response to radiation in a rat model of spinal metastasis.

Hypothesis
We hypothesize that changes in ctDNA titers will accurately demonstrate the degree of radiation-induced tumor killing in this rat model of metastatic spine disease, with radiosensitive (breast, endometrial) cell-lines having greater post-radiation decreases in ctDNA compared to radioresistant cell-lines (lung, colorectal). Furthermore, we hypothesize that these radiation-induced changes will correlate to the degree of tumor necrosis on pathological analysis.

Method of Research
We will use both radiation sensitive and radiation resistant cell lines to generate small tumor masses to be implanted into the lumbar spines of athymic rats. After allowing time for growth of the lumbar lesion, the animals will be irradiated and changes in ctDNA will be tracked across the radiation treatment regimen. ctDNA levels will be correlated with tumor size at 1-week and 2-weeks following radiation and with the extent of necrosis seen on histology. If shown to be an effective fiduciary of radiation-induced tumor necrosis, ctDNA could be routinely used as a marker of radiation response in human patients.

Expected Results
We expect that the radiosensitive cell-lines will display steeper “drop-offs” in the amount of ctDNA after radiation, which will correlate with tumor size on imaging and degree of necrosis on pathologic analysis. We further expect that we will identify the optimal time window to measure ctDNA titers after radiation to accurately indicate final tumor killing.