This work in its simplest form is evaluating whether two therapies (radiotherapy and chemotherapy), that are almost always administered to women with brain metastases of breast cancer, can be given in a coordinated manner to improve efficacy.

Current therapies for brain metastases of breast cancer consist of surgery, systemic chemotherapy, and radiation therapy. Unfortunately, there is limited long-term survival benefit of all therapies, leaving patients with significant morbidity and mortality. A major limitation of the effectiveness of chemotherapy for brain metastases is restriction of drug accumulation by the blood-brain barrier. In this preclinical work we set out to determine if standard radiation therapy protocols compromise the blood-brain barrier resulting in increased drug accumulation in brain metastases of breast cancer.

We have shown in this work that:

* Permeability of the blood-brain barrier was increased 12 hours after irradiation.
* Efflux transport at the blood-brain barrier was reduced at 12 hours after irradiation as well.
* Radiation induced changes at the blood-brain barrier were dependent on an intact immune system.
* The molecular size of molecules that could penetrate the disrupted blood-brain barrier were size dependent (smaller >larger)
* TNF-α concentrations increased in serum immediately and remained til approximately 12 h post-radiation.
* Chemotherapeutics administered at 12hours post irradiation resulted in decreased tumor burden but not changes in survival.

To date radiation and chemotherapy are often seen as distinct and separate. The impact of the work if translated will improve the amount of chemotherapeutic getting to the brain metastases which should improve tumor kill, reduce local failure rates, and potentially distal failure rates as well. Moreover, it could revolutionize the current standard of care as it will promote interdisciplinary treatments.