Dr. Emerson Lim (Mentor: Dr. Dawn Hershman)

Abstract:
In early stage breast cancers, there are a number of benefits for women who receive chemotherapy before undergoing surgery. It may shrink the primary tumor and allow for breast conservation, allow doctors to assess the responsiveness of the tumor to chemotherapy, and provide information on prognosis. The Residual Cancer Burden (RCB) score is an indicator of the amount of tumor remaining at the time of surgery. A lower score indicates fewer remaining cancer cells and has been shown to correlate with improved survival. However, those women who do not respond to chemotherapy are exposed to months of ineffective treatment and unnecessary side effects. A method to assess early tumor response would provide physicians with the ability to make evidence-based changes in treatment and thus reduce the number of women receiving ineffective chemotherapy and possibly improve tumor responses and survival. Currently, methods of detecting tumor response to chemotherapy are either based on measuring changes in tumor size and are not sensitive to early changes, or expose women to ionizing radiation and radioactive agents. Diffuse optical tomography (DOT) is a non-invasive, three dimensional imaging technique that can quickly and inexpensively measure concentrations of oxygenated and deoxygenated blood, water, and fat without the use of radiation or injected radioactive dyes. It consequently provides information on the vascular composition of tumors. Ongoing studies show that changes in tumor vascularity occur before measurable changes in tumor size. Thus, DOT can potentially be used to evaluate tumor response to chemotherapy and may do so earlier than previously possible. Our hypothesis is that early changes in DOT measurements will predict the pathologic response to chemotherapy as measured by the RCB score and may do so better than current imaging (mammogram or magnetic resonance imaging – MRI). We will conduct a pilot study of 20 women with newly diagnosed breast cancer receiving standard chemotherapy with 12 cycles of paclitaxel, followed by 4 cycles of doxorubicin with cyclophosphamide (AC). Subjects will have mammograms, MRIs and DOT measurements at the start and end of chemotherapy. Additional DOT measurements will be performed two weeks after starting paclitaxel, after the completion of paclitaxel, and two weeks after starting AC, and an additional mammogram with be done at the midpoint of treatment (after completing paclitaxel). We will compare changes in DOT measurements at each of these time intervals and see if there is a correlation between these changes and the RCB score. We will also compare changes over time in the mammograms and MRIs and see if there is a correlation between these changes and the RCB score. By doing this, we will be able to see which imaging method has a better correlation with the RCB score. We also plan to compare changes in DOT measurements to other prognostic indicators. Ki-67 is a marker of proliferating cells, and microvessel density is a measurement of the vascularity of tumors as seen under the microscope. A decrease in both these measurements has been shown to correlate with improved survival. We plan to see if there is a correlation between changes in DOT measurements and changes in these prognostic indicators. This study is significant because it has the potential to give oncologists a tool that will allow them to tailor individualized treatments for women with breast cancer, depending on their response. It may even be used as a tool for future studies evaluating the efficacy of new drugs and may one day be used as a more sensitive tool to screen for breast cancer.