Specialty area: Clinical Cancer MRI: Case-Based
Speaker Name: Nola Hylton, PhD

Talk Title: ***Theranostics: Chemotherapy Response in Breast Cancer***

In the past two decades, there has been a shift in the clinical management of breast cancer to greater use of pre-operative or neoadjuvant chemotherapy (NACT). In clinical trials, while the administration of NACT showed no difference in disease-free or overall survival compared to traditional post-operative or adjuvant chemotherapy [1, 2], NACT not only enabled tumor downgrade for breast conservation surgery, it also provided means to evaluate the effectiveness of chemotherapy in patients. In the NACT setting, intact primary breast cancers treated with systemic therapy can be monitored by imaging. Breast cancer NACT presents a valuable opportunity to apply and refine imaging techniques to accelerate new drug development for breast cancer.

MRI of the breast is a sensitive method for assessing both tumor morphology and physiology. The most common MRI technique for functional assessment of breast tissue is based on DCE-MRI and involves serial acquisition of MR images before, and at multiple time points following intravenous injection of gadolinium contrast agent. DCE-MRI is the technique used today as the clinical standard for breast MRI. Clinical interpretation of breast MRI is primarily based on visual interpretation according to the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) system for MRI[3]. For more quantitative assessment, DCE-MRI data can be fit to an appropriate pharmacokinetic model, allowing *in vivo* measurement of physiological parameters related to tissue perfusion, microvascular permeability, and extracellular/extravascular volume fraction. These measurements can be used to characterize tumor neovascularization and can detect changes in tumor vascular properties resulting from treatment. Numerous studies using DCE-MRI have found that changes in kinetic parameters measured early in treatment are associated with response[4-6]. Most of these studies were done in small cohorts of patients using approaches that differed in imaging acquisition protocol, variables measured, timing of early response measurement relative to treatment, and response endpoints. Together they suggest that DCE-MRI may offer a sensitive and quantitative method for assessing response to treatment.

Diffusion-weighted imaging (DWI) is an alternative MRI technique that can be used to measure the mobility of water molecules *in vivo*. DWI is sensitive to tissue characteristics such as cell density, membrane permeability, and microstructure. As such, DWI provides different but complementary biologic information about tumors and their response to treatment in comparison to DCE-MRI. With DWI, the MRI signal is sensitized to water diffusion using varying levels of a magnetic field gradient. DWI studies of the breast have shown decreased diffusivity in malignant breast lesions relative to normal breast tissue, primarily attributed to the increased cell density associated with solid tumors, including breast tumors[7-9]. DWI has also been used to evaluate response to treatment. Separate studies have found that the apparent diffusion coefficient (ADC) in tumors measured from DW images, increases in response to treatment earlier than detectable changes in tumor size or vascularity measured by DCE-MRI [10-13]. The increase in ADC is thought to be due to cell death and necrosis, and may be a valuable early indicator of treatment efficacy that can precede measurable changes in tumor size. Indeed, a growing number of studies have found ADC measures to be predictive of breast cancer treatment outcome[12, 14-20]. DWI has the attractive feature of being a non-contrast technique that can be added to the MRI exam with little time or cost penalty, while providing information distinct from DCE-MRI.

This talk will discuss the emerging applications of functional MRI techniques for assessing breast tumor response to neoadjuvant treatment and the application of MRI metrics as biomarkers of response and risk-of-recurrence. Current findings from the I-SPY (ACRIN 6657/CALGB 150007) trial, a multi-center study integrating biomarkers and imaging to maximize effectiveness of neoadjuvant treatment for patients with locally-advanced breast cancer will be presented. The experience implementing standardized MRI protocols in the multi-center setting will be discussed. This course is intended for imaging scientists and clinical researchers involved in the diagnosis and treatment of breast cancer. It is expected that the audience will gain knowledge leading to the appropriate application of breast MRI techniques in the neoadjuvant treatment setting.

Learning Objectives:

- Evaluate and compare functional MRI techniques for evaluating breast cancer
- Apply quantitative MRI approaches to measure breast tumor response to neoadjuvant treatment
- Critically assess the role of breast MRI for measuring neoadjuvant treatment response and its potential as a predictive biomarker

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