Systematic Analysis of Breast Neoplasia with Lightsheet Microscopy

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Breast cancer is a leading cause of cancer death among women. The current system for diagnosing breast cancer based on the pathological analysis of microscopic images has changed little over the past several decades. Recently, a new state-of-the-art microscopy platform (fluorescent lightsheet microscopy) has been developed, which enables the rapid acquisition of high-resolution three-dimensional (3D) images directly from tissue samples up to several millimeters in thickness. The primary aim of our project is to determine the ability to perform fluorescent lightsheet microscopy directly on archival patient tissue samples and to use the method to identify 3D morphological hallmarks of breast carcinogenesis. To achieve these goals, we will perform lightsheet microscopic analysis on a total of 175 breast tissue samples, including: normal breast, usual ductal hyperplasia, atypical ductal hyperplasia, ductal carcinoma in situ, and invasive ductal carcinoma. We will develop and implement machine learning-based image analysis procedures to measure quantitative 3D morphologic phenotypes from the images, and we will perform statistical analyses to identify lightsheet microscopy-derived features significantly associated with progression of breast neoplasia from normal breast to intra-ductal proliferative lesions to invasive breast cancer. If successful, this project will lay the ground work for future larger scale studies to use lightsheet microscopy to identify novel breast tissue-based 3D quantitative morphologic phenotypes to predict future breast cancer risk (in the setting of benign and pre-invasive breast lesions) and to predict patient survival (in the setting of invasive breast cancer).