MULTIPARAMETER OPTICAL IMAGING OF THE BREAST TUMOR MICROENVIRONMENT

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KEY WORDS: Multiphoton microscopy, second harmonic generation imaging, fluorescence lifetime imaging, intravital imaging, tumor microenvironment, collagen, tumor-associated collagen signatures.

1. IMAGING THE TUMOR MICROENVIRONMENT

Increased breast density is correlated to a 4-6 fold increased risk in developing breast cancer, yet the physical and molecular mechanisms are poorly understood [1]. We have found that alignment changes in the collagen matrix that contribute to this density can be specifically correlated to poor clinical prognosis [2]. These changes in collagen alignment can be uniquely probed with advanced optical imaging techniques such as Second Harmonic Generation (SHG) and Multiphoton Microscopy (MPM) that can non-invasively examine collagen and cells respectively in physiologically relevant in vitro and in vivo cancer models. Cellular metabolism is known to be a key factor in cancer cell progression [3]. To study metabolism, Fluorescence Lifetime Imaging Microscopy (FLIM) [4] can be used to examine NADH and FAD, intermediate metabolites with fluorescence properties.

2. MPM, SHG, AND FLIM IMAGING IN VITRO AND IN VIVO

Advanced imaging techniques such as MPM, SHG, and FLIM are ideal for examining the cellular microenvironment and investigating the connection between cancer cell progression and key factors in the microenvironment. MPM is a laser-scanning microscopy technique that uses nonlinear excitation to non-invasively image a narrowly defined optical plane deep within intact tissues. Spatially: MPM has resolution of less than a micron. Temporally: resolution is on the order of an image per second. Physically, MPM systems are capable of collecting SHG signals which are a nonlinear optical property of collagen. Chemically, MPM is compatible with spectral and lifetime approaches that can provide a quantitative readout of environmental changes such as pH, hydrophobic changes, and protein interactions. Unlike invasive biochemical methods, FLIM can be used in vivo to detect local changes such as NADH binding. Together these techniques are being used to examine the invasion and progression of breast cancer in the context of the chemical and physical microenvironment. These techniques are compatible with examining not only biopsied human and animal tissue but with in vivo mouse models through advanced intravital methods.