Experimental, computational, and analytical techniques for diagnosing breast cancer using optical spectroscopy

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This dissertation presents the results of an investigation into experimental, computational, and analytical methodologies for diagnosing breast cancer using fluorescence and diffuse reflectance spectroscopy. First, the optimal experimental methodology for tissue biopsy studies was determined using an animal study. It was found that the use of freshly excised tissue samples preserved the original spectral line shape and magnitude of the fluorescence and diffuse reflectance.

Having established the optimal experimental methodology, a clinical study investigating the use of fluorescence and diffuse reflectance spectroscopy for the diagnosis of breast cancer was undertaken. In addition, Monte Carlo-based models of diffuse reflectance and fluorescence were developed and validated to interpret these data. These models enable the extraction of physically meaningful information from the measured spectra, including absorber concentrations, and scattering and intrinsic fluorescence properties. The model was applied to the measured spectra, and using a support vector machine classification algorithm based on physical features extracted from the diffuse reflectance spectra, it was found that breast cancer could be diagnosed with a cross-validated sensitivity and specificity of 82% and 92%, respectively, which are substantially better than that obtained using a conventional, empirical algorithm. It was found that malignant tissues had lower hemoglobin oxygen saturation, were more scattering, and had lower beta-carotene concentration, relative to the non-malignant tissues. It was also found that the fluorescence model could successfully extract the intrinsic fluorescence line shape from tissue samples.

One limitation of the previous study is that *a priori* knowledge of the tissue's absorbers and scatterers is required. To address this limitation, and to improve upon the method with which fiber optic probes are designed, an alternate approach was developed. This method used a genetic optimization algorithm to design a fiber optic probe that was optimally suited for the extraction of optical properties from tissue. The optical properties were extracted using a neural network, which relates the measured diffuse reflectance to the absorption and scattering coefficients. It was found that using this approach, the absorption and reduced scattering coefficients could be extracted with RMS errors of 0.6 and 0.5 cm^{-1} for the absorption and reduced scattering coefficients, respectively.