PhD DISSERTATION DEFENSE

Implementation of 3D SHG Imaging Microscopy for Tissue Characterization and Disease Diagnostics: Experiment and Simulations

By

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Abstract:

This work encompasses the integrated use of 3D Second Harmonic Generation (SHG) imaging microcopy, Monte Carlo simulations and novel heuristic and phenomenological models to quantifiably characterize biological tissues and develop diagnostics for diseased states. A novel tissue characterization technique is developed which utilizes experimental data as inputs to Monte Carlo based models to decouple laser tissue interactions and link changes in phenotype between healthy and diseased tissue to SHG descriptors. To accomplish this, thin tissue biopsies from diseased and control tissue are used to generate 3D SHG images and used for experiments designed to estimate bulk optical parameters (through inverse Monte Carlo techniques). The complete experimental data set is used in conjunction with Monte Carlo simulations and phenomenological and physical models to decouple photon-tissue interactions. Utilizing this approach, SHG creation attributes including efficiency and initial directivity are obtained which when combined with experimental data establish a comparative diagnostic suitable to quantifiably differentiate normal from diseased tissues. The application of this technique leads to a quantifiable diagnostic linking disease inspired alterations to the extracellualr matrix (ECM), bulk optical parameters, SGH creation attributes and 3D-SHG images, applicable for disease staging. Two collagen based tissue diseases are investigated in this work, Osteogenesis Imperfecta in mice and Ovarian Cancer in humans, quantifiable diagnostics are developed for both cases. In addition to disease diagnostics, this metric is applicable to investigate a wide range of laser tissue interactions in SHG producing media including the polarization properties of biological tissues and optical clearing.