SHG Microscopy and Scattering Spectroscopy to Probe Extracellular Matrix Alterations in Ovarian Cancer

Paul J. Campagnola*, Karissa Tilbury, Kirby Campbell, Chi-Hsiang Lien, Gunnsteinn Hall
University of Wisconsin-Madison, Madison, WI 53706

We show that characteristic changes in the architecture of collagen (concentration, fibril/fiber structure) and isoform distribution in ovarian cancer can be probed quantitatively by several metrics based on Second Harmonic Generation (SHG) imaging microscopy. Using forward-backward (F/B) directional measurements and polarization anisotropy, we found that the stromal collagen is extensively remodeled with the synthesis of new collagen. To better understand this process, we have utilized both in vitro models and human tissues. 3D F/B measurements were utilized to measure changes in the fibril/fiber assembly in self-assembled gel models of the stroma, which consisted of mixtures of type I (Col I) and type III (Col III) collagen, where up-regulation of the latter has been implicated in ovarian cancer. Increasing concentration of Col III resulted in smaller fibers and weaker SHG intensity, corresponding to decreased organization. The F/B concurrently becomes smaller, consistent with the morphological changes. These results are further consistent with observations of Col III having faster turnover and defective crosslinking in ovarian cancer. We also use polarization resolved SHG to successfully differentiate gels of differing Col III concentration, where the premise is that Col III has a different α-helical pitch angle than Col I. Lastly, we have measured the spectral dependence of the reduced scattering coefficient in normal and malignant ovaries and found the respective spectral slopes are consistent with the changes seen by SHG imaging. Taken together, changes in collagen may be an important biomarker in ovarian cancer that can be measured by SHG directional measurements and polarization analysis.