PROBING ATHEROSCLEROTIC PLAQUE BURDEN USING MULTI-MODAL NONLINEAR OPTICAL MICROSCOPY

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KEYWORDS: Nonlinear optical microscopy; coherent anti-Stokes Raman scattering; two photon excited fluorescence; second harmonic generation; atherosclerosis; plaque classification

Atherosclerosis is a chronic progressive disease associated with plaque accumulation in the arteries.[1] Conventional clinical imaging modalities such as x-ray fluorescence angiography, multi-detector computed tomography (MDCT) and intravascular ultrasound (IVUS) are not optimized for differentiating atherosclerotic plaque burden due to low spatial resolution, radiation toxicity or low specificity and sensitivity towards early lesions. Recent efforts made in the development of MDCT, IVUS and OCT to differentiate plaque types underlines the need for both morphological and compositional information for understanding plaque development, plaque burden and predicting the risk of plaque rupture or erosion. Nonlinear optical microscopy (NLOM) provides a minimally invasive, label-free method for fast biochemical imaging at sub-cellular resolution.[2] NLOM with its intrinsic 3-D optical sectioning capability can interrogate the morphology and biochemical composition at or near the surface of intact tissue. In this study, we used a single-laser, femtosecond-CARS based nonlinear optical microscope to simultaneously image extracellular structural proteins and lipid-rich structures within intact aortic tissue obtained from myocardial infarction-prone rabbits. Clear differences in the NLOM images were observed between healthy arterial tissue and regions dominated by atherosclerotic lesions.(Figure) We also developed an optical parameter for classifying atherosclerotic plaque burden within the vessel using the measured NLOM signals. This parameter is calculated from the individual CARS, SHG and TPEF signal intensities and intensity differences between these imaging channels. Using this parameter we were able to distinguish plaques relative to the age of the rabbit. Complementary OCT B-scan images and histology sections of the same measured tissue area are compared with the NLOM images.