Acoustic Characterization and Nonlinear Imaging of Ultrasound Contrast Agents for Intravascular Assessment of Atherosclerosis

Himanshu Shekhar

Supervised by
Professor Marvin Doyley

Cardiovascular disease kills more Americans than all cancers combined, and is estimated to cost over 300 billion dollars annually. The majority of these deaths are caused when the rupture of atherosclerotic plaques triggers life-threatening conditions such as myocardial infarction and stroke. Although the histopathological features of life-threatening plaques are known, detecting them in vivo is challenging. The abnormal proliferation of the adventitial vasa vasorum, the microvessels that nourish arterial walls — may destabilize atherosclerotic plaques. Therefore, visualizing the vasa vasorum could help assess atherosclerotic plaques. Contrast-enhanced ultrasound can characterize the neovascular vasa vasorum in atherosclerotic arteries. However, the translation of vasa vasorum imaging to the clinic is hampered by the absence of techniques capable of reliably detecting microbubble contrast agents. The goal of the research reported in this thesis is to develop methods for the intravascular detection of the vasa vasorum. To achieve this goal, we conducted physical characterization and imaging studies with Targestar-P®a commercial contrast agent. Specifically, we 1) investigated the impact of the size distribution of the agent on its nonlinear response; 2) discovered that temporal changes in the agent can be harnessed to xii enhance nonlinear emissions; 3) demonstrated using numerical simulations and acoustic measurements that chirp-coded pulsing can substantially enhance the nonlinear response of microbubbles; and 4) developed a prototype intravascular ultrasound system for vasa vasorum imaging. We validated the vasa vasorum imaging system by conducting experiments with hydrogel flow phantoms. Further, we compared the performance achievable with this system in subharmonic and ultraharmonic imaging modes. The findings reported in this thesis could accelerate the development of efficacious contrast agents for intravascular ultrasound imaging. The vasa vasorum imaging system developed in this work can be useful in preclinical research and clinical imaging — for improving our understanding of the pathophysiology of atherosclerosis, evaluating new therapies, and assessing cardiovascular risk.