

ABSTRACT

The organization of fibrillar collagen changes over the course of various cancers, heart diseases, and other pathologies. Imaging these changes can provide physicians knowledge on how a disease may progress or react to treatment. However, it is often difficult to image these changes because current imaging tools either image collagen in high enough resolution to detect small microscale changes, or over large more macro regions of the disease, but cannot do both at the same time. This limits what changes can be used in the clinic and slows research into how collagen organization changes throughout a disease. There is a need for tools that can image across multiple spatial scales. This dissertation covers the development of instruments and computational methods to perform this multiscale imaging of collagen.

We have built two multiscale imaging systems. The first system combines four different imaging methods: Second Harmonic Generation, Optical Coherence Tomography; Ultrasound; and Enhanced Backscattering. This system acquires complementary information on collagen and surrounding biology across scales. The second system performs multiscale imaging using multi-resolution Mueller Matrix Polarimetry. This system speeds up multiscale imaging by allowing users to scan for regions of interest at low resolutions, and then to acquire high resolution images of the regions. In addition, we have developed computational methods to register and analyze the images from these two instruments. The registration includes a protocol, software, and a design for a fiducial phantom that can be seen with both optical and acoustic contrast. The analysis methods use the registration to make point-to-point comparisons between scales, allowing the direct comparison of quantitative variables.

Finally, we have validated these instruments and methods using mouse breast cancer models. The models were imaged in Ultrasound and Second Harmonic Generation to show how collagen density affects Ultrasound signal. In addition, the models are used to show that Mueller Matrix Polarimetry is correlated with collagen signal but can be confounded by imaging parameters such as tissue thickness or collagen type, and that further study is needed for its use as a collagen imaging tool.