**Abstract**

The most common causation of episodic stroke and cerebral ischemia is thought to be microemboli from carotid plaque. The bifurcation at the carotid bulb is a location prone to atherosclerosis. Some carotid plaques may be prone to rupture, which generates thrombi or plaque particulate that produce neural infarction. There is significant clinical need for a method to determine which plaques are vulnerable to disruption so that surgical intervention or other prophylactic actions can be taken. In this dissertation, advances in diagnostic ultrasound imaging tools to address this need are proposed.

Focus is placed primarily on non-invasive, *in vivo* strain imaging techniques to quantify plaque vulnerability. It is hypothesized that strain, mechanical distortion of tissue, is a direct measure of the tissue’s proximity to fatigue failure. A hierarchical block-matching motion tracking algorithm is developed with a number of novel features. Displacements are estimated with improved robustness and precision by advancing a Bayesian regularization algorithm and an unbiased subsample interpolation technique. A modified least-squares strain estimator is proposed to estimate strain images from a noisy displacement input while addressing the motion discontinuity at the wall-lumen boundary. Methods to track deformation over the cardiac cycle with a dynamic frame skip and use the result to accumulate strain on particles in a region of interest are explained. New methods to visualize and characterize the deformation measured with the full 2D strain tensor are presented.

Other diagnostic ultrasound techniques, high-frequency 3D ultrasound and transcranial Doppler ultrasound, which have the potential to support the strain findings are also studied. Experimental methods to characterize the high-frequency acoustic properties of a tissue-mimicking reference phantom are shown to be effective. The reference phantom is used to create 3D integrated backscatter coefficient images of excised carotid plaques. Transcranial Doppler is studied as method to detect intracranial microemboli and hemodynamics.

Initial results from patients imaged prior to endarterectomy suggest that strain imaging detects conditions that are traditionally considered high risk including soft plaque composition, unstable morphology, abnormal hemodynamics, and shear of plaque against tethering tissue that can be exacerbated by neoangiogenesis. Non-invasive carotid strain imaging is a potentially useful tool for detecting unstable carotid plaque.

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