Development of Laser Speckle Imaging: A Novel Technique for the Detection of Unstable Atherosclerotic Plaque

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Introduction: Ischemic cardiovascular disease, the leading cause of death worldwide is frequently preceded by the rupture of unstable atherosclerotic plaque. Laser Speckle Imaging (LSI), a new technique we are investigating, measures an index of plaque stability, related to plaque viscoelasticity, composition and morphology. Laser speckle is a granular pattern formed by the interference of coherent laser light scattered from tissue. The speckle pattern is dynamically modulated by Brownian motion of endogenous particles, which is governed by the viscoelasticity of tissue.

Innovation: We are developing LSI as a new technique for detection of unstable coronary plaques. This technology utilizes an inexpensive laser source, optical fiber bundles and CCD camera to evaluate the arterial wall. In this abstract, we describe our studies in the development of LSI, which will potentially yield a single platform to evaluate coronary plaque biomechanics, composition and structure in patients.

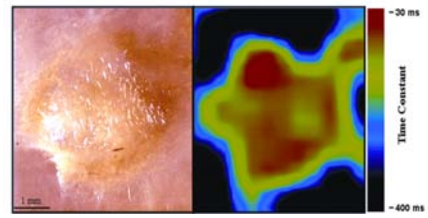

Figure 1: *Time constant distribution over a plaque compared with gross pathology*

<u>*1. Characterization of Atherosclerotic Plaque using LSI:*</u> We demonstrated the capability of LSI for differentiating atherosclerotic plaque type, and for assessing plaque morphology and composition by analyzing laser speckle patterns of 118 aortic specimens obtained from 14 human cadavers. The speckle decorrelation time constant, τ, inversely dependent on the rate of change of the speckle image was determined. The plaques were histologically classified into: necrotic core fibroatheroma (NCFA), pathological intimal thickening, non-necrotic fibroatheroma, intimal hyperplasia, fibrous plaque and fibrocalcific plaque.[1] The average speckle decorrelation time constant, $\bar{\tau}$, was computed for each plaque group. The results of the analysis of variance (ANOVA) and Dunnetts t-tests demonstrated highly significant differences in $\bar{\tau}$ between all the plaque groups. LSI demonstrated high diagnostic sensitivity (100%) and specificity (92%) for identifying unstable plaques. We also obtained time constant maps by scanning the illumination beam and computing τ at each beam location (Fig. 1), which may potentially aid in evaluating the spatial variation in plaque viscoelasticity to detect focal weak spots within the plaque.

<u>*2. Relationship between plaque composition and laser speckle decorrelation*</u>: The time constant, τ, showed high correlation with plaque collagen content *($R=0.73$; $p<0.0001$)* measured using polarized light microscopy of Picrosirius Red stained sections. Since fibrous cap thickness in necrotic core lesions is closely related to plaque collagen content, we similarly found a high correlation between τ and minimum cap thickness *($R=0.87$; $p<0.001$)*. Likewise, a strong negative correlation *($R=-0.81$; $p<0.0001$)* was demonstrated between τ and necrotic core area. These results demonstrate that LSI provides measurements related to plaque collagen content, fibrous cap thickness and necrotic core area.

<u>*3. Depth measurement using LSI*</u>: To obtain depth-resolved measurements we developed a method to combine spatio-temporal analysis of LSI with Diffusion theory and Monte Carlo models of light propagation, and have demonstrated this method to measure fibrous cap thickness in NCFA's (published in *JBO*).[36] Using this method, we demonstrated that LSI measurements of fibrous cap thickness were highly correlated with histological measurements (*$R=0.78$, $p<0.0001$*). Using these methods it may be possible to obtain depth-resolved viscoelasticity measurements using LSI.

<u>*4. Development of intracoronary LSI*</u>: We investigated the use of optical fiber bundles for intravascular LSI and evaluated the influence bundle motion over the cardiac cycle. Results of the two-way ANOVA tests showed no statistically significant difference in LSI measurements measured during the stationary and moving conditions of the fiber bundle ($p = 0.74$). These results show that optical fiber bundles reliably transmit laser speckle images even in the presence of motion during the cardiac cycle, providing a viable option to conduct intracoronary LSI.

Summary and Conclusions: Based on its ability to evaluate composition and morphology of atherosclerotic plaques, and its capability for intracoronary use, we anticipate LSI will prove highly useful in the identification of high-risk coronary lesions in patients.