**C. INNOVATION**

The major innovation in this proposal is that a low-cost ECG-based measure (*Dyx*) will provide a robust measure of autonomic regulation in disturbances of the neurocardiac axis. *Dyx* is an innovative, novel measure and has advantages to other HRV indices. We include the effect of time of day, unlike prior studies, as *Dyx* follows a circadian pattern. This tool, as it is ECG-based, will have a low barrier to wide-spread implementation. The data for this study can also be collected non-invasively, using the Biostamp patch, and the generation of the *Dyx* index can be performed by current commercial technology (HeartTrends algorithm). Overall, *Dyx* will serve as a better clinical tool for risk prediction for IHD as well as a better research tool in understanding autonomic mechanisms in IHD.

Autonomic dysfunction, measured by abnormal HRV, has not yet been used as a clinical tool to stratify patients at risk for developing IHD. This project not only studies a novel, non-linear HRV index *Dyx*, it advances the field by correlating HRV with coronary angiography findings. Currently, risk-stratification for IHD is based on traditional risk factors, such as the Framingham risk score, and other well-known contributors to cardiovascular disease. Although *Dyx* is an independent prognostic marker,1 we can evaluate its diagnostic utility in IHD. Other older HRV indices, such as geometric and frequency domain, are less prognostic for cardiovascular mortality and are not successful at predicting IHD.

Our approach also allows us to look at the effects of brain-correlates on autonomic function using a quantifiable measure. There are many studies that demonstrate psychological factors can increase cardiac risk,2,3 such as through ventricular arrhythmia, but there are no readily-available tools to study the underlying mechanism. *Dyx*, which has not yet been studied, shows promise as a more robust HRV index and future work will help to identify directionality and causality.