

Validation of a standardized protocol for early diagnosis of cardiovascular risk with intracoronary imaging and a whole-body in silico metabolic model

Project Lead: Prof. K. V. Venkatesh

Project Summary: Cardiovascular disease has emerged as the number one cause of morbidity and mortality in India, affecting even the younger population with a high fatality rate. India lost 9.2 million productive years and 1% of its GDP in 2000 due to ischemic heart disease (IHD). There exists no inexpensive early-stage diagnostic tool for cardiovascular diseases today. Current technologies rely on expensive and/or invasive techniques at late stages for assessing plaque buildup and cardiovascular risk. We propose a novel early-stage inexpensive screening and diagnostic tool for cardiovascular risk assessment. Using one's lifestyle data in combination with a specific biomarker expression level as inputs to our physiological whole-body metabolic model, we aim *to develop a robust standardized test to predict the current and future cardiovascular disease risk*. This will be validated by intracoronary imaging, which will correlate the model with the actual measurement of the atherosclerotic plaque burden.

Specific problem being addressed: Our group has developed a human whole-body physiology-rich metabolic model that captures the effect of lifestyle on metabolism. This model incorporates various metabolic and signaling pathways in various tissues and organs (brain, liver, kidney, adipose tissues, muscles) of the body, with blood being the common connecting medium. This is further connected via gastrointestinal absorption incorporating the effect of diet on the metabolism. Exercise effects are incorporated into the energy burning mechanisms in the muscles. Moreover, immune and inflammation pathways are also incorporated in the model. This model is validated from the data available in the literature.

We take a person's physical details (BMI, fat and muscle mass, abdomen-to-hip ratio), lifestyle details (diet, exercise, water intake, smoking and drinking, health conditions) and blood parameters (CBC, vitamins, cholesterol, metabolic/immune/transcriptional markers) as inputs to the model. Using this model, we predict the current and future risk of heart disease. We see a trend that a few lifestyles lead to high cardiovascular risk and hypercholesterolemia. We have now come together since we wish to simultaneously study the effects of both of these factors (specifically lifestyle and mRNA expression) on the cardiovascular disease risk in people.

We strongly believe that incorporating both these factors will have a symbiotic effect on the prediction accuracy of such a method. Hence, we now want to work towards defining a standard procedure to measure cardiovascular disease risk in people. Moreover, using our model, the molecular-level effects due to the over-expression of this specific mRNA on the signaling and metabolic pathways will be evaluated. Coronary angiography is currently the gold standard test for diagnosing coronary artery disease. Our approach towards quantifying early-stage cardiovascular risk is novel since the methodology utilizes a combination of novel biomarkers and a state-of-the-art human physiology silicon platform. We believe that such an approach would revolutionize the management of cardiovascular risk in India by providing a much more affordable solution.

Primary aims of the projects are

- Establish the feasibility for a standardized protocol for early-stage diagnosis of cardiovascular disease, non-invasively and put efforts towards developing a web-based platform to calculate this risk online
- Establish a risk score to initiate early preventive strategies in patients categorized as elevated risk by this screening test.
- Correlate the data collected non-invasively with direct assessment of athero-sclerotic plaque measured invasively.
- Validate this correlation developed among an Indian population sample.

Impact of this innovation: We want to develop a standardized protocol for early-stage cardiovascular risk assessment. Using our technology, a person's lifestyle data would be captured, along with a blood-draw for biomarkers (inflammatory and genetic). This would serve as an input to our metabolic model. Our model, using all this data combined with the physiology information incorporated, would be able to output the cardiovascular disease risk of that person. This correlation will be validated with measurement of the actual plaque burden in the coronary artery of the patient by intravascular ultrasound (a well validated technology for quantitative and qualitative assessment of the plaque). This would translate into a standardized test for cardiovascular disease risk assessment once it is tested and validated in this project.
