



## Electrochemical approach for acute myocardial infarction diagnosis based on direct antibodies-free analysis of human blood plasma

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### ABSTRACT

A novel direct antibodies-free electrochemical approach for acute myocardial infarction (AMI) diagnosis has been developed. For this purpose, a combination of the electrochemical assay of plasma samples with chemometrics was proposed. Screen printed carbon electrodes modified with didodecyldimethylammonium bromide were used for plasma characterization by cyclic (CV) and square wave voltammetry and square wave (SWV) voltammetry. It was shown that the cathodic peak in voltammograms at about  $-250$  mV vs. Ag/AgCl can be associated with AMI. In parallel tests, cardiac myoglobin and troponin I, the AMI biomarkers, were determined in each sample by RAMP<sup>®</sup> immunoassay. The applicability of the electrochemical testing for AMI diagnostics was confirmed by statistical methods: generalized linear model (GLM), linear discriminant analysis (LDA) and quadratic discriminant analysis (QDA), artificial neural network (multi-layer perception, MLP), and support vector machine (SVM), all of which were created to obtain the “True–False” distribution prediction where “True” and “False” are, respectively, positive and negative decision about an illness event.

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### 1. Introduction

AMI is a part of acute coronary syndrome which is the most common cause of death all over the world. Classical symptoms of acute myocardial infarction include sudden chest pain, shortness of breath, nausea, vomiting, palpitations, sweating, and anxiety (Mallinson, 2010). However, about a quarter of all the AMI cases are “silent” and do not show noticeable symptoms. This calls for the development of reliable and simple methods for AMI diagnostics. At present, the diagnosis of AMI is based on WHO-criteria ([www.who.int](http://www.who.int)) which involve characteristic chest pain, diagnostic electrocardiogram (ECG) changes, and elevation of the biochemical markers in the blood samples. Cardiac troponins (cTn), creatine kinase-MB (CK-MB), and cardiac myoglobin (cMb) are typical cardiac markers used for the AMI diagnostics. New approaches intensively investigated cover two additional groups of markers, i.e. (i) inflammation markers (C-reactive protein, myeloperoxidase, placental growth factor, pregnancy-associated plasma protein A) and (ii) cardiac ischemia markers (heart-type fatty acid binding

protein, ischemia modified albumin, b-typed natriuretic peptide) (Yang and Zhou, 2006; McDonnell et al., 2009).

Three different troponins (Tn) are found in the striated muscle. They form a complex that regulates the actin–myosin interaction needed for muscle contraction. TnT and TnI each have two distinct isoforms specific for cardiac and skeletal muscle, respectively. In contrast, the two isoforms of TnC do not discriminate between cardiac and skeletal muscle but are specific for fast-twitch skeletal muscle or to cardiac and slow-twitch skeletal muscle. Since 2000, cardiac troponin (cTn) has been declared as a preferred biomarker for myocardial infarction by the American College of Cardiology and the European Society of Cardiology due to its high sensitivity and nearly absolute specificity (O’Brien, 2008). On the other hand, the specificity of troponins has recently been questioned, because other clinical situations, such as sepsis, hypovolemia and renal failure may also cause an increase in troponin level (Jeremias and Gibson, 2005).

CK-MB, specific for cardiac tissue, is still used for the AMI diagnosis. As total creatine kinase activity, CK-MB typically begins to rise 4–6 h after the onset of infarction but not more than 12 h after. An elevated serum CK-MB level is relatively specific for myocardial injury, particularly in patients with ischemic symptoms when skeletal muscle damage is not observed. These elevations return to baseline within 36–48 h against up to 10 days seen for Tn. This

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