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Recent Advances in Cardiac Troponin I Based Sensors for Detection of Human Heart Attack

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Abstract

Cardiovascular disease (CVD) is considered as a major life threat in human globally, and with time more sophisticated technique for estimating and therapeutics is still desirable. There has been rising attention in detection of diagnostic biomarker for cardiac injury to predict risk of heart attack. Cardiac troponin I (cTnI) has established to be a convincing biomarker for acute myocardial infarction (AMI) detection. An immunoassay and aptamer based biosensors for cTnI can play a significant role in diagnosis of AMI. Over the past decades, several approaches concerning cTnI detection have been investigated, including colorimetric, fluorescence, electrochemical, surface plasmon resonance and paramagnetic. This review focussed more on recent methodologies about surface immobilized detection of cTnI.

Keywords: Cardiovascular disease; Cardiac troponin I; Heart attack; Heart attack sensor; Myocardial infarction

Abbreviations: ACS: Acute Coronary Syndrome; cTnI: Cardiac Troponin I; CVD: Cardiovascular Disease; ECG: Electrocardiogram; MI: Myocardial Infarction; WHO: World Health Organization

Introduction

The World Health Organization (WHO) indexed cardiovascular disease (CVD) as a leading foundation of human death in developing as well as developed countries. An annual number of deaths estimate above 17.5 million to 25 million from 2015 to 2030 representing 40% of all global deaths due to heart disease and stroke [1]. Cardiac related diseases are the major financial burden on clinical resources and cost approximately 192 billion Euros per year. The CVD, heart and blood vessel diseases are mainly associated to artherosclerosis, a plaque build-up within the arteries that limits the blood flow, can lead to atherosclerosis. There are several reasons, including lifestyle that may cause CVD. Myocardial infarction (MI), commonly called 'heart attack' is one of the clinical forms and also among instant life threatening kinds of acute coronary syndromes (ACS). It triggers the most serious adverse cardiac events like irreversible tissue injury in the myocardium [2].

Primarily, the WHO has established criteria for the diagnosis of CVD, whereby patients must encounter a minimum two out of three conditions: characteristic chest pain, electrocardiogram (ECG) changes and elevation in biomarkers level in their blood samples [3]. The MI examined mainly by electrocardiography (ECG) though only 57% of patients can be diagnosed accurately for acute myocardial infarction (AMI). Besides this, AMI patients can even show normal or non-diagnostic ECG when conferred to the Emergency Department that makes early diagnosis of CVD more difficult [4-9]. About 25% of AMI have occurred devoid of any symptoms like pain in chest, back, or jaw [10,11]. Consequently, a sensitive and rapid diagnosis of CVD is extremely essential and crucial not only for patient's survival but also for saving cost and ample amount of time in efficacious early prognosis of AMI.

Biomarkers plays an important role in identification of pathologic processes resulted from different diseases [12]. Neither the clinical presentations nor the ECG had adequate clinical sensitivity and specificity for detecting MI without the use of biomarkers. Cardiac biomarker assays help medical professionals to understand and differentiate between myocardial infarction and angina, which assists in the diagnosis or treatment of CVD. Any minor alteration in biomarkers measured in the blood can conclude the resultant on-going disease relatively, precisely and quickly. In the myocardium, the model biomarker for AMI should be in high concentration and not exist in the non-cardiac tissues [13]. The initially used cardiac biomarkers include aspartate aminotransferase, lactate dehydrogenase isoenzymes and total lactate dehydrogenase [14]. However, in 2000 the European Society of Cardiology and the American College of Cardiology (ESC/ACC) declared new measures for the implication of AMI diagnosis as none of them showed high specificity for AMI [15,16]. Currently, myoglobin, creatine kinase-MB, cardiac forms of troponin (T and I) are relevant AMI diagnostic biomarkers. Among them, cardiac troponin I (cTnI) is recognized as the 'gold standard' biomarker for AMI, since it is normally produced only in the myocardium and displays high specificity to cardiac injury [17]. Cardiac troponin I is one of the unit of troponin complex, including cTnT and cTnC, organized with tropomyosin are situated on the actin filament and play a vital role in contraction of skeletal and cardiac muscle facilitating calcium regulation as a molecular switch. Human cTnI is made up of 209 amino acid residues, with a molecular weight of 24 kDa that can inhibit the actomyosin ATPase, and this property can be increased in the presence of tropomyosin [18,19]. The cTnI isoform sequence present in myocardial tissue varies from those in skeletal muscles [20,21]. This allows the generation of highly specific cTnI antibodies with no cross reaction with other isoforms of troponin. On the incidence of cardiac injury (MI), cTnI is released into the bloodstream and the death risk is

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directly linked to troponin level in serum which increases drastically up to 50 ng/mL within 3–6 h, lastly to a level around 550 ng/mL, peak at 24–48 h and return to baseline over 5–14 days [22-24]. In a recent study, 0.5 to 2.0 ng/mL cTnI concentrations is considered as the borderline between normal people and patients [3]. The traditional cTnI detection method include enzyme-linked immunosorbent assay (ELISA) and radioimmunoassay (RIA) that has many drawbacks, including low sensitivity,high cost, and slow turnaround time that prevents their future practical use.

Current methods for diagnosis of AMI depend greatly on conventional approaches which are based on examinations conducted in laboratories that may take several hours or even days from when tests are ordered to when results are obtained [25]. The development of biosensors is probably one of the most promising ways to elucidate some of the difficulties concerning fast, sensitive and cost effective measurements [26]. Biosensors lead to quick diagnosis, contributing better health care and decreasing the turnaround time for results declaration which is extremely stressful to the patients. Currently, lab-on-a chip based biosensor technology with the ability for point-of-care testing (POCT) is studied for the detection of cTnI in blood [27]. A POCT is defined as a test performed immediate to the patients [28]. There might be slight modifications in the definition, depending on the several POCT operating locations, such as doctor offices and emergency departments. According to the instructions and recommendations directed by the National Academy of Clinical Biochemistry (NACB), the total time taken by POCT should be within 1 h with a specimen of serum or whole blood [29].

In the present paper, we reviewed the developed biosensors over the past 10 years for the detection of cardiac troponin I in early diagnosis of heart attack. This review also summarized the commercial cTnI assays manufactured by various industries various biosensor platforms and emphasized the chief clinically significant parameters, such as their detection limit and designing of bioassay [30].

Biosensors for cardiac troponin I (cTnI)

A biosensor is a device aimed to distinguish and quantify target analytes that is broadly used as an influential analytical tool in medical diagnostics [25]. It allows detection of proteins, nucleic acids and monitoring antigen–antibody interaction. It is commonly fabricated by immobilizing a biological receptor molecule, such as antibody, DNA, or RNA on the surface of an appropriate transducer that convert biochemical signal into quantifiable electronic signals. A range of sensors for cTnI detection has been developed including techniques like optical, electrochemical, colorimetric, surface plasmon resonance, chemi-resistive, etc. [31-34]. A summary of different types of sensor platforms reported for the detection of cTnI are summarised (Figure 1).

Colorimetric based biosensors

The principle of colorimetric biosensor is based on the amount of light absorbed by the chromogenic response at the specific wavelength in the presence of analyte. To avoid the hazardous procedure in radioimmunoassay such type of assay was not developed until the year 1971in general; the colorimetric assay is now well-known as enzyme-linked immunosorbent assay (ELISA) [35]. The principle is also similar to the sandwiched assay, antigen is captured by the primary antibody at first, and the secondary enzyme linked antibody will be further added to form a sandwich complex. Lastly, the change in color and related measurements can verify the antigen quantitatively. For example, to the above principle, horseradish peroxidase (HRP)

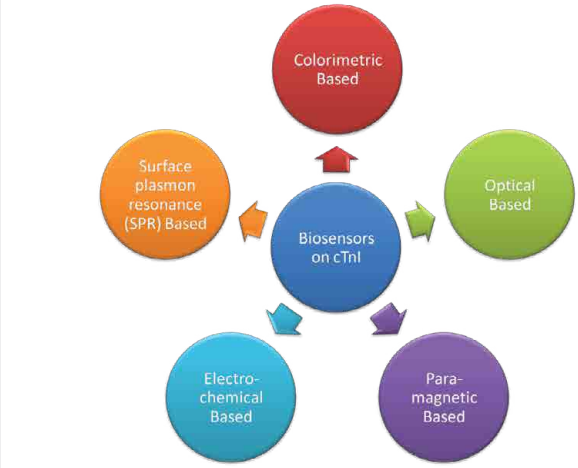

Figure 1: Most frequently studied techniques in relation to the detection of cardiac troponin I in CVD risk.

which can begin a chemi-luminometric signal was widely exploited to assemble a colorimetric assay [36-39]. In 2010, Wu et al. developed a poly-(dimethylsiloxane) (PDMS)-gold composite film-based biosensor for cTnI in which anti-cTnI and cTnI were captured individually on the surface of PDMS-AuNPs [40]. The process has small size, cost effectiveness, and high sensitivity (0.01 ng/mL) characteristics, but above 1 h incubation time is needed. Similarly, Kim et al., used the lateral flow assay (LFA) method when adding cTnI to the sample pad, the flow would pass through conjugate pads which has two different AuNP conjugates, and the cTnI reacted first with the anti-troponin I antibody bearing AuNP without a further operation step to analyze cTnI [41]. The color intensity was measured for concentrations of cTnI followed by dropping LFA strip into troponin I containing well plates. The detection limit from the patient samples was effectively determined as low as 0.01 ng/mL. For this assay, only 10 min is needed for the detection as compared to previous method. Another method was introduced by Cho et al. on an ELISA-on-a-chip (EOC) biosensor for cTnI [42]. The sensor was based on cross-flow chromatography technique in which one monoclonal cTnI antibody (BD clone 12) was functionalized with biotin and another BD clone 12 was labeled by HRP, which is used to catalytically oxidize a luminogenic substrate luminol. The cTnI antigen, biotin-labeled antibody, and HRP labeled antibody were sandwiched onto the substrate via biotin–streptavidin interaction. Luminol passed through the immobilized surface, and the generated chemiluminometric signal was captured by installed detector. On addition of cTnI antigen, only 20 min is needed for the incubation and measurement process.

Optical based biosensors

An optical biosensor is fluorescence based immunoassays for the detection of particular analyte. The potential signal molecules like fluorescence organic dye and fluorescent nanoparticles are mainly used to monitor the presence of target antigen. Various commercially available cTnI detection instruments based on fluorescence assay can offer examination in just 20 min, for instance Roche Cardiac Reader, Abbott i-STAT and Singulex Erenna System etc. Recently Bhatnagar et al., developed a fluorescence resonance energy transfer (FRET) based biosensor for early detection of heart attack using graphene quantum dots (GQDs) and graphene (Figure 2) [43]. The bioprobe was formed by conjugating anti-cTnI monoclonal antibody to amine functionalized GQDs, and monitored their fluorescence as switch on condition.

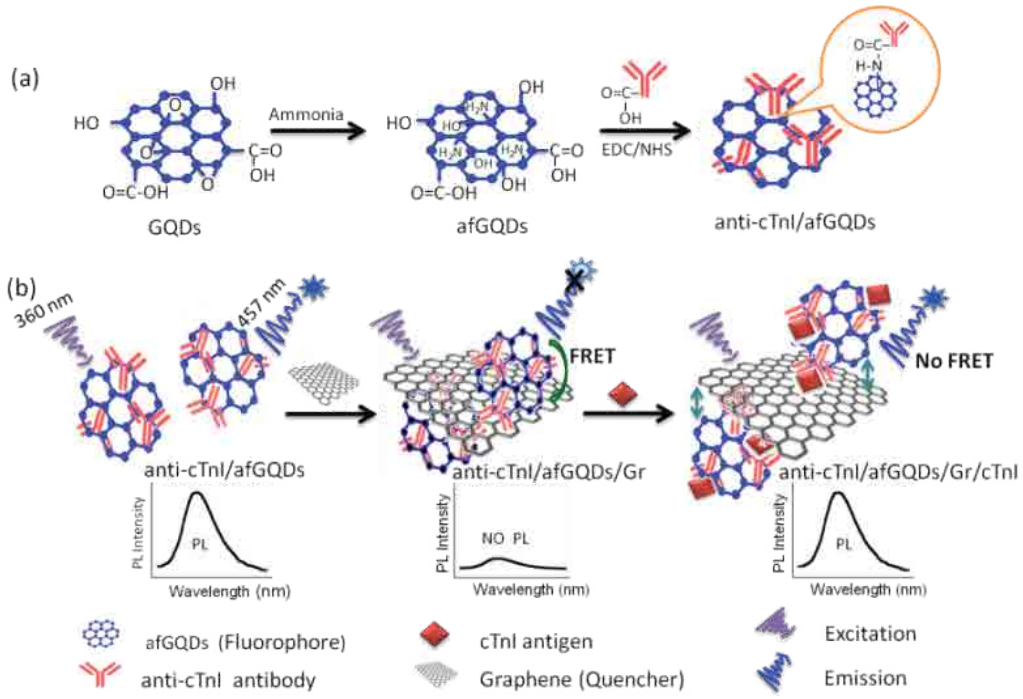

Figure 2: Schematic illustration of FRET based cTnI [43].

Further, on adding graphene sheets to the prepared bioprobe the fluorescence was recorded as switch off and after addition of various concentrations of cTnI, again the fluorescence recovered in photo-luminescence spectra. The sensor takes only 10 min with low detection limit of 0.192 pg/mL. Similarly, Shankar et al., proposed immobilized a 16-phosphonohexadecanoic acid self-assembled monolayer (SAM) onto a TiO_2 array to constitute a low-cost biosensor [44]. On this ultrasensitive platform, the detection of cTnI concentrations as low as 0.1 pg mL^{-1} was accomplished with the help of enzymatic amplification. The reported study takes over 2 h to complete the analysis. Similarly, another way to design a biosensor when a fluorophore is close to the metal surface, its optical properties will significantly alter. Based on this metal quenching effect, the detection sensitivity can be improved. Lee and Kang deposited gold onto the glass substrate, followed by immobilizing protein A, anti-cTnI, cTnI antigen, and fluorescence labeled anti-cTnI, respectively [45]. Depending on the distance between the dye and the gold surface, the fluorescent dye was not greatly quenched, but adsorption of dye led to the quenching of its fluorescence. Therefore, such enhanced fluorescence was detectable about 7000 times lower in the detection limit compared to the traditional method. However, it is still a time-consuming procedure. Alkaline phosphatase (ALP) has been largely exploited for the fluorescent based cTnI immunoassay, especially in commercial products and recently has explored the ALP chemiluminescence chemistry for the cTnI detection [25,46-48]. The combination of magnetic and fluorescence strategy is promising for the quick and sensitive for cTnI detection. In both the cases, the investigation time is about 40 min which is better in comparison to the TiO_2 nano-array and the limit of detection for both can attain as low as 1 ng/mL.

Recently, aptamer has widely been studied and vigorously developed for probable therapy and diagnosis of diseases. Due to its high specificity and stability are generally better to those of the antibodies. An aptamer is a peptide sequence, a single-stranded DNA (ssDNA) or RNA (ssRNA) which can recognize a wide variety of target molecules specifically, such as chemical molecules, proteins, and cells [49]. In 2015, Dorraj et al. most recently have chosen an aptamer (79 bpssDNA) that was used to combine the human cTnI from a synthetic nucleic acid library by systematic evolution of ligand exponential enrichment (SELEX) [50]. Results showed that the detection limit using aptamer-AuNPs-based assay was 5 ng/mL, though take over 1 h detection process which is still a drawback for this method. The potential of either approaches can be seen as promising outlook for the progress of cTnI detection.

Electrochemical based biosensors

Electrochemical assay based biosensors operated by the detection of electrochemical signals from the specific reaction primarily rely on the interaction between transducer and target analytes. When captured by the immobilized antibody, charge transfer takes place between antibody and antigen molecules, leading to the alteration in the current resistance the surface. Thus, an electrochemical biosensor converts any reaction into a measurable electrical signal. A versatile novel cTnI detection platform using nanoparticles has been reported. In 2011, Ahammad et al. developed a highly sensitive cTnI biosensor using AuNPs modified ITO surface with different linkers like cystamine and glutaraldehyde self-assembled on it [51]. Then the anti-cTnI antibodies were immobilized by linker molecules and on adding cTnI, immunocomplex formed onto the AuNPs-ITO electrode. Then, to detect the concentration of cTnI, the horseradish peroxidase (HRP) labeled secondary anti-cTnI antibody used to measure the changes in open circuit potential during H_2O_2 electro-reduction. These optical immunoassays take more incubation time though the high sensitivity could achieve upto 1 ng/mL. Recently, Shan et al. reported a cTnI biosensor with a higher sensitivity of 0.4 pg/mL [52]. Two specific peptides as capture peptide and report peptide were used and self-assembled onto the gold nanoparticles electrodeposited onto the gold electrode. Ruthenium labeled at lysine position of the report peptide via acylation and after adding cTnI on the electrode surface and the probe

peptide, the response was electrochemically generated. Additionally, various immunoassays can be integrated to microfluidics. Recently, AuNPs poly(dimethylsiloxane) (PDMS) composite microfluidic systems based approach has been developed [53]. A sandwich structure formed between anti-cTnI antibodies absorbed on GNP containing micro-reactor cells to capture the cTnI and secondary anti-cTnI antibodies labeled with CdTe and ZnSe quantum dots (QDs). The QDs were dissolved into Cd^{2+} and Zn^{2+} that could be detected on the localized surface by square-wave anodic stripping voltammetry. This cTnI immunosensor established the success of combination of microfluidics with electrochemistry for clinical application. The limitations of currently developed sensing platforms include slow-turnaround time, expensive equipment, and use of toxic or fluorescent labels. Recently, Periyakaruppan et al. have developed an inexpensive, simple and label-free approach to detect cTnI biomarker using nanoelectrode arrays made up of vertically aligned carbon nanofiber (CNF) [54]. The detection of human-cTnI in assay was attained by the anti-cTnI Ab immobilized on CNFs and measured electrochemically with impedance spectroscopy and cyclic voltammetry techniques. The sensing system established a good selectivity and sensitivity against cTnI analyte at 0.2 ng/mL cTnI concentration as the lower limit detection. Electrochemical based biosensors can also provide highly sensitive and fast sensing response, however the results can be disturbed by detection environment including the pH and ionic strength.

Surface plasmon resonance based biosensors

Surface plasmon resonance (SPR) is an exceptional optical transduction technique, which has been commercially employed for optical biosensors SPR biosensors involve special surface plasmon electromagnetic waves to probe changes in the refractive index (RI) at surfaces of metals [44]. Kwon et al. recently fabricated an SPR sensor for cTnI by using monoclonal anti-cTnI antibody as an epitope peptide onto a chemically modified thin gold film [32]. The cTnI concentration is detected by the SPR signal intensity and found that this intensity was directly proportional to the cTnI concentration range of 0–160 ng/mL. According to the author, the detection limit of the sensor was equivalent to ELISA-based commercial cTnI detection systems that was calculated as low as 0.068 ng/mL. Similarly, Masson et al. developed a fiber optic based SPR sensor for cTnI detection where anti-cTnI specific to cTnI were immobilized on carboxymethylated dextran layer on a gold SPR surface [55]. The assembled sensor shows a lower detection limit of 1.4 ng/mL. The advantage of this sensor in comparison to other was that the antibody immobilized probe was stable for few weeks in a wide pH range (pH 2–12).

Paramagnetic based biosensors

Paramagnetic particles (PMPs) have being used in applications like MRI contrast agents and separation of biomolecules [56,57]. Usually, PMPs have an iron oxide core with a high biocompatibility layer outside [58,59]. Thus, magnetic nanoparticles have been broadly utilized as a carrier for biomolecule detection and to increase the sensitivity [60,61]. In general, PMPs reagent and antigen are supplied into a chamber containing antibodies coated at the bottom and antigen can be transported rapidly to the bottom surface by the driving force generated from the bottom magnetic field. On characterizing the surface, the antigen is able to be detected successfully after washed away the unbound PMPs. Most recent, Prin's group developed a multiplexed immunoassay for cTnI using actuated PMPs [62]. Initially, anti-cTnI antibodies coated magnetic nanoparticles were allowed to mixed with the cTnI sample to capture. After the fast and efficient binding of cTnI due to the large surface area of the particles, the mixed solution was distributed by the driving force of electromagnets. In this way, the particles concentrate to capture the cTnI on the binding molecule, which lead to consume lesser time. Finally, unbound cTnI molecules would be washed away and examined the cTnI concentration which is proportional to that of the magnetic nanoparticles. The sensing of cTnI was achieved by reflected light intensity from the surface by the mechanism of total internal reflection (TIR). A fast and highly sensitive detection with a limit of 0.03 ng/mL cTnI is achieved through the combination of magnetic and optical detection. Furthermore, Kiely et al. reported another novel PMPs based immunoassay for cTnI with an advantage of short time process. The sensor was constructed using two reaction coil surfaces, for detection and reference respectively that were mounted onto the substrate [63]. Two anti-cTnI molecules were immobilized onto the detection coil and PMP surface, respectively. Addition of cTnI to the device form sandwiched between the PMP and the surface and the magnetic field of PMPs can able cTnI can be detected. The technique is highly sensitive, fast as it takes only 4 min with recognition of 0.5 ng/mL cTnI. Paramagnetic assay is more appropriate in clinical diagnostics due to its non-magnetic properties with the surrounding biological molecules. Todd et al., used another combination of magnetic and optical approach for the fast detection of cTnI. Streptavidin functionalized PMPs were tagged to fluorescent dye Labeled cTnI by streptavidin–biotin coupling approach [64]. Magnetic bed was used to separate MPs after incubating samples in a 96-well plate. Prior to measurements, urea was added to release the cTnI from the MPs by disrupting antibody–analyte interactions using Erenna Immunoassay System which is a single molecule counting technology based system. In this system, samples were pumped into a capillary flow cell through an interrogation space and after passing through a dichroic mirror or confocal lens, light reached the interrogation space. When fluorescent dye labelled cTnI encounter the light, fluorescence could be measured by the confocal microscope lens and the detector. The approach results in high sensitivity detection and attained a low detection limit of 0.6 ng/L.

Conclusion

This is significantly important to diagnose cardiovascular diseases precisely heart attack at the early stage, in order to provide successful treatment for recovery of patients. Cardiac troponin I (cTnI) has recognized to be most specific biomarker for myocardial infarction (MI). Thus, it is essential to develop a cTnI biosensor which is fast, sensitive, and give POCT support to the diagnosis of acute MI at very low concentration (<0.04 ng/mL) in the whole blood. This review revealed a varied research in respect to the detection of cTnI for diagnosis of AMI. In spite of the substantial developments in fabrication of biosensor, there is no ideal device has been used so far in clinical diagnostics. Since, patient's data is an important factor to analyse and improvise the performance and reliability of a device. The key challenges for a technology are the sensitivity and POCT assessment which introduces a mini bench top device and hand-held instrumentation. Additionally, cTnI detection equipment can be focussed to (1) portable, specific and highly sensitive biosensors, (2) efficient process and shorter turnaround time, (3) cost effective, (4) POCT analysis, and (5) stability of the immunoassay. On merging all the traits, the succeeding decades will get a breakthrough in the domain of cTnI biomarker detection for early diagnosis of AMI.

References

1. Facts about cardiovascular diseases.
World Health Organization, 2007, http://www.who.int/mediacentre/factsheets/fs317/en/index.html.

2. Song S.Y., Han Y.D., Kim K., Yang S.S. & Yoon H.C.
A fluoro-microbead guiding chip for simple and quantifiable immunoassay of cardiac troponin I (cTnI).
Biosens. Bioelectron. 2011, **26**: 3818-3824.

3. Yang Z. & Zhou D.M.
Cardiac markers and their point-of-care testing for diagnosis of acute myocardial infarction.
Clin. Biochem. 2006, **39**: 771-780.

4. McDonnell B., Hearty S., Leonard P. & O' Kennedy R.
Cardiac biomarkers and the case for point-of-care testing.
Clin. Biochem. 2009, **42**: 549-561.

5. Suprun E., Bulko T., Lisitsa A., Gnedenko O., Ivanov A., Shumyantseva V. & Archakov A.
Electrochemical nanobiosensor for express diagnosis of acute myocardial infarction in undiluted plasma.
Biosens. Bioelectron. 2010, **25**: 1694-1698.

6. Yusuf S., Pearson M., Sterry H., Parish S., Ramsdale D., Rossi P. & Sleight P.
The entry ECG in the early diagnosis and prognostic stratification of patients with suspected acute myocardial infarction.
Europ. Heart J. 1984, **5**: 690-696.

7. Foy S.G., Kennedy I.C.S., Ikram H., Low C.J.S., Shirlaw T.M. & Crozier I.G.
The early diagnosis of acute myocardial-infarction.
Aus. N. Z. J. Med. 1991, **21**: 335-337.

8. Stubbs P. & Collinson P.O.
Point-of-care testing: A cardiologist's view.
Clin. Chim. Acta 2001, **311**: 57-61.

9. Kost G.J. & Tran N.K.
Point-of-care testing and cardiac biomarkers: the standard of care and vision for chest pain centers.
Card. Clin. 2005, **23**: 467-490.

10. Wan Z.F., Yang L.Y., Sun P., Ren L.L., Li M.L., Wu H., Wang J.F. & Zhang L.
Conjugation of biomolecules with magnetic protein microspheres for the assay of early biomarkers associated with acute myocardial infarction.
Anal. Chem. 2009, **81**: 6210-6217.

11. Bottenus D., Jubery T.Z., Ouyang Y.X., Dong W.J., Dutta P. & Ivory C.F.
10000-fold concentration increase of the biomarker cardiac troponin in a reducing union microfluidic chip using cationic isotachophoresis.
Lab. Chip 2011, **11**: 890-160.

12. Strimbu K. & Tavel J.A.
What are biomarkers?
Curr. Opin. HIVAIDS 2010, **5**: 463-466.

13. Daubert M.A. & Jeremias A.
The utility of troponin measurement to detect myocardial infarction: review of the current findings.
Vasc. Health Risk Manage. 2010, **6**: 691-699.

14. Apple F.S., Wu A.H., Jaffe A.S., Panteghini M., Christenson R.H., Cannon C.P., Francis G., Jesse R.L., Morrow D.A. & Newby L.K.
National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine, Practice Guidelines: Analytical issues for biomarkers of heart failure.
Circulation 2007, **116:** e95-e98.

15. Alpert J.S., Thygesen K., Antman E. & Bassand J.P.
Myocardial infarction Redefined - A Consensus Document of the Joint European Society of Cardiology, American College of Cardiology Committee for the Redefinition of Myocardial Infarction.
J. Am. Coll. Cardiol. 2001, **37**: 973-973.

16. Alpert J.S., Antman E., Apple F., Armstrong P.W., Bassand J.P., de Luna A.B., Beller G., Breithardt G., Chaitman B.R., Clemmensen P., Falk E., Fishbein M.C., Galvani M., Garson A., Grines C., Hamm C., Hoppe U., Jaffe A., Katus H., Kjekshus J., Klein W., Klootwijk P., Lenfant C., Levy D., Levy R.I., Luepker R., Marcus F., Naslund U., Ohman M., Pahlm O., Poole-Wilson P., Popp R., Pyorala K., Ravkilde J., Rehnquist N., Roberts W., Roberts R., Roelandt J., Ryden L., Sans S., Simoons M.L., Thygesen K., Tunstall-Pedoe H., Underwood R., Uretsky B.F., deWerf F.V., Voipio-Pulkki L.M., Wagner G., Wallentin L., Wijns W., Wood D. & Amer J.E.S.C.
Myocardial infarction Redefined – A Consensus Document of the Joint European Society of Cardiology/American College of Cardiology, Committee for the Redefinition of Myocardial Infarction.
Eur. Heart J. 2000, **21**: 1502-1513.

17. Panteghini M., Pagani F., Yeo K.T.J., Apple F.S., Christenson R.H., Dati F., Mair J., Ravkilde J. & Wu A.H.B.
Evaluation of imprecision for cardiac troponin assays at low-range concentrations.
Clin. Chem. 2004, **50**: 327-332.

18. Wilkinson J.M. & Grand R.J.A.
Comparison of amino-acid sequence of troponin-i from different striated muscles.
Nature 1978, **271**: 31-35.

19. Apple F.S. & Collinson P.O.
Analytical characteristics of high-sensitivity cardiac troponin assays.
Clin. Chem. 2012, **58**: 796-796.

20. Vallins W.J., Brand N.J., Dabhade N., Butlerbrowne G., Yacoub M.H. & Barton P.J.R.
Molecular-cloning of human cardiac troponin-i using polymerase chain-reaction.
FEBS Lett.1990, **270**: 57-61.

21. Babuin L. & Jaffe A.S.
Troponin: The biomarker of choice forthe detection of cardiac injury.
Can. Med. Assoc. J. 2005, **173**: 1191-1202.

22. Sasse S., Brand N.J., Kyprianou P., Dhoot G.K., Wade R., Arai M., Periasamy M., Yacoub M.H. & Barton P.J.
Troponin I gene expression during human cardiac development and in end-stage heart failure.
Circ.Res.1993, **72**: 932-938.

23. Vichairuangthum K., Leowattana W., Ajyooth L.O. & Pokum S.
The relationship between serum concentration of cardiac troponin I in chronic renal failure patients and cardiovascular events.
J.Med.Assoc. Thail. 2006, **89**: 714-720.

24. Mahajan V.S. & Jarolim P.
How to interpret elevated cardiac troponin levels
Circulation 2011, **124**: 2350-2354.

25. Mascini M. & Tombelli S.
Biosensors for biomarkers in medical diagnostics.
Biomarkers 2008, **13**: 637-657.

26. Mohammed M.I. & Desmulliez M.P.
Lab-on-a-chip based immunosensor principles and technologies for the detection of cardiac biomarkers: a review.
Lab Ona Chip 2011,**11**: 569-595.

27. St-Louis P.
Status of point-of-care testing: Promise, realities and possibilities.
Clin.Biochem.2000, **33**: 427-440.

28. Von Lode P.
Point-of-care immunotesting: Approaching the analytical performance of central laboratory methods.
Clin. Biochem. 2005,**38**: 591-606.

29. Maqsood A., Kaid K. & Cohen M.
Clinical significance of borderline cardiac troponin (CTNI) in patients presenting with acute coronary syndrome who are referred for cardiac catheterization.
Internet J. Cardiovasc. Res. 2006, **4**: 1-4.

30. Tate J., Barth J. & Bunk D.
Analytical characteristics of commercial and research cardiac troponin I and T assays declared by the manufacturer, 2012; http://www.ifcc.org/media/218177/IFCC Troponin Tables ng/L Update December 2012.pdf.

31. Daniels J.S. & Pourmand N.
Label-free impedance biosensors: opportunities and challenges.
Electroanal. 2007, **19**: 1239-1257.

32. Kwon Y.C., Kim M.G., Kim E.M., Shin Y.B., Lee S.K., Lee S.D., Cho M.J. & Ro H.S.
Development of a surface plasmon resonance-based immunosensor for therapid detection of cardiac troponin I.
Biotechnol. Lett. 2011, **33**: 921-927.

33. Krishnamoorthy S., Iliadis A.A., BeiT. & Chrousos G.P.
An interleukin-6ZnO/SiO(2)/Si surface acoustic wave biosensor.
Biosens. Bioelectron. 2008, **24**: 313-318.

34. Monson C.F., Driscoll L.N., Bennion E., Miller C.J. & Majda M.

Antibody–antigen exchange equilibria in a field of an external force: Design of reagentless biosensors
Anal. Chem. 2009, **81**: 7510-7514.

35. Engvall E. & Perlmann P.
Enzyme-linked immunosorbent assay (ELISA) quantitative assay of immunoglobulin-G.
Immunochem. 1971, **8**: 871-874.

36. Torabi F., Far H.R.M., Danielsson B. & Khayyami M.
Development of a plasma panel test for detection of human myocardial proteins by capillary immunoassay.
Biosens. Bioelectron. 2007, **22**: 1218-1223.

37. Chen C.C., Do J.S. & Gu Y.
Immobilization of HRP in mesoporous silica and its application for the construction of polyaniline modified hydrogen peroxide biosensor.
Sens. 2009, **9**: 4635-4648.

38. Larue C., Calzolari C., Bertinchant J., Leclercq F., Grolleau R. & Pau B.
Cardiac-specific immunoenzymometric assay of troponin I in the early phase of acute myocardial infarction.
Clin. Chem. 1993, **39**: 972-979.

39. Davies E., Gawad Y., Takahashi M., Shi Q.W., Lam P., Styba G., Lau A., Heeschen C., Usategui M. & Jackowski G.
Analytical performance and clinical utility of a sensitive immunoassay for determination of human cardiac troponin I.
Clin. Biochem. 1997, **30**: 479-490.

40. Wu W.Y., Bian Z.P., Wang W., Wang W. & Zhu J.J.
PDMS gold nanoparticle composite film-based silver enhanced colorimetric detection of cardiac troponin I Sens.
Actuat. B Chem. 2010, **147**: 298-303.

41. Choi D.H., Lee S.K., Oh Y.K., Bae B.W., Lee S.D., Kim S., Shin Y.B. & Kim M.G.
A dual gold nanoparticle conjugate-based lateral flow assay (IFA) method for the analysis of troponin I.
Biosens. Bioelectron. 2010, **25**: 1999-2002.

42. Cho I.H., Paek E.H., Kim Y.K., Kim J.H. & Paek S.H.
Chemiluminometric enzyme-linked immunosorbent assays (ELISA)-on-a-chip biosensor based on cross-flow chromatography.
Anal. Chim. Acta 2009, **632**: 247-255.

43. Bhatnagar D., Kumar V., Kumar A. & Kaur I.
Graphene quantum dots FRET based sensor for early detection of heart attack.
Biosens. Bioelectron. 2016, **79**: 495-499.

44. Kar P., Pandey A., Greer J.J. & Shankar K.
Ultrahigh sensitivity assays for human cardiac troponin I Using TiO_2 nanotube arrays.
Lab Chip 2012, **12**: 821-828.

45. Lee S. & Kang S.H.
Quenching effect on gold nano-patterned cardiac troponin I Chip by total internal reflection fluorescence microscopy.
Talanta 2013, **104**: 32-38.

46. Liu J., Zhang L.L., Wang Y.S., Zheng Y. & Sun S.H.
An improved portable biosensing system based on enzymatic chemiluminescence and magnetic immunoassay for biological compound detection.
Measurement 2014, **47**: 200-206.

47. Dispenzieri A., Kyle R.A., Gertz M.A. Therneau T.M., Miller W.L., Chandrasekaran K., McConnell J.P., Burritt M.F. & Jaffe A.S.
Survival in patients with primary systemic amyloidosis and raised serum cardiac troponins.
Lancet 2003, **361**:1787-1789.

48. Dasgupta A., Chow L., Wells A., Datta P.
Effect of elevated concentration of alkaline phosphatase on cardiac troponin I assays.
J. Clin. Lab. Anal. 2001, **15**: 175-177.

49. Keefe A.D., Pai S. & Ellington A.
Aptamers as therapeutics.
Nat. Rev. Drug Discov. 2010, **9**: 537-550.

50. Dorraj G.S., Rassaee M.J., Latifi A.M., Pishgoo B. & Tavallaei M.
Selection of DNA aptamers against human cardiac troponin I for colorimetric sensor based dot blot application.
J. Biotechnol. 2015, **208**: 80-86.

51. Ahammad A.J.S., Choi Y.H., Koh K., Kim J.H., Lee J.J. & Lee M.
Electrochemical detection of cardiac biomarker troponin I at gold nanoparticle-modified ITO electrode by using open circuit potential.
Int. J. Electrochem. Sci. 2011, **6**: 1906-1916.

52. Shan M., Li M., Qiu X.Y., Qi H.L., Gao Q. & Zhang C.X.
Sensitive electrogenerated chemiluminescence peptide-based biosensor for the determination of troponin I with gold nanoparticles amplification.
Gold Bull. 2014, **47**: 57-64.

53. Zhou F., Lu M., Wang W., Bian Z.P., Zhang J.R.& Zhu J.J.
Electrochemical immunosensor for simultaneous detection of dual cardiac markers based on a poly(Dimethylsiloxane)-gold nanoparticles composite microfluidic chip: A proof of principle.
Clin. Chem. 2010, **56**: 1701-1707.

54. Periyakaruppan A., Gandhiraman R.P., Meyyappan M. & Koehne J.E.
Label-free detection of cardiac troponin-i using carbon nanofiber based nanoelectrode arrays.
Anal. Chem. 2013, **85**: 3858-3863.

55. Masson J.F., Obando L., Beaudoin S. & Booksh K.
Sensitive and real-time fiber-optic-based surface plasmon resonance sensors for myoglobin and cardiac troponin I.
Talanta 2004, **62**: 865-870.

56. Eveness J., Kiely J., Hawkins P., Wraith P. & Luxton R.
Evaluation of paramagnetic particles for use in a resonant coil magnetometer based magneto-immunoassay.
Sens. Actuat. B Chem. 2009, **139**: 538-542.

57. Luxton R., Badesha J., Kiely J. & Hawkins P.
Use of external magnetic fields to reduce reaction times in an immunoassay using micrometer-sized paramagnetic particles as labels (magnetoimmunoassay).
Anal. Chem. 2004, **76**: 1715-1719.

58. Senyei A., Widder K. & Czerlinski G.
Magnetic guidance of drug-carrying microspheres.
J. Appl. Phys. 1978, **49**: 3578-3583.

59. Pankhurst Q.A., Connolly J., Jones S.K. & Dobson J.
Applications of magnetic nanoparticles in biomedicine.
J. Phys. D: Appl. Phys. 2003, **36**: R167-R181.

60. Graham D.L., Ferreira H. A. & Freitas P.P.
Magnetoresistive based biosensors and biochips.
Trends. Biotechnol. 2004, **22**: 455-462.

61. Do J. & Ahn C.H.
A polymer lab-on-a-chip for magnetic immunoassay with on-chip sampling and detection capabilities.
Lab. Chip 2008, **8**: 542-549.

62. Bruls D.M., Evers T.H., Kahlman J.A.H., van Lankvelt P.J.W., Ovsyanko M., Pelssers E.G.M., Schleipen J.J.H.B., de Theije F.K., Verschuren C.A., van der Wijk T., van Zon J.B.A., Dittmer W.U., Immink A.H.J., Nieuwenhuis J.H. & Prins M.W.J.
Rapid integrated biosensor for multiplexed immunoassays based on actuated magnetic nanoparticles.
Lab. Chip 2009, **9**: 3504-3510.

63. Kiely J., Hawkins P., Wraith P. & Luxton R.
Paramagnetic particle detection for use with an immunoassay based biosensor.
IET Sci., Meas. Technol. 2007, **1**: 270-275.

64. Todd J., Freese B., Lu A., Held D., Morey J., Livingston R. & Goix P.
Ultrasensitive flow-based immunoassays using single-molecule counting.
Clin. Chem. 2007, **53**: 1990-1995.

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