Development of a rapid, high sensitive point-of-care test for NT-proBNP based on Magnotech

Hefti MH¹, Nieuwenhuis JH², Raymond F³, de Theije FK², Immink AHJ², İncorporograt B³
¹Future Diagnostics, ²Philips Healthcare Incubator, and ³bioMérieux France
hefti.m@future-diagnostics.nl

Introduction

Point-of-care (POC) in vitro diagnostic applications are very demanding in a number of areas: performance, time-to-result, and reliability. The Magnotech technology enables developing immunoassays that can meet these requirements. Here we present the current status for the assay development of NT-proBNP, a specific marker for the diagnosis and monitoring of heart failure. This NT-proBNP assay is rapid, sensitive and shows a good correlation when compared to immunoassays currently on the market.

Method

Magnetism is the driving force behind each Magnotech immunoassay. A magnetic concentration step ensures fast binding kinetics whereas the active assay control based on magnetic actuation ensures good precision. The NT-proBNP assay uses 2 different monoclonal antibodies. One is coupled to magnetic particles, and the other one is bound to the cartridge surface (“print spot”). A surface sensitive technique involving frustrated total internal reflection (f-TIR) is used to detect the presence of magnetic particles attached to the sensor surface.

Time to result

One of the key requirements for point-of-care tests is a short time-to-result. The current NT-proBNP assay time is less than 4 minutes, when using plasma.

Flexibility

The system is able to read out a signal prior to the end of the measurement time, without disturbing the end result. This creates flexibility allowing for increased dynamic range by using two or more intermediate time points as read out signal (depicted by arrows in the picture below).

Assay performance

To be a viable alternative for automated system analysers, for POC applications the assay sensitivity is important. Our Magnotech NT-proBNP assay has an analytical sensitivity in the same range (currently around 10 pg/mL) as for example the bioMérieux VIDAS NT-proBNP assay ref. 30449 (20 pg/mL).

In February the status of the assay was compared with VIDAS NT-proBNP assay (bioMérieux) by Passing and Bablok fit using a set of 65 Lithium Heparin patient plasma samples. The corresponding slope was 1.19 (95% CI 1.04 to 1.34) and an intercept of 147.5 (95% CI -6.56 to 307.43) with a correlation of R=0.88 over the range 20 to 6518 pg/mL (see correlation graph, left panels).

The last months we targeted on an extended dynamic range up to 25000 pg/mL. Evaluated using a limited set of 39 Lithium Heparin patient plasma samples we are able to measure over the range of 59 to 20372 pg/mL without significant impact on the correlation with VIDAS. The corresponding slope was 1.03 (95% CI 0.89 to 1.21) and an intercept of 4.98 (95% CI -355.27 to 158.89) also with a correlation of R=0.88 (see correlation graph, right panels).

Oncoming improvements

In the next phase a filter will be added to the cartridge allowing measuring whole blood as well as plasma. First experiments showed that when using whole blood the filling time of the disposable cartridge is less than 30 seconds, resulting in a total time-to-result of less than 5 minutes.

Another functionality that will be explored is the introduction of 1 (or more) additional print spots on the cartridge surface. These print spots can be optimized to react less intense to exposure of NT-proBNP analyte, allowing another possibility to work on dynamic range in combination with high sensitivity.