Performance Evaluation of the NT-proBNP Assay* Using Acridinium Ester Technology on the ADVIA Centaur XP Immunoassay System


Abstract

Background: The measurement of NT-proBNP is a useful aid in the diagnosis and assessment of severity of congestive heart failure. Siemens Healthineers is currently developing an NT-proBNP assay for serum and plasma on the ADVIA Centaur® Immunoassay Systems.

Methods: The ADVIA Centaur NT-proBNP (PBNP) assay* is a fully automated two-site sandwich immunoassay using direct chemiluminescent technology and a new acridinium ester (TSP-AE). NT-proBNP reagents include a biotinylated sheep monoclonal antibody in the Ancillary reagent, a second sheep antibody labeled with the newly developed acridinium ester in the Lite reagent, and streptavidin-coated paramagnetic latex particles in the solid phase. Samples are incubated with the Ancillary reagent and solid phase to form a PBNP/biotinylated antibody/solid phase complex. Lite reagent is added and allowed to incubate, resulting in the formation of an acridinium ester/PBNP/biotinylated antibody/solid phase complex. Separation occurs, and the signal is proportional to the concentration of NT-proBNP in the sample.

Results: The method requires 20 μL of serum or plasma. Time to first result is 18 minutes, with stable calibration for 28 days. 28-day open-well stability has been achieved. Linearity was demonstrated over the range of <LOQ to >35,000 pg/mL. With automated dilution, the measuring interval is extended to 350,000 pg/mL. Equivalent results were obtained among serum, lithium heparin plasma, and EDTA plasma. Reproducibility was assessed using the CLSI EP5-A2 protocol with serum samples ranging from 84 to 30,145 pg/mL. Repetitivities CIs ranged from 1.4 to 3.5%. Within-lab CIs ranged from 2.0 to 4.3%. In accordance with the CLSI EP5-A2 protocol, no interference was observed with 75 ng/mL biotin.

Precision

• CLSI protocol EP05-A2
• Nine samples, two runs/day for 20 days
• 11 samples tested, n = 5

• Assay precision. Repeatability CVs ranged from 1.4 to 2.3%. In subjects with left ventricular dysfunction, serum and plasma concentrations of BNP and proBNP increase, as do the concentrations of the N-terminal fragment NT-proBNP. Studies indicate that NT-proBNP can be used in diagnostic and prognostic applications.

Introduction

The World Health Organization (WHO) lists cardiovascular disease as the leading cause of death worldwide.1 Heart failure (HF) is a clinical syndrome resulting from cardiac disease that compromises ventricular function. It is often considered the end stage of cardiac disease, brought on by a number of different conditions including cardiomyopathy, hypertension, and acute myocardial infarction. Heart failure is also a disease that is more prevalent in older patients, with a worldwide prevalence of 10% in patients >75 years old.2 Thus, as the population ages, incidence of heart failure is expected to grow. In subjects with left ventricular dysfunction, serum and plasma concentrations of BNP and proBNP increase, as do the concentrations of the N-terminal fragment NT-proBNP. Studies indicate that NT-proBNP can be used in diagnostic and prognostic applications.

Materials and Methods

Figure 1. Principle of the assay.

Linear regression was demonstrated for the assay. The percent bias from the weighted linear fit was <10% or ≤10 pg/mL across the assay range.

Sample-Type Equivalence

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Conclusion

• Fully automated assay on the ADVIA Centaur Immunoassay Systems
• Repeatability ≤3.5%; within-lab precision ≤4.3%
• No interference to 75 ng/mL biotin
• Correlation with the proBNP II assay on the Roche cobas e 411 system

References


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