

Development of a High Sensitivity Cardiac Troponin I Method for the Dimension Vista™ Intelligent Lab System

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Introduction

Cardiovascular disease is the leading cause of death in the United States and is a major cause of disability. More than two of every five Americans die of cardiovascular disease with 2,500 Americans dying from heart disease each day. In 2006, heart disease is projected to cost more than \$258 billion, including health services, medication, and lost productivity.

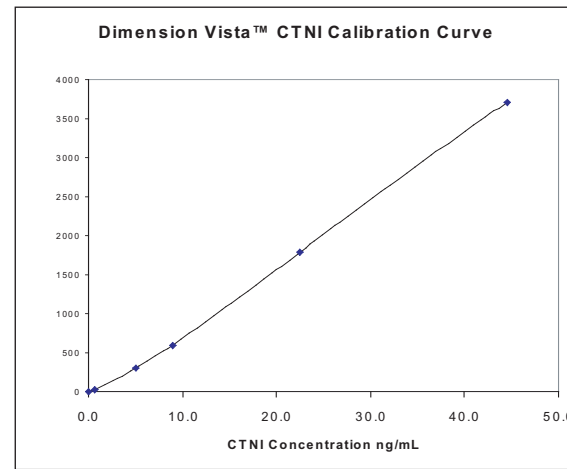
Cardiac troponin is the cornerstone for the detection of myocardial injury, risk stratification in acute coronary syndromes (ACS), and for the diagnosis of acute myocardial infarction (AMI). In order to ensure accurate identification of troponin positive patients, the laboratory must utilize an assay which is highly sensitive, specific, and precise. The ability to deliver accurate troponin results allows for early diagnosis, which can guide treatment resulting in improved patient outcomes.

This poster describes the design and performance of the cardiac Troponin I assay for the Dimension Vista™ Intelligent Lab System. The excellent sensitivity and precision of the method make it a useful monitor of troponin I levels throughout all stages of cardiovascular disease.

Dimension Vista™ cTnI (CTNI) methodology

The CTNI method is a homogeneous, sandwich chemiluminescent immunoassay based LOCI™ technology. The LOCI™ reagents include two latex bead reagents and a biotinylated anti-cardiac troponin I monoclonal antibody fragment. The first bead reagent (Sensibeads) is coated with streptavidin and contains photosensitizer dye. The second bead reagent (Chemibeads) is coated with a second anti-cardiac troponin I monoclonal antibody and contains chemiluminescent dye. Sample is incubated with Chemibeads and biotinylated antibody to form bead-cardiac troponin I-biotinylated antibody sandwiches. Sensibeads are added and bind to the biotin to form bead-pair immunocomplexes. Illumination of the complex at 680 nm generates singlet oxygen from Sensibeads, which diffuses into the Chemibeads, triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is a direct function of the cardiac troponin I concentration in the sample. The time to first result is 10 minutes.

Calibration Curve



General Performance Characteristics

Assay Range	0 – 40.0 ng/mL
Analytical Sensitivity	< 0.015 ng/mL
Calibration Interval	30 Days
Time To First Result	10 Minutes
Sample Size	20 µL Serum

Reproducibility

Reproducibility of the method was evaluated using CLSI protocol EP5-A2. The protocol consisted of taking one replicate from each of two sample cups at two time points per day for twenty days. The time points during each day were separated by a minimum of two hours. All results were based on a single calibration done at the start of the study. The data were treated by analysis of variance to determine within-run (repeatability) and total (within-lab) reproducibility estimates.

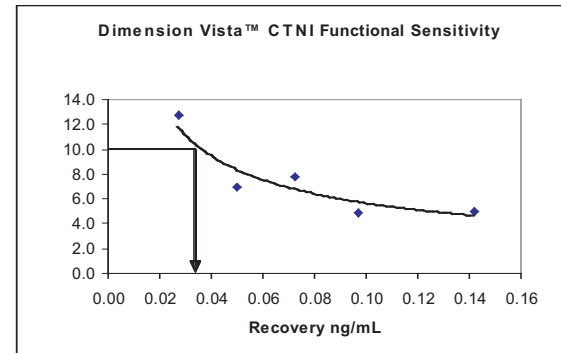
	Serum QC		QC Level 1*	
Mean Recovery ng/mL	0.067	0.39	22.7	0.073
Repeatability % CV	5.24	1.79	1.09	5.34
Within Lab % CV	7.77	6.20	4.32	7.36

*Bio-Rad Liquichek™ Cardiac Markers Control LT

Analytical and Functional Sensitivity

Analytical sensitivity was evaluated by running 20 replicates of normal serum with the Dimension Vista™ CTNI assay. Analytical sensitivity was calculated as the mean recovery plus two standard deviations. The analytical sensitivity was determined to be less than 0.015 ng/mL.

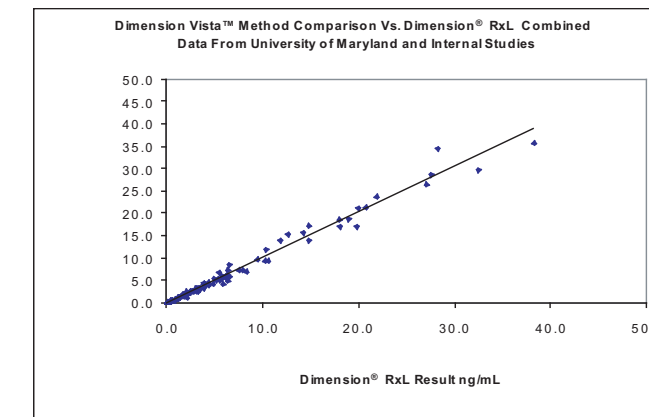
Functional sensitivity is defined as the lowest concentration of troponin I with a total precision (%CV) of 10%, based on a two replicate per run, one run per day, 20 day reproducibility study. Five serum samples were tested, and the troponin I concentration with a 10% total CV was read from the curve. The functional sensitivity was determined to be approximately 0.04 ng/mL.



Method Comparison

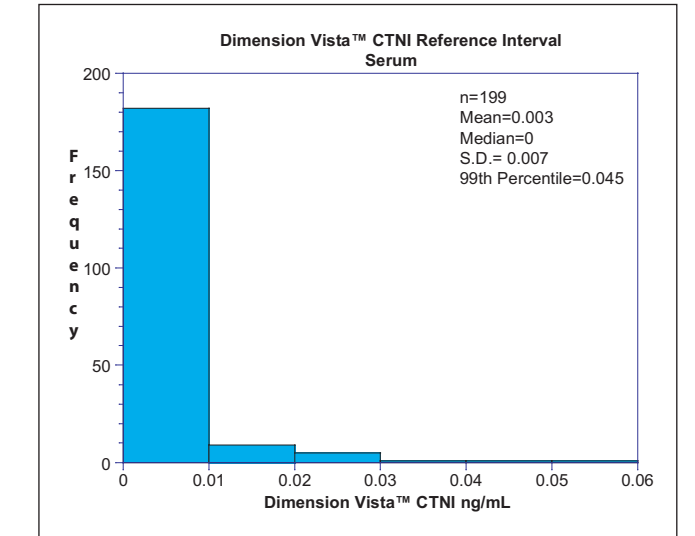
The Dimension Vista™ CTNI assay was compared to the Dimension® RxL through a split sample correlation study using patient serum. The data include samples processed at University of Maryland Medical Center and samples processed at Dade Behring. Analysis by linear regression shows excellent agreement between the methods.

Slope: 1.01 ± 0.009
Intercept: -0.003 ± 0.06
 $r = 0.993$
 $S_{y,x} = 0.76$
 $N = 197$



Reference Interval

A reference interval study was done with serum samples from 199 apparently normal individuals. The 99th percentile was determined to be 0.045 ng/mL.



Conclusions

The Joint European Society of Cardiology/American College of Cardiology Committee recognizes troponin as the preferred biochemical marker for myocardial damage, and also recommends an imprecision level (coefficient of variation or CV) for troponin assays of <10% at the 99th percentile of normal. The Dimension Vista™ CTNI method meets those requirements and has the performance characteristics of a high sensitivity troponin I method.