

Development of an easy-to-use C-reactive protein (CRP) point-of-care test (POCT) for analysis from easily accessible capillary whole blood samples

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Background

C-reactive protein (CRP) has been extensively studied and compared for its efficacy as a marker of inflammation and bacterial infection [1, 2]. In a point-of-care setting, a serial monitoring of patients' CRP values is vital to patient outcomes. The optionally battery-assisted DiaSys InnovaStar® setup [Figure 1] allows access to CRP values through a convenient and minimally-invasive capillary puncture even in remote settings. Assisting in antibiotic treatment decisions by ensuring easy access to a patient's CRP value, InnovaStars' CRP point-of-care-test (POCT) will help to protect against the mounting global problem of antibiotic resistance. The detection of untreated bacterial infections remains the primary cause of death of children below the age of 5 [3, 4]. More than 90% of these deaths occur in the poorest countries of Asia and Africa [5].

Objective

Development of a CRP POCT that additionally detects the hemoglobin concentration to calculate plasma corrected values, thus allowing the measurement of CRP from easily accessible capillary whole blood samples.

Methods & Results

We developed a latex-enhanced immunoturbidimetric assay on the DiaSys InnovaStar POC analyzer and evaluated the results of whole blood / plasma pairs and correlated these to CRP plasma values from an automated clinical Hitachi 917 analyzer. The performance characteristics were evaluated according to the CLSI guidelines which included analytical sensitivity, linearity, precision and accuracy.

For whole blood we acquired the following results for CRP IS POCT: CRP IS® showed a limit-of-blank (LoB) of 1.27 mg/L and a limit-of-quantitation (LoQ) of 2.76 mg/L [9]. The upper limit of linearity was 365 mg/L ($R^2 = 0.99$) [Figure 2] [7]. At a CRP concentration of 5, respectively 40 mg/L we established for whole blood a CV of 3.7 respectively 3.1% for repeatability and between-run and between-day CVs of below 2% [6].



Figure 1: Battery assisted InnovaStar POC

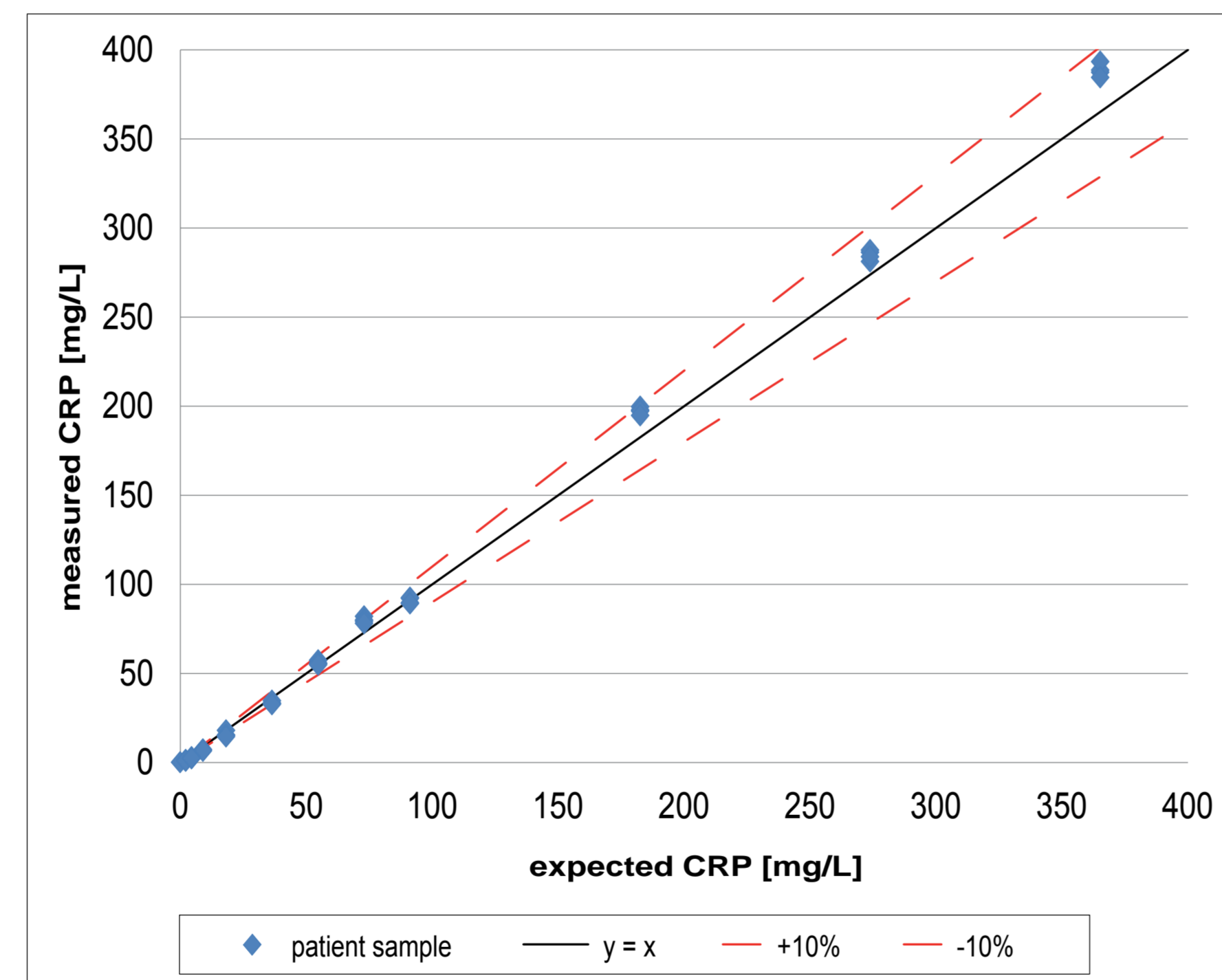


Figure 2: CRP linearity for whole blood within $\pm 10\%$ limits

Table 1: Tolerable interferences [8].

Interferent	CRP 5 mg/L	CRP 40 mg/L
Lipid	2000 mg/dL	2000 mg/dL
Bilirubin, unconjugated	60 mg/dL	60 mg/dL
Bilirubin, conjugated	60 mg/dL	60 mg/dL
Rheumatoid Factor	500 IU/mL	500 IU/mL
Hemoglobin	20 g/dL	20 g/dL

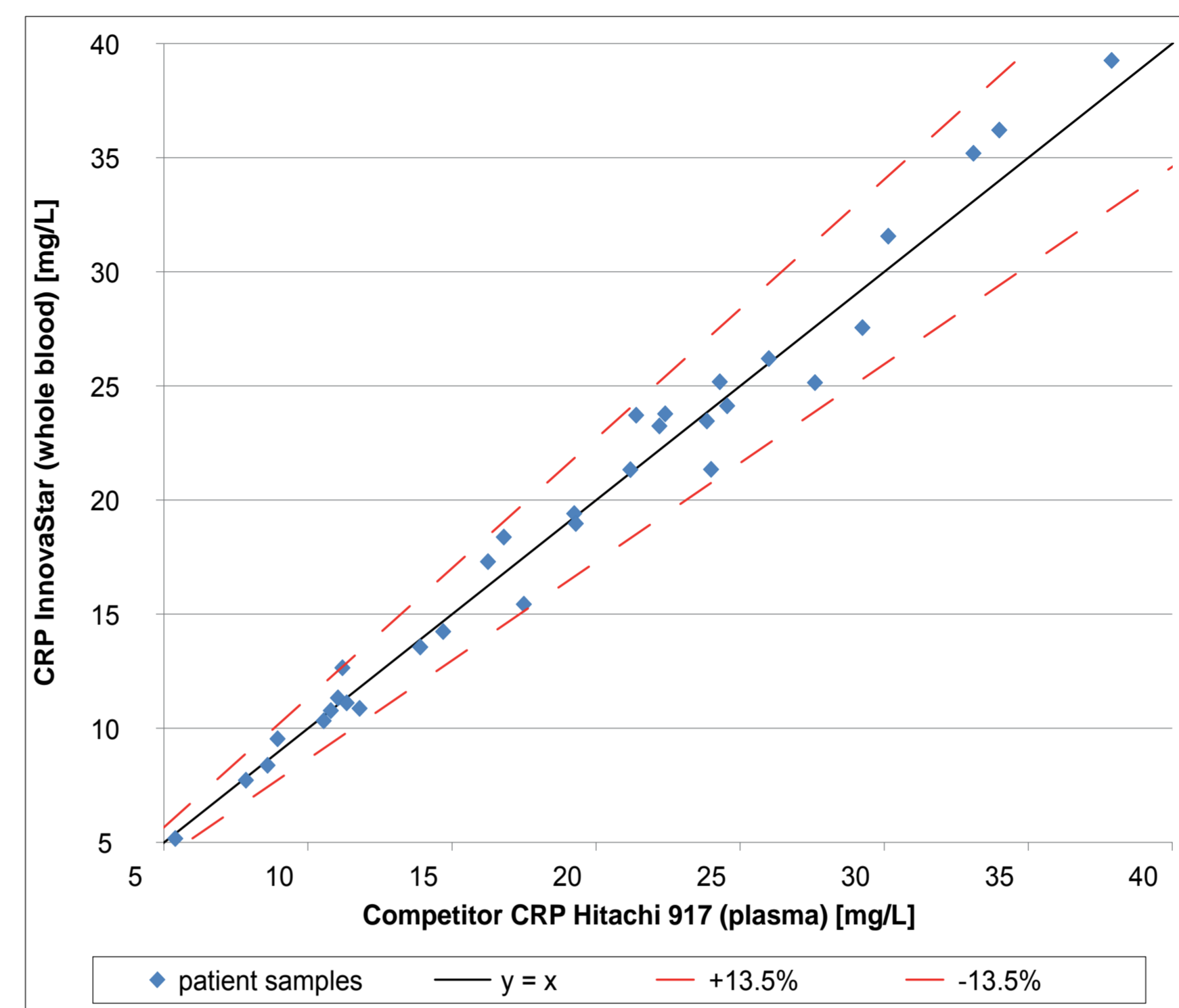


Figure 3: Method comparison to competitor CRP measuring whole blood [10]

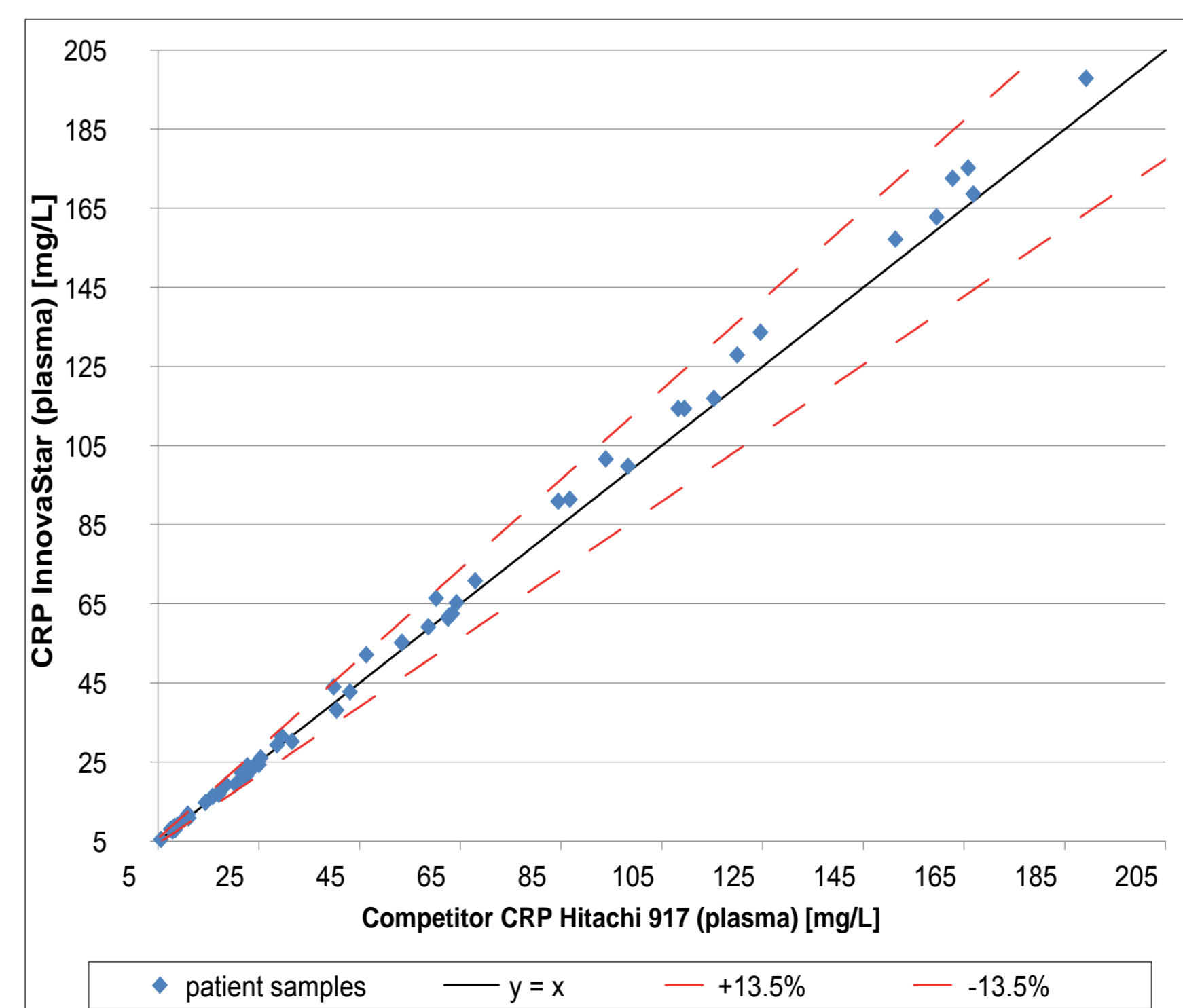


Figure 4: Method comparison to competitor CRP measuring plasma [10]

A preliminary method comparison applying whole blood ($n = 38$) or plasma samples ($n = 60$) on CRP IS against plasma values from a competing CRP reagent (Hitachi 917) showed a linear correlation with a slope of 1.0576 and an intercept of -0,8793 ($R^2 \geq 0.98$) [Figure 3, 4]. Tolerable interferences [Table 1] have been evaluated at a concentration of 5 and 40 mg/L CRP [8]. No prozone effect was observed for CRP concentrations of up to 1800 mg/L.

Conclusion

Our results clearly demonstrated that the DiaSys InnovaStar CRP IS POC analyzer's performance characteristics are comparable to a fully-automated clinical chemistry analyzer. The CRP IS is an easy-to-use POCT. Utilized in a point-of-care setting, the emergency room, in rural and remote areas or for serial monitoring of patients it provides a substantial benefit for treatment decisions.

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