PT/INR Test Performance of the Xprecia Stride Coagulation Analyzer

Demonstrates Equivalency with Established Laboratory Hemostasis and Point-of-care Methods

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Introduction

Primary care, urgent care, and other point-of-care (POC) locations demand fast, reliable prothrombin time/international normalized ratio (PT/INR) test results to support oral anticoagulant therapy (OAT).

The Xprecia Stride™ Coagulation Analyzer* from Siemens Healthcare Diagnostics is a handheld POC device that generates rapid PT/INR test results from fingerstick samples.

This external validation study, conducted under ICH/GCP† guidelines, assessed the clinical substantial equivalence of the Xprecia Stride analyzer PT/INR test against an established laboratory hemostasis method (BCS® XP System, Siemens Healthcare Diagnostics).

Summary

Method comparison between the Xprecia Stride analyzer and the BCS XP System demonstrated excellent correlation (r^2 = 0.89) and 0.0 PT/INR bias at medical decision levels.

Reproducibility/intermediate precision demonstrated that liquid quality control (LQC) met the industry-standard acceptance criterion of ≤10%. In addition, repeatability was also found to be well within the same acceptance criterion.

The data and subsequent analysis validate the intended clinical use of the Xprecia Stride Coagulation Analyzer for near-patient PT/INR testing using capillary blood.

The Increasing Demand for Oral Anticoagulant Therapy (OAT)

OAT is prescribed on a long-term basis for people who have experienced recurrent abnormal blood clotting, or for those who are at high risk of developing clots. For example, patients with atrial fibrillation (AF), a common cardiac arrhythmia that affects more than 6 million people in Europe and 2.6 million in the USA,[1] are at risk for blood clots, including those that cause ischemic stroke. OAT is frequently prescribed to reduce these stroke risks, but the medications usually necessitate frequent patient PT/INR monitoring.

The Xprecia Stride Analyzer is an accurate, convenient, easy-to-use handheld instrument with enhanced safety features designed to protect operators during the testing process.

More than 800 million PT/INR tests are conducted annually worldwide.[2] An increasing population of patients on warfarin (COUMADIN) therapy and the trend toward testing away from the central laboratory have escalated the demand for PT/INR tests at the point of care:

- POC PT/INR test settings include the physician's office, outpatient clinics, and diverse hospital locations, including the emergency room, coronary care unit, operating rooms, and the radiography department.
- PT/INR testing at the point of care facilitates rapid interventions that may help to optimize patient therapy.

Clinical Utility

The Xprecia Stride Coagulation Analyzer is intended for near-patient monitoring of PT/INR testing on capillary blood samples. It is an accurate, convenient, easy-to-use handheld instrument with enhanced safety features designed to protect operators during the testing process:

- Fast results across the 0.8–4.5 INR reporting range
- Small, 6 µL sample size
- Push-button ejection of used test strips to minimize biohazard exposure
- Easy-to-use color touchscreen interface and clear display of results as INR units
- Integrated bar-code scanner to facilitate rapid, error-free data capture
- Seamless, secure bidirectional data transfer via USB connection

Test Technology

The Xprecia Stride analyzer uses electrochemical technology and single-use reagent test strips to measure the prothrombin time. A sample chamber in the test strip is filled with the blood sample by capillary action.

The strip contains dried reagents consisting of thromboplastin, an electroactive thrombin substrate, and other reagents. An electroactive group, released from the thrombin substrate, is detected electrochemically at the electrodes in the strip; the current produced is analyzed by an algorithm to determine the coagulation time. Each test strip is analyzed by two on-strip quality control checks when a sample is applied to check for presence of adequate test sample and reagents on the test strip and for test strip degradation due to exposure to environmental factors. If either control fails, the analyzer will report an error and cancel the test.

Liquid quality control (LQC) material offers users the option of testing in accordance with local, state, federal, or national guidelines.

Siemens Healthineers has been a market leader in laboratory hemostasis solutions for more than 30 years and now can provide a POC solution for coagulation testing. The Xprecia Stride Coagulation Analyzer extends our hemostasis expertise into the POC arena and gives customers the choice of a broad portfolio of analyzers from the same manufacturer.

The Xprecia Stride analyzer uses the Dade® Innovin® reagent—the same reagent used by Siemens Healthineers lab analyzers—removing a potential area for variability between lab and POC test results.

Study Purpose

The PT/INR test on the Xprecia Stride Coagulation Analyzer must demonstrate clinical substantial equivalence to the clinical reference method. Accurate results—in terms of precision and low bias—facilitate optimal use of the analyzer for clinical decision making. The study investigated:

- Agreement versus a proven reference laboratory method used for PT/INR testing
- Reproducibility/intermediate precision (LQC levels 1 and 2)
- Repeatability
- Expected INR range for study subjects not on anticoagulation therapy

Methods

General

364 study subjects, comprising patients receiving warfarin therapy and individuals not on warfarin therapy, were enrolled at four clinical sites[‡] over an 11-month period. At each site, subjects provided two separate whole-blood capillary samples via finger puncture for immediate PT/INR testing by qualified POC operators on the Xprecia Stride Coagulation Analyzer. Each subject also provided a whole-blood sample collected in a citrated tube. These samples were centrifuged to generate platelet-poor plasma and then frozen. Frozen samples were shipped to a laboratory[§] for PT/INR testing on the reference Siemens Healthcare Diagnostics BCS XP System using Dade Innovin reagent. The same aliquot of sample was measured twice and the INR results averaged to give the laboratory INR value. Subsequent data analysis was performed by Universal Biosensors Pty Ltd (Rowville, Victoria, Australia).

The study was conducted using reagent test strips, analyzers, and INR liquid quality control materials manufactured on validated lines.

Method comparison study

Results from the first drop of fingerstick whole blood from study subjects (n = 364) were used to determine agreement and bias in INR measurement. Xprecia Stride analyzer results across two INR ranges (<2.0, and 2.0–4.5) were used for method comparison. These ranges provided a distribution of subject results across the measuring range. Study subjects were allocated to a range based on their averaged laboratory INR reference value.

Results from both analytical methods were used to perform a Passing-Bablok regression. The slope (95% CI), y-intercept (95% CI), correlation coefficient (r), and coefficient of determination (r^2) were calculated. Passing-Bablok regression acceptance criteria up to 4.5 INR were defined as:

- Slope: 95% confidence interval within 0.80–1.20
- Intercept: +0.3 to -0.3
- Coefficient of determination (r^2) ≥0.82

Bias of the Xprecia Stride analyzer PT/INR test was calculated at two medical decision points (INR = 2.0 and INR = 4.5; see Table 1).

Reproducibility/intermediate precision study

Reproducibility/intermediate precision data was generated by qualified operators at each site performing tests on the Xprecia Stride analyzer with LQC levels 1 and 2 in duplicate at the beginning and end of 20 days of testing. Across the four sites, testing was conducted using three lots of reagent test strips and three lots of PT liquid quality control kits. The multiple parameters calculated from complete datasets for each site analyzer at each LQC level are shown in Table 3.

Repeatability study

The difference between results from pairs of capillary samples obtained from two separate fingersticks and tested on the same analyzer was used to assess repeatability. Valid pairs from 364 study subjects (all clinical sites) were used for repeatability data analysis. Mean INR, the standard deviation, and the %CV were calculated across three INR ranges (<2.0, 2.0–3.0, and 3.1–4.5; see Table 2).

Expected range

Xprecia Stride analyzer PT/INR test results (n = 120, 84 results sourced from this study, combined with 36 results from an in-house study) were used to evaluate the expected range for nontherapeutic individuals. The normal range was reported as lower and upper INR values enclosing 95% of results.

Results

Method comparison study

Figure 1 shows a plot of the Passing-Bablok regression performed on capillary blood PT/INR results from Xprecia Stride analyzers compared to PT/INR results with the reference BCS XP System. Table 1 presents method comparison regression statistics and calculated bias.

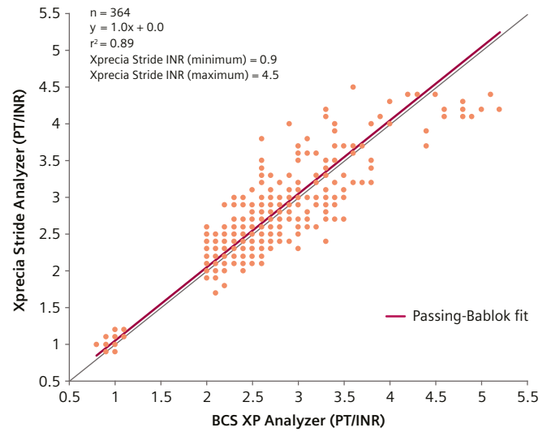

Figure 1. Plot of Passing-Bablok regression fit (red) and line of identity (gray).

This study demonstrated excellent correlation (r^2 = 0.89) of the Xprecia Stride Coagulation Analyzer PT/INR test with the reference laboratory BCS XP System method.[3]

Table 1. Xprecia Stride analyzer versus BCS XP System method comparison regression statistics and calculated bias.

Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r)	Coefficient of Determination (r^2)	Calculated Bias at 2.0 INR	Calculated Bias at 4.5 INR
1.0 (0.95 to 1.00)	0.0 (0.0 to 0.1)	0.944	0.89	0.0	0.0

The study also showed the low bias of the test compared with laboratory BCS XP System INR measurement. At the medical decision points of 2.0 INR and 4.5 INR, 0.0 INR bias was observed, well within the acceptance criterion defined as not to exceed a median bias of ±0.3.

Repeatability study

Table 2. INR results for the Xprecia Stride analyzer on paired samples of capillary blood.

Summary of Repeatability SDs and %CVs for Xprecia Stride Analyzer PT/INR Results									
Site-PT/INR Range (BCS XP)	INR (<2.0)			INR (2.0–3.0)			INR (3.1–4.5)		
	Xprecia Stride Analyzer Within Run			Xprecia Stride Analyzer Within Run			Xprecia Stride Analyzer Within Run		
	N	SD	%CV	N	SD	%CV	N	SD	%CV
Combined Sites	168	0.06	5.8	418	0.14	5.3	120	0.15	4.5

Data analysis demonstrated that, across the three INR ranges, repeatability %CVs were ≤5.8, well below the industry-standard criterion of acceptance of %CV ≤10%.

Expected range

For capillary blood, the Xprecia Stride analyzer INR test range of 0.9 to 1.1 encompassed 95% of results for subjects not on oral anticoagulation therapy.

Reproducibility/intermediate precision study

Table 3. Reproducibility/intermediate precision of PT liquid quality control (LQC) testing across study locations.

				Repeatability (formerly called Within Run)		Within Laboratory (formerly called Total)	
Control Level	Site	N	Mean	SD	%CV	SD	%CV
PT Control 1	1	80	1.27	0.03	2.5	0.05	3.9
	2	80	1.29	0.03	2.3	0.04	2.8
	3	80	1.20	0.02	1.8	0.02	1.9
	4	80	1.24	0.04	3.3	0.06	5.0
PT Control 2	1	80	3.18	0.06	1.8	0.15	4.7
	2	80	3.22	0.07	2.2	0.10	3.1
	3	80	3.18	0.05	1.6	0.09	2.7
	4	80	3.11	0.11	3.6	0.26	8.3

Discussion and Conclusions

The Xprecia Stride Coagulation Analyzer was validated according to its intended use with capillary blood. All test acceptance criteria over the measuring range were passed, with the following Passing-Bablok regression results:

- Slope: 1.0 (95% CI 0.95 to 1.0)
- Intercept: 0.0 (95% CI 0.0 to 0.1)
- Coefficient of determination (r^2) ≥0.89

The PT/INR test showed equivalency when compared to the PT/INR test of the reference BCS XP System. Bias was notably low at two key PT/INR medical decision points (2.0 PT/INR and 4.5 PT/INR, bias 0.0). Reproducibility/intermediate precision was ≤8.3% CV, meeting an acceptance criterion of ≤10% CV. Test repeatability was ≤5.8% CV, also well below this criterion of acceptance.[3]

The Xprecia Stride analyzer PT/INR test has equivalent performance to a reference lab test. Trained healthcare practitioners can confidently use the test at the point of care to monitor patients on warfarin oral anticoagulant therapy.

The reliable, lab-quality performance of the Xprecia Stride Coagulation Analyzer is complemented by its speed, simplicity, efficiency, and overall practicality in point-of-care settings.

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The reliable, lab-quality performance of the Xprecia Stride analyzer is complemented by its speed, simplicity, efficiency, and overall practicality in POC settings.

*Product availability varies by country.
†International Conference on Harmonization/Good Clinical Practice.
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