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# Evaluation of the Atellica COAG 360 coagulation analyzer in a central laboratory of a maximum care hospital

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## Abstract

**Introduction:** Fully-automated coagulation analyzers are key components of a high-throughput central laboratory. The novel Atellica COAG 360 (Siemens Healthineers) is a high-volume coagulation analyzer approved for hemostasis diagnostics. The aim of the study was to evaluate the analytical performance of this coagulation analyzer in a central laboratory.

**Methods:** Intra (n = 10)- and inter (n = 20)-assay precision of the Atellica COAG 360 was determined using commercially available control samples. Patient samples (n = 74-104) were used for comparison analyses with the Sysmex CS-5100 (Siemens Healthineers). Effects of visual interferences on coagulation testing were assessed and the sample throughput rate of the Atellica COAG 360 was determined.

**Results:** Intra- and inter-assay precision of the Atellica COAG 360 showed coefficient of variations (CVs) < 5% for most of the coagulation parameters comparable to CVs of the Sysmex CS-5100. Passing-Bablok and Bland-Altman analyses revealed high correlation and good agreement between both coagulation analyzers in determination of coagulation parameters. Results of coagulation measurements determined in optically abnormal samples were comparable between the Atellica COAG 360 and the Sysmex CS-5100 and were confirmed by mechanical measurements on a STart Max (Stago Diagnostics) coagulation analyzer. A sample throughput rate of about 190 tests per hour in a routine setting including five coagulation parameters was determined for the Atellica COAG 360 integrated in a total laboratory automation system.

**Conclusion:** The Atellica COAG 360 provides high analytical performance as high-throughput analyzer for routine and specific coagulation parameters and is suitable to be connected to a total laboratory automation.

KEYWORDS

Atellica COAG 360, automated analyzer, coagulation, hemostasis, total laboratory automation

## 1 | INTRODUCTION

Assessment of blood clotting function is crucial in numerous routine and emergency situations including diagnostic and therapeutic management of hemostasis disorders, unexplained bleeding situations, and the perioperative management.[1,2] The most widely and frequently used tests are prothrombin time (PT) and activated partial thromboplastin time (aPTT), representing

the extrinsic and intrinsic coagulation system, respectively. Besides global coagulation tests, determination of specific coagulation parameters, such as single coagulation factor activities, von Willebrand (vWF) activity, or protein C, are essential for diagnosis and management of hemostatic disorders. Increasing centralization and consolidation of hemostasis diagnostics together with a growing global hemostasis market require fully-automated coagulation analyzers for high-throughput coagulation testing.[3,4] Nowadays, high-volume coagulation testing can be performed by fully-automated coagulation analyzers, which allow the fast, accurate, and reliable measurement of coagulation parameters thereby maintaining high quality.[4-8] However, pre-analytical issues are still challenging and have to be considered in laboratory medicine and in particular in hemostasis testing.[4] Besides control of sample transportation, this includes primary tube check, sample volume check, and the detection of interfering substances in plasma samples. Therefore, most of the clinical chemistry and coagulation analyzers provide plasma indices for detection of interferences, such as hemolysis (H-index), icterus (I-index), and lipemia (L-index). Total laboratory automation was first developed for analyzers in clinical chemistry and immunochemistry reflecting the need for an efficient and optimized workflow.[9] Coagulation analyzers are increasingly becoming part of laboratory automation in central laboratories reducing the number of stand-alone coagulation analyzers and the total turnaround time, thus being cost and labor saving.[4]

The novel coagulation analyzer Atellica COAG 360 (Siemens Healthineers) is a fully-automated hemostasis system and the first analyzer combining five different analytical technologies on one platform. Coagulation testing can be performed by use of clotting (optical and optomechanical) and immunologic assays, by LOCI (Luminescent oxygen channeling assay) technology-based high-sensitivity immunoassays or by aggregation tests. It features plasma quality assessment by determination of plasma indices and allows continuous access to cooled reagents and consumables. For the use in a central laboratory, the Atellica COAG 360 can be connected to a track line of a laboratory automation.

The aim of the present study was to evaluate the analytical performance and throughput capability of the Atellica COAG 360 analyzer connected to a total laboratory automation in a central laboratory on 24/7 duty.

## 2 | MATERIALS AND METHODS

### 2.1 | Study design and sample collection

The study was conducted at the Institute for Clinical Chemistry and Pathobiochemistry in the Department for Diagnostic Laboratory Medicine at the University Hospital in Tübingen. Measurement of coagulation parameters was performed using citrate-containing plasma patient samples (Sarstedt) from clinical routine (n = 74-104). All samples were centrifuged for 10 minutes at 2500 *g* and anonymized using individualized identification numbers for each sample tube to ensure anonymity of patients. Plasma supernatants were transferred into at least two identical aliquots and were immediately measured. Determination of sample throughput rate was performed using freshly collected citrate-containing plasma samples from healthy volunteers (n = 45). Written informed consent was obtained from healthy volunteers prior to blood sample collection. The study was conducted in accordance with the Declaration of Helsinki from 1964 and its later amendments and approved by the local Ethics Committee of the medical faculty of Tübingen (protocol number: 113/2014BO1).

### 2.2 | Reagents, calibrators, and controls used on coagulation analyzers

Reagents, calibrators, and controls were used on the Atellica COAG 360 according to the instructions of the manufacturer and standard operating procedures (see Table S1). The same reagents were used on the Sysmex CS-5100 (Siemens Healthineers) and the STart Max (Diagnostica Stago SAS) coagulation analyzers. Reference ranges (5th-95th percentiles) and onboard reagents stabilities are provided according to the manufacturer for the Atellica COAG 360. A gender-specific reference range is provided for protein S (free) and a 90th percentile for D-dimer.

### 2.3 | Atellica COAG 360 coagulation analyzer

The Atellica COAG 360 coagulation analyzer provides 25 flexible reaction detector positions of which 24 positions are intended for clotting, chromogenic, and immunologic assays (340, 405, 630, and 850 nm) and one specific position for LOCI (680 nm) measurements. In total, the analyzer has a maximum load capacity of 150 samples (30 racks à five samples). Furthermore, one rack is defined as STAT sample rack with five priority positions. According to the manufacturer, the Atellica COAG 360 is able to perform 210 single tests of PT/aPTT, 350 simultaneous tests of PT/aPTT, and 310 simultaneous tests of PT/aPTT/AT/DD per hour. For assessment of sample quality, the analyzer performs a primary-tube volume check and a hemolysis, icterus, and lipemia ("HIL") check. Therefore, a 4-channel photometer with simultaneous multiwavelengths scanning (365, 415, 470, and 645 nm) is used. For each HIL-index, nine levels are defined and assay-specific thresholds are provided. Furthermore, the Atellica COAG 360 provides automated reflex, redilution, multidilution analysis and repeat testing using laboratory-specific rules. Cooled chambers and anti-evaporation caps can be used for most of the reagents. For integration into existing laboratory infrastructures, the Atellica COAG 360 can be connected, according to the manufacturer, to various laboratory automation and online data management systems.

### 2.4 | Assessment of linearity and of intra- and inter-assay precision and accuracy

Linearity of coagulation measurements was evaluated using samples from clinical routine with high levels of fibrinogen, antithrombin, D-dimer and FXIII. Samples were manually diluted (1:2, 1:4, 1:8, 1:16; and 1:32), and measurement results were correlated with theoretical assigned concentrations. A curve was determined by linear regression analysis, and linearity was assumed as acceptable when $R^2 > 0.95$.

Commercially available control samples (see Table S1) in the normal and abnormal range of respective parameters were used for determination of intra- and inter-assay precision and accuracy. Intra-assay precision was calculated for all indicated parameters by repeated measurements of the respective control samples 10 times in a single batch and reported as mean ± SD and the calculated coefficient of variation (CV%). Inter-assay precision was determined by measuring control samples twice a day over 20 days and reported as mean ± SD and the calculated CV%. Intra-assay and inter-assay accuracy was calculated as mean percentage difference between measurement results and known target values of commercially available control samples.

### 2.5 | Pre-analytical assessment of sample quality

Centrifuged samples from clinical routine were selected according to optical properties and defined as hemolytic, icteric, or turbid (lipemic) by visual inspection. Triglyceride and total bilirubin concentrations were determined on an ADIVA Centaur XPT clinical chemistry analyzer using enzymatic methods, and plasma hemoglobin concentrations were determined on a Dimension EXL 200 system using a spectrophotometric method (both Siemens Healthineers). INR, aPTT, fibrinogen, antithrombin, and D-dimer measurements were performed using the Atellica COAG 360 and the Sysmex CS-5100 coagulation analyzers, and results of both analyzers were compared. Furthermore, the STart Max, a coagulation analyzer based on mechanical clot detection was included in the study. The same reagents and calibrators, as provided in Table S1, were used for measurements of INR, aPTT and fibrinogen in the same hemolytic, icteric, and lipemic samples on the STart Max. Results were compared with previously obtained measurement results of the Atellica COAG 360.

### 2.6 | Sample throughput rate and STAT analysis

Plasma samples from healthy volunteers were used to determine sample throughput rate of the Atellica COAG 360 and the Sysmex CS-5100. In total, 45 citrated plasma samples were collected and subsequently centrifuged for 10 minutes at 2500 *g*. Five parameters (INR, aPTT, fibrinogen, antithrombin, and D-dimer) were measured in each sample. Centrifuged plasma samples were entered via an input/output module on the track-line system of the laboratory automation (Aptio Automation; Siemens Healthineers) and transported to the Atellica COAG 360 or Sysmex CS-5100 platform. Five samples with high priority (STAT samples) were also included in the performance study of the Atellica COAG 360.

### 2.7 | Statistical analysis

Results of coagulation measurements are presented as mean values with standard deviation (SD) for normally distributed data. Passing-Bablok regression and Bland-Altman analyses were performed for comparison of coagulation measurement results.[10,11] Statistical analyses were performed and figures were created using GraphPad Prism 7.03 (GraphPad Software).

## 3 | RESULTS

### 3.1 | Assessment of linearity and carryover

Routine coagulation parameters, like fibrinogen ($R^2$ = 0.998; 0.5-4.5 g/L), antithrombin ($R^2$ = 0.996; 6.1%-127%), D-dimer ($R^2$ = 0.994; 0.2 µg/mL FEU-16.0 µg/mL FEU), and FXIII ($R^2$ = 0.973; 5.2%-150%) showed high linearity in broad and clinically relevant concentration ranges. To evaluate potential carryover, aPTT was measured five times after determination of a heparin-spiked sample (>2 U/mL of unfractionated heparin). No prolongation of aPTT could be detected.

### 3.2 | Analytical accuracy and intra-assay and inter-assay precision

Intra- and inter-assay precision of the Atellica COAG 360 was calculated using commercially available control samples with normal and abnormal levels in regard of reference intervals or threshold concentrations of respective parameters (see Table 1). Calculations revealed intra-assay coefficients of variation (CV) <5% for most of the coagulation parameters. Slightly increased CVs were observed for D-dimer (normal level, 7.1%), FV (normal level: 6.6%; abnormal level, 7.8%), FVIII chromogenic (normal level, 5.6%), FIX (low level, 6.2%), and FX (low level, 6.7%). Calculation of inter-assay precision on 20 consecutive days revealed CVs < 5% for the majority of investigated coagulation parameters. Again, D-dimer (normal level, 5.7%), FV (normal level, 7.9%), FX (low level, 5.4%; normal level, 5.4%) and FXIII (low level, 8.5%), and von Willebrand factor antigen (low level, 7.7%) showed slightly increased inter-assay CVs. Intra- and inter-assay precision CVs of six frequently requested hemostasis parameter were also calculated for the Sysmex CS-5100 coagulation analyzer (see Table S2). These parameters were used for the comparison with the Atellica COAG 360 coagulation analyzer. Intra-assay CVs of the Sysmex CS-5100 were >5% for fibrinogen (low level, 7.4%; high level 7.1%), D-dimer (low level, 5.8%; high level 6.6%), and FXIII (low level, 6.3%). Inter-assay CVs were >5% for fibrinogen (low level, 6.7%), D-dimer (low level, 6.2%; high level 5.3%), and FXIII (low level, 6.0%; high level, 6.4%).

**TABLE 1** Intra- and inter-assay precision and accuracy of coagulation parameters determined by the Atellica COAG 360

| | Intra-assay (n = 10) | | | | Inter-assay (n = 20) | | | |
|---|---|---|---|---|---|---|---|---|
| Parameter | Target value | Mean ± SD | CV (%) | Difference to target value (%) | Target value | Mean ± SD | CV (%) | Difference to target value (%) |
| PT ratio | 1.06 | 1.10 ± 0.01 | 0.9 | 3.8 | 1.06 | 1.11 ± 0.03 | 2.4 | 4.7 |
| | 3.87 | 4.00 ± 0.06 | 1.4 | 3.4 | 3.87 | 3.95 ± 0.12 | 2.9 | 2.1 |
| INR | 1.05 | 1.08 ± 0.01 | 0.9 | 2.9 | 1.05 | 1.09 ± 0.02 | 1.7 | 3.8 |
| | 3.16 | 3.25 ± 0.04 | 1.2 | 2.8 | 3.16 | 3.21 ± 0.08 | 2.5 | 1.6 |
| aPTT (s) | 25.7 | 25.80 ± 0.33 | 1.3 | 0.4 | 25.7 | 25.80 ± 0.35 | 1.4 | 0.4 |
| | 48.5 | 49.70 ± 0.77 | 1.5 | 2.5 | 48.5 | 49.80 ± 0.76 | 1.5 | 2.7 |
| aPTT ratio | 0.99 | 0.95 ± 0.01 | 1.3 | −4.0 | 0.99 | 0.93 ± 0.01 | 1.3 | −6.1 |
| | 1.95 | 1.84 ± 0.02 | 1.2 | −5.6 | 1.95 | 1.81 ± 0.04 | 1.9 | −7.2 |
| Fibrinogen (g/L) | 0.9 | 0.88 ± 0.04 | 4.5 | −2.2 | 0.9 | 0.87 ± 0.03 | 3.0 | −3.3 |
| | 2.4 | 2.26 ± 0.07 | 3.1 | −5.8 | 2.4 | 2.30 ± 0.07 | 2.8 | −4.2 |
| Antithrombin (%) | 37 | 36.72 ± 0.41 | 1.1 | −0.8 | 37 | 36.81 ± 1.15 | 3.1 | −0.5 |
| | 99 | 106.21 ± 3.68 | 3.5 | 7.3 | 99 | 107.09 ± 3.27 | 3.1 | 8.2 |
| D-Dimers (µg/mL FEU) | 0.3 | 0.34 ± 0.02 | 7.1 | 12.0 | 0.3 | 0.32 ± 0.02 | 5.7 | 6.8 |
| | 2.73 | 2.79 ± 0.04 | 1.5 | 2.2 | 2.73 | 2.82 ± 0.05 | 1.9 | 3.3 |
| FXIII (%) | 27 | 29.82 ± 0.63 | 2.1 | 10.4 | 27 | 30.45 ± 2.58 | 8.5 | 12.8 |
| | 87 | 83.23 ± 2.60 | 3.1 | −4.3 | 87 | 85.93 ± 3.12 | 3.6 | −1.2 |
| FII (%) | 34 | 35.02 ± 0.94 | 2.7 | 3.0 | 34 | 34.80 ± 0.56 | 1.6 | 2.4 |
| | 100 | 97.30 ± 1.30 | 1.3 | −2.7 | 100 | 98.17 ± 1.45 | 1.5 | −1.8 |
| FV (%) | 27 | 25.02 ± 1.95 | 7.8 | −7.3 | 27 | 25.85 ± 1.25 | 4.8 | −4.3 |
| | 90 | 89.67 ± 5.90 | 6.6 | −0.4 | 90 | 90.16 ± 7.15 | 7.9 | 0.2 |
| FVII (%) | 34 | 35.89 ± 0.70 | 1.9 | 5.6 | 34 | 36.49 ± 1.46 | 4.0 | 7.3 |
| | 98 | 93.09 ± 2.26 | 2.4 | −5.0 | 98 | 94.21 ± 3.04 | 3.2 | −3.9 |
| FVIII (%) | 27 | 28.22 ± 0.55 | 1.9 | 4.5 | 27 | 26.75 ± 0.51 | 1.9 | −0.9 |
| | 96 | 90.84 ± 2.14 | 2.4 | −5.4 | 96 | 90.70 ± 4.38 | 4.8 | −5.5 |
| FVIII chromogenic (%) | 28 | 27.96 ± 0.62 | 2.2 | −0.1 | 28 | 27.17 ± 1.21 | 4.5 | −3.0 |
| | 94 | 86.39 ± 4.80 | 5.6 | −8.1 | 94 | 85.04 ± 4.52 | 5.3 | −9.5 |
| FIX (%) | 36 | 36.05 ± 2.25 | 6.2 | 0.1 | 36 | 36.40 ± 1.73 | 4.8 | 1.1 |
| | 100 | 102.94 ± 1.87 | 1.8 | 2.9 | 100 | 105.27 ± 4.32 | 4.1 | 5.3 |
| FX (%) | 29 | 26.31 ± 1.76 | 6.7 | −9.3 | 29 | 26.47 ± 1.44 | 5.4 | −8.7 |
| | 89 | 82.94 ± 1.25 | 1.5 | −6.8 | 89 | 81.85 ± 4.38 | 5.4 | −8.0 |
| FXI (%) | 32 | 30.46 ± 0.77 | 2.5 | −4.8 | 32 | 30.96 ± 1.30 | 4.2 | −3.3 |
| | 98 | 94.08 ± 1.65 | 1.8 | −4.0 | 98 | 93.68 ± 3.09 | 3.3 | −4.4 |
| FXII (%) | 31 | 30.39 ± 0.40 | 1.3 | −2.0 | 31 | 30.05 ± 0.48 | 1.6 | −3.1 |
| | 107 | 109.70 ± 1.25 | 1.1 | 2.5 | 107 | 108.67 ± 2.84 | 2.6 | 1.6 |
| Protein C (%) | 33 | 35.09 ± 0.85 | 2.4 | 6.3 | 33 | 35.98 ± 1.61 | 4.5 | 9.0 |
| | 98 | 103.20 ± 0.90 | 0.9 | 5.3 | 98 | 103.64 ± 1.67 | 1.6 | 5.8 |
| Protein S (%) | 30 | 31.43 ± 0.59 | 1.9 | 4.8 | 30 | 32.23 ± 0.81 | 2.5 | 7.4 |
| | 91 | 90.53 ± 1.69 | 1.9 | −0.5 | 91 | 90.35 ± 2.12 | 2.3 | −0.7 |
| vWF antigen (%) | 37 | 39.76 ± 1.22 | 3.1 | 7.5 | 37 | 40.32 ± 3.10 | 7.7 | 9.0 |
| | 126 | 132.98 ± 2.85 | 2.1 | 5.5 | 126 | 131.01 ± 6.07 | 4.6 | 4.0 |
| vWF activity (%) | 30 | 28.98 ± 0.59 | 2.0 | −3.4 | 30 | 29.23 ± 0.62 | 2.1 | −2.6 |
| | 93 | 89.44 ± 1.33 | 1.5 | −3.8 | 93 | 89.92 ± 1.91 | 2.1 | −3.3 |

*Note:* Two commercially available control samples with different target values were used and mean values ± standard deviation (SD). The corresponding coefficients of variation (CV) and differences to target values were calculated. Inter-assay precision of single factor activities (FII-XII), Protein C/S and vWF Ag/Ac was calculated measuring control samples on 10 consecutive days.

Abbreviations: aPTT, activated partial thromboplastin time; FII-XIII, factor II-XIII; INR, international normalized ratio; PT, prothrombin time; vWF, von Willebrand factor.

**TABLE 2** Comparison of results measured by the Atellica COAG 360 and the Sysmex CS-5100 for determination of coagulation parameters

| Parameter | Unit | N | Bias ± SD | Intercept | Slope | Spearman's *r* |
|---|---|---|---|---|---|---|
| INR | — | 104 | 0.06 ± 0.11 | −0.14 (−0.33 to 0.02) | 1.14 (1.00 to 1.33) | .882 |
| aPTT | s | 103 | 3.2 ± 5.0 | −2.80 (−4.90 to −1.15) | 1.20 (1.14 to 1.27) | .990 |
| Fibrinogen | g/L | 89 | 0.3 ± 0.2 | 0.14 (0.01 to 0.26) | 1.05 (1.02 to 1.10) | .990 |
| Antithrombin | % | 90 | 11.2 ± 4.8 | 8.65 (3.00 to 12.83) | 1.03 (0.98 to 1.10) | .969 |
| D-dimer | µg/mL FEU | 90 | 0.5 ± 0.6 | 0.05 (−0.02 to 0.08) | 1.14 (1.11 to 1.17) | .995 |
| FXIII | % | 74 | 4.0 ± 7.3 | −7.03 (−10.25 to −3.32) | 1.13 (1.09 to 1.17) | .977 |

Intra- and inter-assay analytical accuracy was calculated as mean percentage differences to target values of commercially available control samples. Calculation of intra-assay accuracy revealed mean differences <10% for all investigated parameters, except for D-dimer (low level, 12.0%) and FXIII (low level, 10.4%). Results of inter-assay accuracy calculations were also

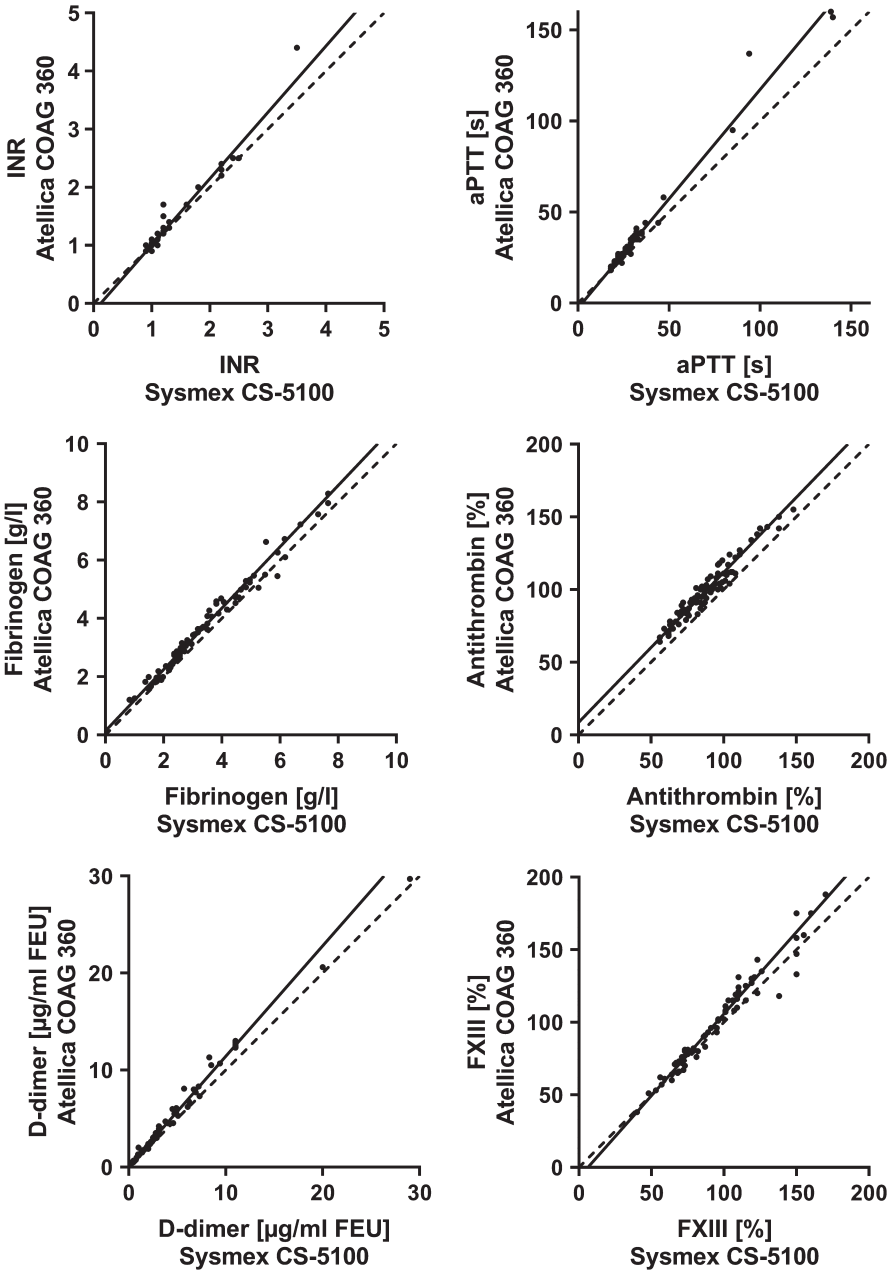


**FIGURE 1** Comparison of coagulation measurements determined by the Atellica COAG 360 and the Sysmex CS-5100. Passing-Bablok regression analyses were performed using measurement results of routine coagulation parameters determined by the Atellica COAG 360 and the Sysmex CS-5100. Details of regression analyses are provided in Table 2

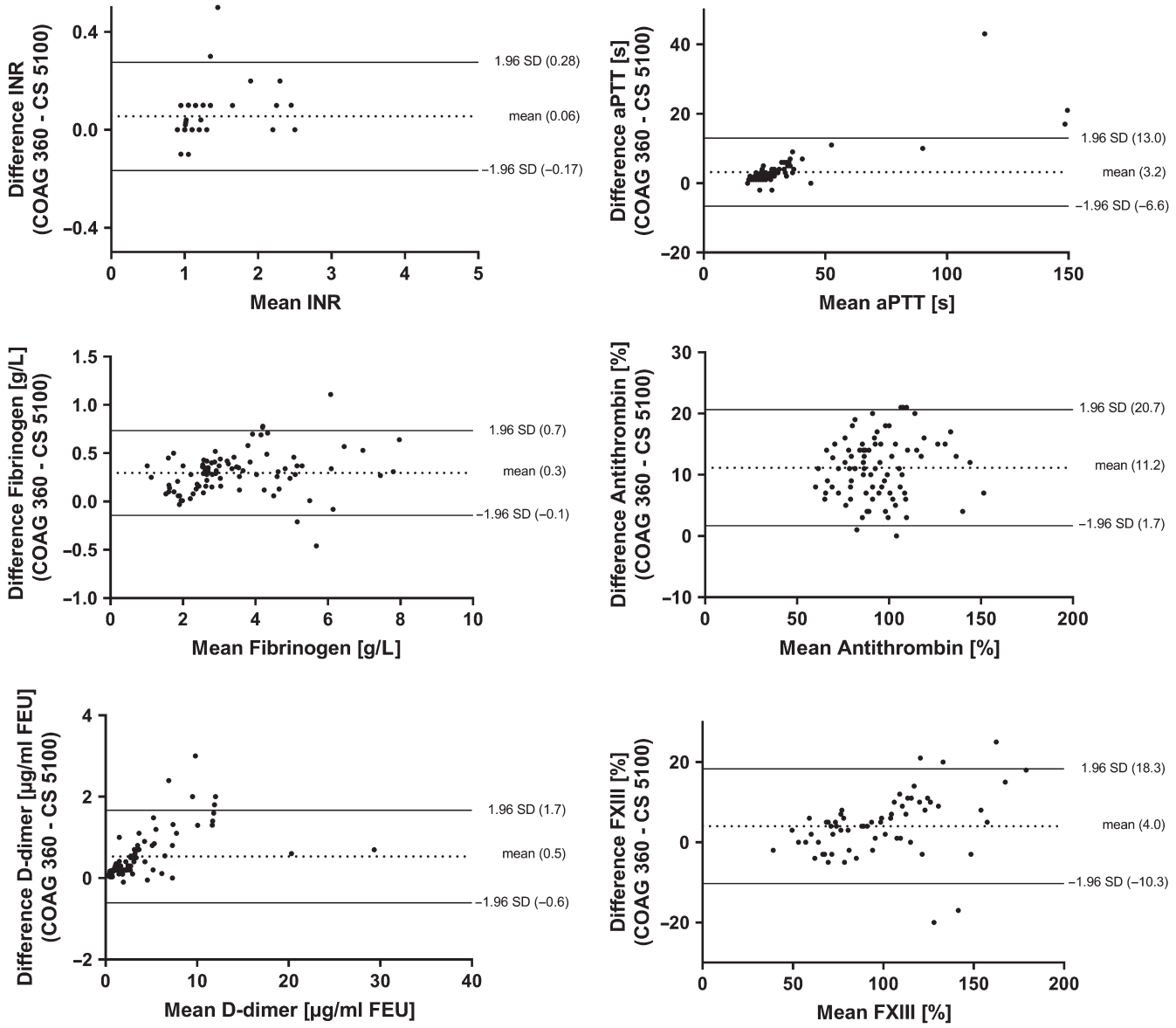


**FIGURE 2** Agreement of coagulation measurement results determined by the Atellica COAG 360 and the Sysmex CS-5100. Shown are Bland-Altman plots for routine coagulation parameters. Details are provided in Table 2

<10% for all investigated parameters, except for FXIII (low level, 12.8%).

### 3.3 | Comparison of coagulation analyzers: Atellica COAG 360 vs Sysmex CS-5100

Plasma samples from clinical routine covering the entire clinically relevant concentration ranges were used for comparison analyses between the Atellica COAG 360 and the Sysmex CS-5100. Results were reported for INR, aPTT, antithrombin, fibrinogen, D-dimer, and FXIII (see Table 2). Passing-Bablok analyses showed good correlation between measurement results of the Atellica COAG 360 and the Sysmex CS-5100 for the indicated parameters ($r > 0.88$; $P < .0001$ for all parameters, see Figure 1). Bland-Altman plots revealed high agreement between analyzers for most parameters (see Figure 2). Fibrinogen (bias: 0.3 g/L; −1.96 SD = −0.1 g/L, 1.96 SD = 0.7 g/L) and antithrombin (bias: 11.2%; −1.96SD = 1.7%, 1.96SD = 20.7%) measurement results determined by the Atellica COAG 360 were higher compared with Sysmex CS-5100 results.

### 3.4 | Detection of interferences and investigation of possible effects on coagulation measurements

Interferences on coagulation measurements were assessed using icteric (total bilirubin concentrations between 7.6 and 45.4 mg/dL; n = 12), hemolytic (plasma hemoglobin concentrations between 25 and 110 mg/dL; n = 10), and lipemic (triglyceride concentrations between 360 and 874 mg/dL; n = 7) plasma samples.

Atellica COAG 360 routinely performs a HIL-check by optical absorbance measurements at specified wavelengths. All icteric (I-index

**TABLE 3** Comparison of routine coagulation parameters determined by the Atellica COAG 360, Sysmex CS-5100, and the STart Max in samples with visual interferences

| | (A) | | | | |
|---|---|---|---|---|---|
| | **INR** | **aPTT [s]** | **Fibrinogen [g/L]** | **Antithrombin [%]** | **D-dimer [µg/mL FEU]** |
| Icteric samples (n = 12) | 0.28 ± 0.32 | 6.5 ± 5.2 | 0.3 ± 0.2 | 5.4 ± 6.8 | 0.56 ± 1.33 |
| Hemolytic samples (n = 10) | −0.01 ± 0.08 | 2.7 ± 2.8 | 0.5 ± 0.7 | −1.7 ± 10.3 | 0.06 ± 0.09 |
| Lipemic samples (n = 7) | −0.03 ± 0.10 | 11.7 ± 15.9 | 0.5 ± 0.4 | 7.9 ± 6.2 | 0.33 ± 0.66 |
| | **(B)** | | | | |
| | **INR** | | **aPTT [s]** | | **Fibrinogen [g/L]** |
| Icteric samples (n = 12) | 0.02 ± 0.11 | | 1.3 ± 7.5 | | 0.1 ± 0.2 |
| Hemolytic samples (n = 10) | 0.01 ± 0.09 | | −0.3 ± 3.4 | | 0.1 ± 0.7 |
| Lipemic samples (n = 7) | 0.04 ± 0.09 | | −1.1 ± 5.5 | | 0.3 ± 0.2 |

*Note:* Shown are biases ± standard deviations determined by Bland-Altman analysis for (A) the comparison between the Atellica COAG 360 and the Sysmex CS-5100 and (B) for comparison between the Atellcia COAG 360 and the STart Max.

2-7) samples were correctly identified by the Atellica COAG 360. Eight of ten samples with visible hemolysis were identified as hemolytic (H-index 3-5). Two samples with free hemoglobin concentrations of 25 and 31 mg/dL, that is close to the upper reference range of 20 mg/dL, were not flagged. Six of seven lipemic samples were correctly flagged (L-index 2-5; all with triglyceride concentrations >400 mg/dL). A lipemic sample with a triglyceride concentration of 360 mg/dL was not detected.

Using these samples, routine coagulation measurement results (INR, aPTT, fibrinogen, antithrombin, and D-dimer) were performed on the Atellica COAG 360 and the Sysmex CS-5100. Furthermore, INR, aPTT, and fibrinogen measurements were also performed using the same samples and reagents on the STart Max coagulation analyzer. Measurement results of optical-based clot-detection coagulation analyzers (Atellica COAG 360 and Sysmex CS-5100) and the mechanical clot-based coagulation analyzer (STart Max) were similar, and comparison of results revealed good agreement. Biases between analyzers were calculated for the investigated parameters (see Table 3A and 3B).

### 3.5 | Performance of the Atellica COAG 360 in a high-throughput central laboratory

The Atellica COAG 360 and the Sysmex CS-5100 coagulation analyzers are fully implemented and connected to the laboratory automation and to the local data management system (CentraLink; Siemens Healthineers). Samples were loaded via the Aptio automated track-line system (Siemens Healthineers) on each platform. We measured a mixed panel consisting of five frequently requested coagulation parameters including INR, aPTT, fibrinogen, antithrombin, and D-dimer in 45 samples.

First results were reported within eight minutes after taking an aliquot from samples on the track-line by both analyzers. Complete results for 45 mixed panels (225 single tests) in a routine setting were provided after 71 minutes by the Atellic COAG 360. In comparison, the Sysmex CS-5100 needed 77 minutes for the same approach. For the evaluation of the STAT capability of the Atellica COAG 360, we measured the same mixed panel in five plasma samples. STAT samples were successively loaded via the track-line after ten routine samples. They were automatically prioritized by the Atellica COAG 360, and results of coagulation measurements were completed within an average time of eight minutes compared to routine samples with an average time of about twenty minutes at the same time. Taken together, the Atellica COAG 360 connected to a laboratory automation shows optimal STAT capability and has a slightly improved throughput rate of about 190 single tests per hour compared with the Sysmex CS-5100 (about 175 single tests per hour) in a routine setting of a mixed panel of coagulation parameters.

## 4 | DISCUSSION

In the present study, the analytical performance of the Siemens Atellica COAG 360, a fully-automated high-throughput coagulation analyzer, was evaluated. Intra- and inter-assay accuracy and precision were determined and compared with the widely used Sysmex CS-5100 automated coagulation analyzer. CVs were optimal (<5%) and accuracy was acceptable (<10%) for most of the routine coagulation parameters. Only few parameters showed slightly elevated CVs in the normal and/or abnormal range. Similar results were obtained for the Sysmex CS-5100 coagulation analyzer. These values are consistent with previously published precision data for the Sysmex CS-5100.[5] Other automated coagulation analyzers, such as the ACL TOP and the Sysmex CA-7000, showed comparable analytical performance.[12,13]

Overall, correlation of coagulation measurement results between analyzers was optimal and mean differences were acceptable

for most of the investigated parameters. Measurements included the major hemostasis parameters, and results covered the entire clinically relevant concentration ranges. Among those, fibrinogen and antithrombin showed largest mean bias regarding total values. These differences between the Atellica COAG 360 and the Sysmex CS-5100 may have a clinical relevance. Therefore, reference ranges for antithrombin and fibrinogen have to be carefully established by each laboratory and validated depending on the coagulation analyzer.

The assessment of pre-analytical sample interferences by the Atellica COAG 360 included primary-tube sample-volume check and HIL-check. Underfilled samples (<20%) were correctly identified during our study period and sample interferences were efficiently detected in most of hemolytic, icteric, and lipemic samples. Recently, Lippi and colleagues extensively validated the assessment of plasma indices determined by the Atellica COAG 360. They provided assay-specific HIL-index interference limits for some coagulation parameters and demonstrated optimal performance of HIL-indices.[14] In our study, measurements of coagulation parameters in these samples showed good comparability between the Atellica COAG 360 and the Sysmex CS-5100. The Sysmex CS-5100 as well as the Atellica COAG 360 utilizes photo-optical clotting detection. Therefore, a systematic bias due to wavelength interferences cannot be ruled out. However, results are consistent to previous data provided by Ratzinger and colleagues comparing the Sysmex CS-5100 with the STA-R coagulation analyzer from Stago, which uses mechanical clotting detection.[5] We also performed mechanical clot detection using the STart Max coagulation analyzer for frequently demanded coagulation parameters (INR, aPTT, and fibrinogen). We could confirm similar results between the Atellica COAG 360 and results obtained by the STart Max for the investigated parameters. Taken together, results of coagulation measurements determined by the Atellica COAG 360 are not affected by optical interferences at least up to concentrations measured in the present study samples.

The Atellica COAG 360 is intended to be used in a high-throughput central laboratory and features the possibility to be connected to track-line systems of total laboratory automations. Most throughput evaluations of coagulation analyzers were performed with directly loaded samples on analyzer platforms. We aimed to imitate real-life conditions of a high-throughput laboratory in a central laboratory with total automation. We determined a sample throughput rate of about 190 tests per hour for a mixed panel including coagulometric (INR, aPTT, fibrinogen and antithrombin) and immunologic (D-dimer) assays. This panel includes frequently requested hemostatic assays and can be assumed as representative for demands in a maximum care hospital. In comparison with other studies, we found a slightly increased sample throughput rate. Ratzinger and colleagues reported a throughput rate of 160 tests per hour for a routing setting consisting of PT, INR, thrombin clotting time, aPTT, antithrombin, and D-dimer using the Sysmex CS-5100.[5] However, plasma throughput rates are hardly comparable due to the lack of standardization for sample throughput studies and due to the laboratory automation setting in our study. The throughput rates provided by the manufacturer are usually much higher as they are performed using samples, which are directly loaded to the analyzer. To our knowledge, this is the first study demonstrating the sample throughput rate of a coagulation analyzer connected to a track-line system of a total laboratory automation. In general, the connection of a coagulation analyzer to a total laboratory automation may a rational and necessary process for central laboratories. Total laboratory automation can improve the efficient sample processing and quality of coagulation measurements. Pre-analytical concerns regarding the transport of coagulation samples via a track-line and automated centrifugation processes should be considered but are assumed not to be relevant. In a study by Da Rin and Lippi, the loading of samples to coagulation analyzers via a track-line did not significantly affect hemostasis testing compared with directly loaded samples.[15]

Furthermore, unifying different methodologies on one coagulation analyzer is a main advantage in the field of hemostasis diagnostics. So far, hemostasis systems for routine and specific coagulation tests were operated separately or were used alternately for routine and specific coagulation tests. Together with markedly increased onboard reagent stabilities, a significantly improved workflow and reduced turnaround times in the laboratory are feasible.

The Atellica COAG 360 was launched as the first analyzer combining five different assay technologies on one platform. We investigated clotting (optical detection), immunologic, and chromogenic assays. Additionally, the Atellica COAG 360 is, according to the manufacturer, intended to use optomechanical clot detection and aggregation testing. However, these technologies have not been released yet and were therefore not evaluated in this study.

From a personal view, this analyzer provides a user-friendly interface and facilitates routine maintenance. The daily maintenance required less than 10 minutes. Compared to the Sysmex CS-5100, the main advantage of the Atellica COAG 360 is the continuous access and loading of reagents and consumables at any time together with markedly increased onboard reagents stabilities (see Table S1). This leads to a simplified handling and an improved workflow.

Taken together, the results of the evaluation demonstrate that the novel Atellica COAG 360 features optimal analytical performance as a high-throughput coagulation analyzer in a central laboratory with total automation. It combines routine and specific high-quality coagulation testing with an effective and efficient workflow.

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## CONFLICT OF INTEREST

The authors state that there is no conflict of interest.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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