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Full Length Article

Analytical and clinical validation of the Tsmart FIB Batrox© assay on the LabPad Evolution analyzer for fibrinogen measurement in whole blood

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ABSTRACT

Background: Fibrinogen is the first coagulation factor to drop during severe hemorrhage, making it an early biomarker for assessing bleeding severity.
Objectives: To evaluate the analytical and clinical performance of the Tsmart FIB Batrox©, a novel point-of-care test using batroxobin, a snake venom-derived enzyme insensitive to heparins and direct thrombin inhibitors, performed on the LabPad Evolution analyzer. The assay delivers results in less than 4 min from citrated whole blood, addressing unmet needs in emergency settings.
Patients and methods: This study included 121 residual citrated (0.109 mol/L) samples collected for routine coagulation testing. Fibrinogen levels measured by the Tsmart FIB Batrox© assay were compared against the Clauss method (gold standard), performed in the central laboratory using the same samples.
Results: The Tsmart FIB Batrox© demonstrated excellent correlation with the Clauss assay ($r = 0.94$), particularly in the clinically critical range for severe bleeding. Bland-Altman analysis revealed negligible bias. No interference from hematocrit variations or anticoagulants was observed. At fibrinogen cut-offs of 1.0 g/L and 2.0 g/L, it exhibited high diagnostic accuracy (area under the ROC curve values of 0.99 and 0.98, respectively). Precision testing confirmed excellent repeatability and reproducibility, with coefficients of variation <10% across all ranges.
Conclusion: The Tsmart FIB Batrox© system enables rapid and accurate fibrinogen measurement from a single drop of citrated whole blood, even at the lowest detectable concentrations. Its strong correlation with the Clauss method, high diagnostic accuracy, and POC feasibility make it a valuable tool for real-time decision-making in hemorrhage management.

1. Introduction

Acquired fibrinogen deficiency resulting from coagulopathy associated with major blood loss is a critical challenge in emergency medicine and intensive care. As the central substrate for clot formation, fibrinogen is essential for initiating and sustaining hemostasis. Importantly, fibrinogen is the first clotting factor to fall to critically low levels during severe hemorrhage, making it a key prognostic biomarker in bleeding patients [1]. Low fibrinogen levels are associated with reduced survival rate [2,3], and early fibrinogen replacement has been reported to improve outcomes in severe trauma [4–15]. Consequently, rapid and accurate measurement of fibrinogen levels is paramount in managing life-threatening bleeding.

Massive hemorrhage remains a leading cause of preventable death across multiple clinical settings. In trauma, hemorrhage accounts for nearly 50% of death occurring within 24 h of injury and up to 80% of intraoperative mortality, affecting 3 to 5% of patients [16]. In cardiothoracic surgery, approximately 5 to 7% of patients undergoing cardiac surgery lose more than 2 L of blood, [17] with 10% of patients consuming 90% of transfusion products [18]. In obstetrics, postpartum

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hemorrhage remains the leading cause of maternal mortality in low-resource countries, and a major source of morbidity in high-resource countries [19,20]. Together, these data underscore massive bleeding as a major public health concern requiring urgent diagnostic and therapeutic interventions [21,22].

Normal plasma fibrinogen levels range from 2.0 to 4.5 g/L in healthy adults [23], and are physiologically increased during pregnancy [24]. Hypofibrinogenemia has been identified as a risk factor for adverse outcomes in trauma [25,26], cardiovascular surgery [5,27,28], and obstetrics [29–33]. Nevertheless, the optimal fibrinogen threshold for intervention remains debated. A consensus threshold of 1 g/L has been widely accepted for fibrinogen supplementation prophylaxis in congenital afibrinogenemia patients, and 1.5 g/L in case of bleeding [34–37]. For acquired fibrinogen deficiency in massive hemorrhage, there is insufficient evidence to establish a definite trigger threshold [38]. Ciavarella et al. first proposed a threshold of 0.8 g/L in 1967, based on a small cohort of 36 massively transfused patients [39]. A threshold of 0.8 to 1 g/L was subsequently recommended by the American Society of Anesthesiologists in 2006 [40], and by the European trauma guidelines in 2007 [41]. As clot strength increases with increasing concentrations of fibrinogen [42], and a minimum level of 2 g/L is required for efficient coagulation and clot formation [7,33,43–45], the threshold for fibrinogen supplementation has been reconsidered. The last European guidelines now recommend a threshold of 1.5 g/L or 1.5 to 2.0 g/ [8,44,45], while current studies and consensus statements recommend a target level of at least 1.5 to 2.0 g/L [7,8,46–49]. A large retrospective cohort study demonstrated that fibrinogen ≥1.3 g/L was associated with improved survival, with an optimal post-treatment target of 2.0–2.5 g/L [3]. The RETIC study further validated this, identifying a post-treatment threshold slightly above 2.0 g/L to minimize the need for massive transfusion [50]. Similar findings have been reported in post-partum hemorrhage [51].

Therefore, accurate fibrinogen measurement, particularly in the range below 2.5 g/L, is critical for guiding timely and appropriate replacement therapy.

The Clauss fibrinogen assay, performed on automated coagulation analyzers, is the gold standard for measuring fibrinogen levels in diluted plasma samples [52]. This method quantifies the time to fibrin clot formation after addition of a high concentration of thrombin. Fibrin clot endpoint is detected by mechanical or photo-optical means due to modifications of plasma samples viscosity or turbidity. Fibrinogen concentration is inversely proportional to clotting times.

However, the Clauss assay requires plasma separation, sample dilution, and transport to a central laboratory, resulting in turnaround times of 30–60 min, a delay that is incompatible with the rapidly evolving dynamics of severe hemorrhage. In this context, point-of-care (POC) testing enables real-time, bedside decision-making, which has been shown to improve clinical outcomes through earlier and more targeted fibrinogen replacement [8]. POC fibrinogen measurement allows clinicians to initiate therapy promptly, reducing time-to-treatment and minimizing reliance on empirical transfusion protocols.

The aim of the present study was to evaluate the analytical and clinical performance of a novel POC fibrinogen assay, the Tsmart FIB Batrox©, performed on the LabPad Evolution analyzer. This assay uses batroxobin, a snake venom-derived enzyme that is insensitive to heparin and direct thrombin inhibitors, and it delivers results from citrated whole blood in less than 4 min. We compared its performance to the Clauss assay, focusing on its accuracy at critical fibrinogen thresholds used to guide massive hemorrhage protocols.

2. Material and methods

2.1. Device technology

The LabPad Evolution analyzer (BIOSYNEX SA, Illkirch-Graffenstaden, France) employs a patented lensless imaging technology to measure coagulation times by detecting the immobilization of blood cells as they become entrapped within the forming clot. This technology builds indeed upon earlier pioneering work from our group, in which laser speckle was first introduced for coagulation monitoring [53]. Since then, this core approach has evolved substantially as we have combined laser speckle analysis with a lens-free imaging architecture, enabling a highly compact and robust device specifically designed for point of care use with microscale blood samples. This innovative approach leverages dynamic speckle pattern analysis, wherein a coherent light source illuminates a dense suspension of randomly distributed diffusing particles generating time-varying interference patterns resulting from multiple light-scattering events. In the case of a blood sample, as the cells are unbounded, their residual motions due to the migration in the chamber induce a constantly changing speckle figure, exhibiting a “swarminglike” behavior. When the blood clot forms, the cells are immobilized leading to a speckle image fixed in time. Briefly, the system monitors microscale Brownian and convective displacements of RBCs within a capillary microfluidic channel following the mixture of whole blood with a freeze-dried procoagulant reagent. As coagulation progresses, RBCs become progressively incorporated into the three-dimensional fibrin network, leading to a measurable reduction in cellular motion. The measurement principle relies on real-time digital image correlation (Fig. 1), wherein normalized cross-correlation coefficients between consecutive frames are computed and plotted as a function of time, yielding a coagulation kinetics curve: latency phase (initiation of coagulation), gel phase (clot formation), plateau phase (stable clot with little motion of the red blood). Finally, coagulation time is automatically calculated from the inflexion point or characteristic transition in the kinetics curve, as derived through quantitative analysis of the time-series image data captured by the integrated image sensor.

The Tsmart FIB Batrox© developed by BIOSYNEX is a quantitative fibrinogen assay performed on the LabPad Evolution analyzer. The method employs batroxobin (Pentapharm, Aesch BL, Switzerland), in the presence of 4.5 mM Ca^{++}. Indeed, batroxobin is a thrombin-like serine protease derived from *Bothrops atrox* venom, which selectively cleaves fibrinogen to form fibrin monomers independent of thrombin. This enzymatic specificity renders the assay insensitive to heparin and

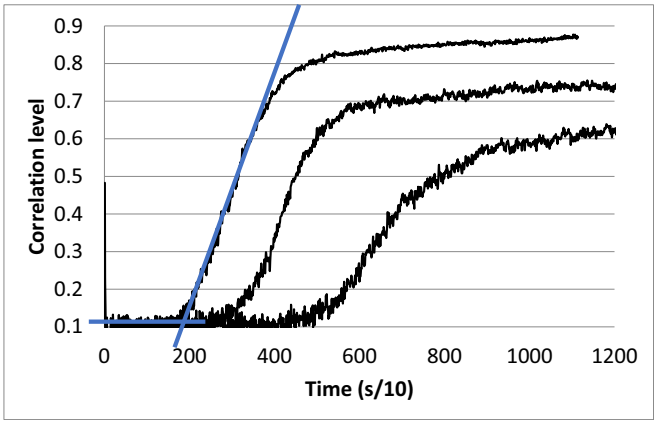

Fig. 1. Typical curves for fibrinogen assay using LabPad Evolution and Tsmart FIB Batrox©. Introduction of the blood sample in the Tsmart trigger coagulation. Similarly to the Clauss method, the longer the coagulation takes, the lower the fibrinogen is. From left to right curves obtained for concentrations of 2, 1.3 and 0.6 G/L of fibrinogen are shown. For the 2 g/L curve, the different phases of the coagulation dynamic are shown: 1, latency phase (initiation of coagulation), 2, gel phase (clot formation), and 3, plateau phase (stable clot with little motion of the red blood cells). The intersection of the tangent to the inflexion point of the curve determines the clotting time. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

direct thrombin inhibitors (e.g. argatroban, dabigatran), making it particularly suitable for patients receiving anticoagulant therapy. The assay is optimized for fibrinogen concentrations between 0.5 and 3.0 g/L. Briefly, the disposable microcuvette containing freeze-dried batroxobin reagent is inserted into the LabPad Evolution, where it is pre-warmed to 37 °C to ensure standardized reaction kinetics. A 20 μL drop of citrated venous blood is applied to the microcuvette, initiating the coagulation reaction. The coagulation time (CT) is determined algorithmically by identifying the intersection of the tangent at the inflexion point of the coagulation curve with the time (X) axis. As in the Clauss method, the clotting time exhibits an inverse proportionality to fibrinogen concentration. However, the Tsmart FIB Batrox© further enhances precision by incorporating a secondary quantitative parameter, namely the plateau amplitude of the coagulation curve, which is directly proportional to fibrinogen levels, providing an additional validation metric for result accuracy (Fig. 1). A dose response calibrating curve was constructed using the SSC/ISTH secondary coagulation standard for fibrinogen in plasma (SSCLOT5).

2.2. Precision study

Within-run precision (repeatability) was evaluated by repeated testing of three different fresh citrated whole blood samples obtained from the local blood bank. Each sample was tested ten times on a single instrument by one qualified operator. The between-run (reproducibility) was evaluated using a standardized mixture of freeze-dried citrated plasma (Hyphen-Biomed, Neuville-sur-Oise, France) and red blood cells (Diagast, Loos, France) to ensure consistent fibrinogen concentrations across five consecutive days, three instruments, and three different batches of Tsmart FIB Batrox©. This controlled matrix maintains the red blood cell component essential for the assay's optical detection principle while minimizing biological variability inherent to fresh whole blood. Five replicates were realized on five consecutive days. The total number of replicates was 225 on each of the two different samples. The within-run and between-run precisions were expressed as coefficient of variation (CV) defined as the standard deviation (SD) divided by the mean multiplied by 100%.

Routine quality control procedures were not assessed in this validation study, which focused on analytical precision under controlled experimental conditions. To date, no dedicated liquid QC material is available for the Tsmart FIB Batrox assay. Clinical laboratories should monitor analytical performance through precision verification using native samples until manufacturer QC materials become available.

2.3. Interference study

The potential interference of endogenous and exogenous substances on fibrinogen measurements was evaluated in accordance with CLSI guidelines EP07 [54] and supplement EP37 [55]. Endogenous substances tested included bilirubin (ACROS Organics™, Fischer scientific, Illkirch, France) up to 40 mg/dL, triglycerides (Sigma Aldrich, Saint Quentin Fallavier, France) up to 15 g/L, haemoglobin (Sigma Aldrich) up to 1000 mg/dL, D-dimer (BBi solution, Crumlin, Gwent, UK), up to 5000 μg/L, Albumin (Sigma Aldrich) up to 60 g/L. Exogenous substances tested were substances known to affect coagulation assays and included unfractionated heparin (sodium heparin from Cheplapharm, Levallois-Perret, France) and low molecular weight heparin (sodium enoxaparin from Sanofi Wintrhrop Industrie, Gentilly, France) up to 12 U/mL, protamine sulphate (Sigma Aldrich) up to 6 AHU/mL, as well as rivaroxaban (Alsachim, Illkirch-Graffenstade, France) up to 2700 ng/mL, dabigatran (Alsachim), up to 9000 ng/mL, and argatroban (Sigma Aldrich) up to 4.5 μg/mL.

Citrated whole blood samples containing 2 g/L of fibrinogen (a medically relevant decision threshold) were spiked with freshly prepared interfering substances. To account for minor volume changes due to the addition of interferents, an equivalent volume of diluent (either HEPES-buffered saline or dimethyl sulfoxide) was added to the control sample, ensuring comparable dilution effects.

For each interfering substance, the bias relative to the control sample was calculated. A substance was considered to have a clinically significant interfering effect when the result in the presence of the interferent differs from the result without the interferent more than twice the within-run precision CV (i.e., 14%).

2.4. Comparison method study design

The multicenter method comparison study was conducted under real-world laboratory routine conditions across three independent clinical sites: the University Hospital of Grenoble-Alpes (CHUGA, Grenoble, France), the Biogroup Laboratory (Saint-Martin-d'Hères, France), and the Pitié-Salpêtrière University Hospital (AP-HP, Paris, France).

A total of 121 residual citrated blood samples (sodium citrate 0.109 mol/L, 9:1 blood-to-anticoagulant ratio) were prospectively collected from routine coagulation testing, including 69 samples from CHUGA, 10 samples from Biogroup Laboratory, and 42 samples from Pitié-Salpêtrière Hospital. Residual citrated samples were collected from hospitalized patients undergoing routine fibrinogen testing for clinical indications including perioperative hemostasis assessment, bleeding evaluation, trauma, liver dysfunction, and critical care management. Fibrinogen levels were determined in each sample using the reference Clauss assay (STA-Liquid Fib, Diagnostica Stago, Asnières, France) on a STA-R Max® analyzer and the Tsmart FIB Batrox© assay (BIOSYNEX SA).

The Clauss assay was performed by routine laboratory technicians following standard operating procedures (SOPs). All measurements were completed within 4 h of plasma separation to minimize pre-analytical variability. The Tsmart FIB Batrox© assay was conducted by trained operators using 20 μL of citrated whole blood per test.

Hematocrit measurements were performed exclusively for CHUGA samples using an automated hematology analyzer (e.g., Sysmex XN-9000, Sysmex France, Villepinte, France).

The study used deidentified residual specimens originally collected for standard-of-care testing, with no additional blood draws performed. In accordance with French bioethics laws (Article L.1243-3), local IRB approvals, and FDA guidance for IVD studies, informed patient consent was waived since the study used discarded excess material with no patient identifiers.

All data were anonymized prior to analysis to ensure compliance with the General Data Protection Regulation (GDPR) and regulatory standards for in vitro diagnostic performance evaluations.

2.5. Statistical analysis

Statistical analyses were performed using the GraphPad Prism software version 8.0.2 (GraphPad Software, San Diego, CA, USA) or the Minitab® software version 21.4.3 (Minitab, Inc., State College, PA, USA).

Continuous data were tested for normality using the Shapiro-Wilk test. Values were expressed as mean and SD. For method comparisons, slope and intercept with 95% confidence interval (95% CI) were calculated using Passing and Bablok regression [56] and Pearson's r correlation coefficient was estimated. Agreement between methods was assessed using Bland-Altman analysis, where systematic bias was defined as the mean difference between paired measurements, and 95% limits of agreement were established as the mean bias ±1.96 times the SD of the differences. The presence of proportional bias was evaluated by examining the relationship between measurement differences and their averages [57].

A paired *t*-test was conducted to determine whether the observed mean bias differed significantly from zero, using a significance threshold of $\alpha = 0.05$.

Decision thresholds for fibrinogen were evaluated using receiver

operating characteristic (ROC) curve analysis using jamovi (Version 2.6, The jamovi project (2025), retrieved from https://www.jamovi.org).

A p-value <0.05 was considered as statistically significant.

3. Results

3.1. Analytical performances

3.1.1. Precision study

The results of the within-run and between-run precision studies are reported in Table 1. Within-run precision CVs ranged from 3.9% to 9.3%, while between-run precision CVs ranged from 7.5% to 8.3%. All CVs met the industry-standard acceptance criteria of <10%.

3.1.2. Interference study

Results of interference studies are summarized in Table 2. Each value corresponds to the mean result (n = 8) at maximum tested concentration.

Of the five endogenous substances evaluated, only albumin exceeded the predefined 14% bias threshold at the maximum concentration of 60 g/L. Lower concentrations demonstrated dose-dependent effects, with biases remaining within acceptable limits (≤14%) up to 52 g/L (data not shown).

None of the six exogenous substances tested, including anticoagulants and reversal agents, demonstrated clinically significant interference at concentrations threefold higher than peak therapeutic levels, as specified by CLSI EP07-A3 and EP37. This result confirms the assay's robustness against common pharmacological interferents at therapeutic doses.

3.2. Comparison with the conventional Clauss method and clinical performances

Across 121 samples examined, fibrinogen concentrations measured with the conventional Clauss method were distributed in the 0.48–4.1 g/L range and the distribution was as follows: 0.5–1 g/L, 27 samples; 1.01–1.50 g/L, 10 samples; 1.51–2.0 g/L, 25 samples; 2.01–2.50 g/L, 25 samples; and 2.51–4.1 g/L, 34 samples.

Fig. 2A shows the Passing-Bablok regression analysis comparing Tsmart FIB Batrox© measurements against the conventional Clauss method across all participating centres. The regression yielded a slope of 0.95 (95% CI: 0.89 to 1.0) and an intercept of 0.082 (95% CI: −0.055 to 0.22), with a Pearson correlation coefficient (r) of 0.94 ($P < 0.001$). The 95% CI for the slope encompasses 1.0, indicating no significant proportional bias, while the intercept CI includes zero, confirming the absence of systematic constant bias. These findings demonstrate excellent concordance between Tsmart FIB Batrox© and the reference Clauss method, supporting the assay's validity for clinical fibrinogen quantification.

According to the Bland–Altman plot (Fig. 2B), the mean difference was _0.013 g/L, and the upper and lower limits of agreement (LOA) were −0.662 g/L and + 0.637 g/L, respectively. All plots were within limits of agreement, except four, which were considered acceptable.

The paired t-test yielded a p-value of 0.68, indicating that there is no significant difference between the mean fibrinogen level obtained using the laboratory reference method and the Tsmart FIB Batrox© method.

The impact of hematocrit values on the fibrinogen measurement was further investigated using CHUGA samples. The median hematocrit was 32%. As illustrated in Fig. 3, the hematocrit value had no statistically significant impact on the Tsmart FIB Batrox© results across the tested hematocrit range of 18–50%. The four outliers observed correspond to fibrinogen levels ≥3.0 g/L with different hematocrits.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic accuracy of the Tsmart FIB Batrox© assay relative to the reference Clauss method at clinically relevant fibrinogen thresholds (i.e., 2 g/L and 1 g/L). As presented in Fig. 4, the assay demonstrated excellent discriminatory performance at both decision thresholds. The area under the ROC curve (AUC) was 0.98 (95% CI: 0.96 to 1.00; $P < 0.001$) for the 2.0 g/L threshold, and 0.99 (95% CI: 0.98 to 1.00; $P < 0.001$) for the 1.0 g/L threshold, respectively. These results indicate that the Tsmart FIB Batrox© assay provides diagnostic equivalence to central laboratory Clauss measurements, with near-perfect classification accuracy for identifying patients requiring fibrinogen supplementation or experiencing critical hypofibrinogenemia.

Table 2
Impact of interference substances on Tsmart FIB Batrox© results.

Interference substances	Concentration	LabPad results (g/L)		% difference
		Control	With interferent	
Triglycerides	1500 mg/dL (16.95 mmol/L)	1.65	1.68	1.52%
Bilirubin	40 mg/dL (474.4 μmol/L)	1.68	1.79	6.72%
Haemoglobin	10 g/L	1.90	2.05	7.89%
D-dimer	5000 ng/mL (26 nmol/L)	1.79	1.78	−0.70%
Albumin	60 mg/dL (902.8 μmol/L)	2.29	2.93	27.87%
Unfractionated heparin	12 U/mL	1.68	1.63	−2.99%
Low molecular weight heparin		1.68	1.66	−0.75%
Protamine sulphate	6 AHU/mL	1.74	1.74	0.00%
Rivaroxaban	2700 ng/mL	1.33	1.38	3.77%
Dabigatran	9000 ng/mL	1.89	1.79	−5.30%
Argatroban	4,5 μg/mL	1.38	1.41	2.73%

4. Discussion

This study evaluated the analytical performance of the Tsmart FIB Batrox© assay for measuring fibrinogen levels in comparison to the gold-standard Clauss method across three independent core laboratories. Our results demonstrate that the batroxobin-based point-of-care Tsmart FIB Batrox© assay achieves analytical equivalence to the reference Clauss method while offering critical advantages for time-sensitive clinical applications.

Table 1
Within-run and between-run precision of the Tsmart FIB Batrox©. Within-run and between-run (reproducibility) studies were performed as described in the materials and methods section.

Native whole blood	Clauss fibrinogen (g/L)	Precision study	Within run				Range
			n	mean	SD	%CV	
1	1.1	Within-run precision (repeatability)	10	1.2	0.047	3.9%	1.1–1.3
2	2.0		10	1.9	0.13	6.7%	1.7–2.1
3	0.5		10	0.7	0.063	9.3%	0.6–0.8
4	1.0 g/L ± 0.2 g/L	Between-run precision (reproducibility)	225	1.1	0.091	8.3%	0.9–1.4
5	2.0 g/L ± 0.2 g/L		225	2.3	0.17	7.5%	1.9–2.8

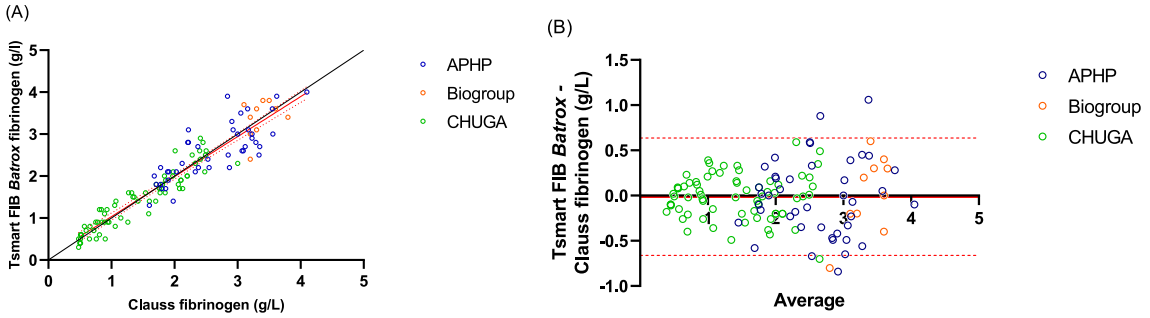

Fig. 2. Tsmart FIB Batrox© results vs standard laboratory result: (A) Passing Bablok regression plot. The continuous red line represents the fit line, and the dashed red lines represent the 95% limits of agreement. (B) Bland-Altman plot. APHP stands for the laboratory of Pitié Salpétrière Hospital, and CHUGA for the one of the University Hospital Grenoble-Alpes. (n = 121). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

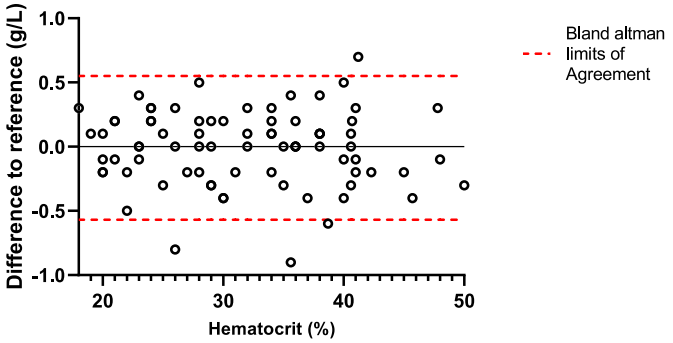

Fig. 3. Percent of bias for Tsmart FIB Batrox© results against laboratory reference plotted against blood hematocrit ($n = 79$).

The Tsmart FIB Batrox© assay exhibited excellent concordance with the Clauss method. Passing-Bablok regression analysis yielded a slope of 0.95 and intercept of 0.082 g/L, with the 95% confidence intervals encompassing 1.0 and zero, respectively, thereby confirming the absence of both proportional and constant bias. The strong Pearson correlation coefficient ($r = 0.94$, $P < 0.001$) further supports this conclusion. Bland-Altman analysis revealed negligible systematic bias across the entire clinical range (0.5–5.0 g/L), with 95% limits of agreement falling within clinically acceptable boundaries.

ROC curve analysis at clinically relevant thresholds for the decision to infuse [8,39–41,44,45] or reinfuse [7,8,46–49] fibrinogen demonstrated near-perfect discriminatory performance. These values substantially exceed the 0.90 benchmark for diagnostic excellence. The high sensitivity and specificity at both cutoffs validate the suitability of the assay for guiding fibrinogen supplementation in the management of acute hemorrhage, allowing clinicians to apply existing Clauss-based treatment algorithms unmodified.

While this study demonstrates excellent correlation with the laboratory Clauss reference method, comparison with viscoelastic whole blood assays such as ROTEM FIBTEM would provide complementary information regarding functional fibrinogen contribution to clot formation in complex coagulopathies. Such head-to-head studies in perioperative and trauma settings are warranted to determine how Tsmart FIB Batrox integrates with existing viscoelastic-guided transfusion algorithms.

In addition, within-run and between-run precision at medically critical fibrinogen concentrations meets the predefined acceptability criteria, ensuring reliable serial measurements for monitoring therapeutic interventions. Between-run reproducibility utilized a standardized reconstituted matrix rather than fresh whole blood to ensure measurement stability across instruments and lots. While this approach differs from routine testing conditions, it provides essential evidence of analytical robustness under controlled multi-day conditions. Furthermore, the assay demonstrated insensitivity to preanalytical interferences (hemolysis, icterus, lipemia) that could typically compromise optical clot detection systems and showed no hematocrit-dependent bias across a clinically relevant range (18–50%).

The assay was found to be insensitive to unfractionated heparin, low-molecular-weight heparins, direct thrombin inhibitors, direct oral anti-Xa inhibitors, and protamine sulphate. This may be advantageous in certain clinical scenarios, such as cardiac and hepatic surgeries, where therapeutic heparinization (>2–4 IU/mL) often renders conventional Clauss measurements unreliable despite plasma dilution strategies,

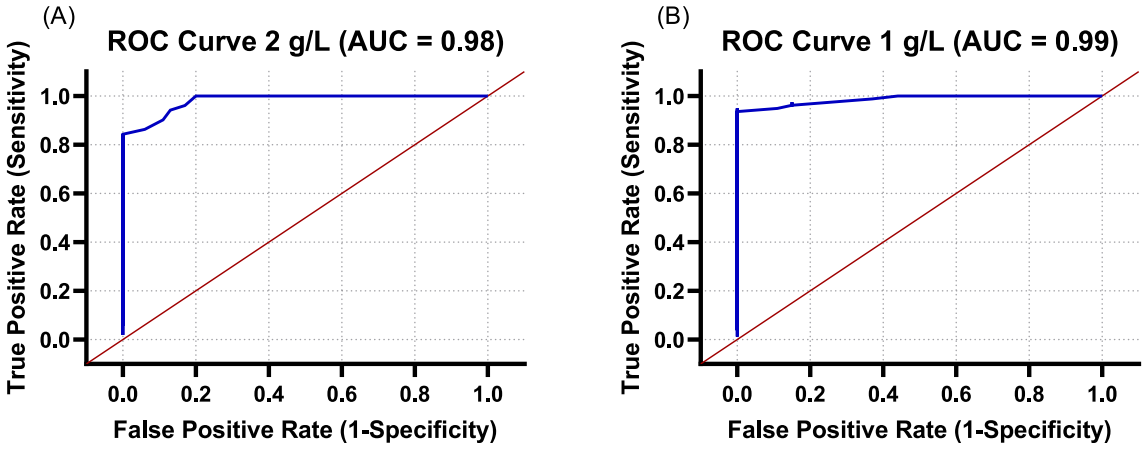

Fig. 4. Receiver operating characteristic analysis ($n = 121$). (A) At a 2 g/L threshold. (B) At a 1 g/L threshold.

trauma and emergency medicine, where anticoagulant medication history may be unavailable and polypharmacy is common, and critical care settings where frequent overlapping anticoagulation occurs.

The <4-minute turnaround time from sample application to result represents a 10- to 15-fold reduction compared to conventional laboratory workflows (30–60 min minimum, including transport, centrifugation, and analysis).

Finally, one must keep in mind that the Tsmart FIB Batrox© device uses a drop of citrated anticoagulated blood from the citated tube for coagulation tests. Therefore, results can be confirmed as soon as the core laboratory issues a validated result. This is a significant distinction from systems that use native blood to approximate the fibrinogen level.

Several limitations must be acknowledged. First, the study population was predominantly hospital-based. The heterogeneous clinical contexts prompting fibrinogen testing may have introduced biological variability reflecting real-world practice. While this enhances the applicability of our findings, future prospective studies in more homogeneous cohorts could further characterize assay performance across specific clinical scenarios, including prehospital settings. Medication exposure data were not systematically available for residual routine samples. However, dedicated interference testing confirmed the assay's insensitivity to major anticoagulants and hemostatic agents at supratherapeutic concentrations, supporting result reliability across diverse pharmacologic contexts.

Second, the hematocrit range tested (18%–50%) may not encompass extreme pediatric or neonatal values. However, dedicated pediatric validation is ongoing in cardiac surgery. Third, although interference testing included commonly used anticoagulants, rare coagulopathies (e.g., dysfibrinogenemias and afibrinogenemia) and pharmacologic thrombolytics require systematic evaluation. Another limitation of the interference study is that testing was conducted using a baseline fibrinogen concentration of 2 g/L. Although this represents a meaningful clinical threshold, assessment of interference effects at lower concentrations around 1 g/L, most relevant for severe bleeding management, should be evaluated in future validation work. Finally, prospective clinical outcome studies comparing point-of-care-guided versus laboratory-guided fibrinogen replacement are essential to demonstrate their impact on mortality, transfusion burden, and cost-effectiveness.

In conclusion, the Tsmart FIB Batrox© assay used with the LabPad Evolution analyzer demonstrates excellent analytical and clinical performance. It obtained the CE mark for professional use in June 2024, and offers a rapid and reliable alternative to conventional fibrinogen measurements. Its insensitivity to hematocrit, hemolysis, and anticoagulants, combined with rapid turnaround times, positions it as a valuable tool for guiding fibrinogen replacement in critical bleeding situations. By enabling real-time fibrinogen monitoring at the bedside, this assay has the potential to enhance patient care and improve outcomes in critical bleeding scenarios.

CRediT authorship contribution statement

Nina Breteau: Writing – review & editing, Writing – original draft, Methodology, Investigation. **Corinne Frère:** Writing – review & editing, Investigation, Conceptualization. **Raphaël Marlu:** Writing – review & editing, Investigation, Conceptualization. **Landry Seyve:** Writing – review & editing, Investigation, Conceptualization. **Stéphane Blachier:** Writing – review & editing, Investigation, Conceptualization. **Vincent Poher:** Writing – review & editing, Project administration, Funding acquisition. **Johanna Spiaczka:** Writing – review & editing, Conceptualization. **Benoît Polack:** Writing – review & editing, Writing – original draft, Supervision.

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Declaration of competing interest

N.B., J.S., and V.P. are employees of AVALUN. All other authors have no conflicts to disclose.

Data availability

Data and information related to this study is available on reasonable request to the authors.

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