Novel capillary blood point-of-care test for adalimumab and infliximab trough levels: Effects of abnormal blood conditions on the test result

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Objective

Patients suffering from inflammatory bowel disease can be treated with the biologics adalimumab (ADL) or infliximab (IFX). Previous studies demonstrated the usefulness of therapeutic drug monitoring (TDM) to adjust the patient's biologic concentration individually. Commercially available rapid assays support laboratories in the fast and easy detection of ADL and IFX concentrations but the assays' dependency on serum as analyte matrix is a general hindrance for TDM, as serum preparation from whole blood is time-consuming and requires laboratory equipment. Patients and clinicians would thus benefit from rapid point-of-care (POC) and easy to use assays that are independent of laboratory equipment. The objective of this project was to expand existing serum lateral flow assays for the analysis of ADL or IFX in capillary blood and investigate potential interactions resulting from the blood matrix.

Methods

ADL and IFX lateral flow serum kits were optimized so that both, capillary blood and EDTA whole blood can be used as analyte matrix by using disposable capillaries for blood collection and for its transfer into dropper bottles that are prefilled with chase buffer. To measure ADL or IFX levels with a POC lateral flow test cassette reader (BÜHLMANN Quantum Blue® Reader) the mixture is then applied on an ADL or IFX lateral flow test cassette (Figure 1). Matrix agreement studies were performed to compare spiked EDTA whole blood and capillary blood samples with spiked serum samples as reference. Additionally, spiked EDTA whole blood samples were treated to obtain three abnormal blood conditions: Icteric, hemolytic and lipemic blood. Bias in results exceeding 30% relative difference to the untreated sample was considered as an interference.

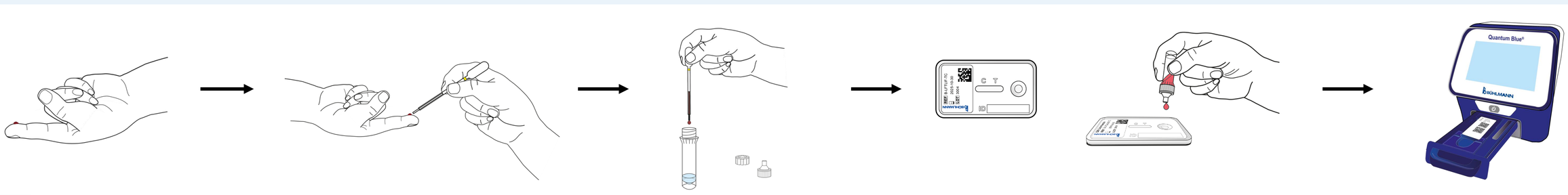

Figure 1: Schematic illustration of the whole blood sampling procedure with Quantum Blue® Adalimumab/Infliximab Capillary Blood using a Quantum Blue® Reader.

Results: Matrix agreement studies

Spiked blood samples showed good agreement with reference serum samples. A Passing-Bablok analysis (Figure 2 and Figure 3) revealed a bias of less than 15% at the clinical decision points for ADL (5 µg/mL and 12 µg/mL) and IFX (3 µg/mL and 7 µg/mL).

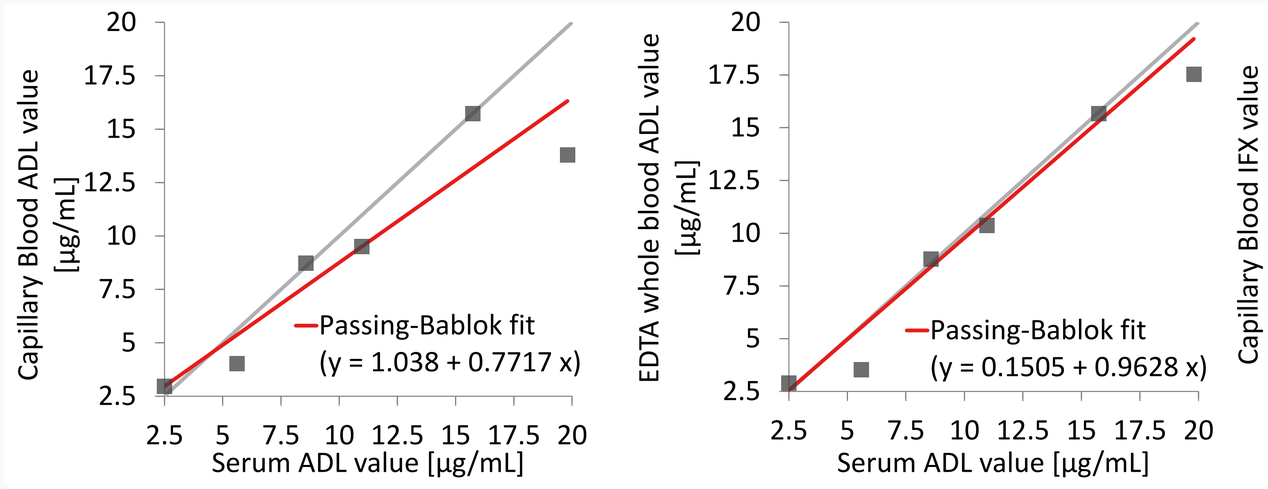

Figure 2: POC ADL assay – Passing-Bablok regression analysis of spiked capillary blood vs serum (left) and spiked EDTA whole blood vs serum (right).

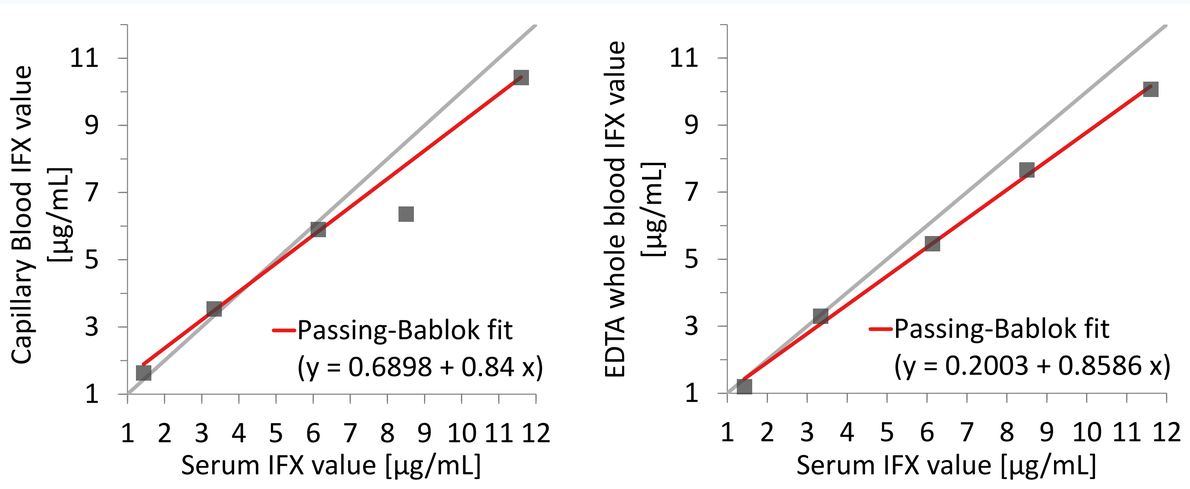

Figure 3: POC IFX assay – Passing-Bablok regression analysis of spiked capillary blood vs serum (left) and spiked EDTA whole blood vs serum (right).

Results: Abnormal blood conditions

Observed relative differences between all tested abnormal blood conditions ranged between -16% and +5% for ADL and -20% and +26% for IFX (Figure 4).

Simulated abnormal blood condition	Compound	Test conc. [mg/mL]
Icteric blood	Bilirubin conjugated	0.29
	Bilirubin unconjugated	0.20
Hemolytic blood	Hemolysis induced by vortexing	N.A.
Lipemic blood	Triglyceride (Intralipid)	13.2

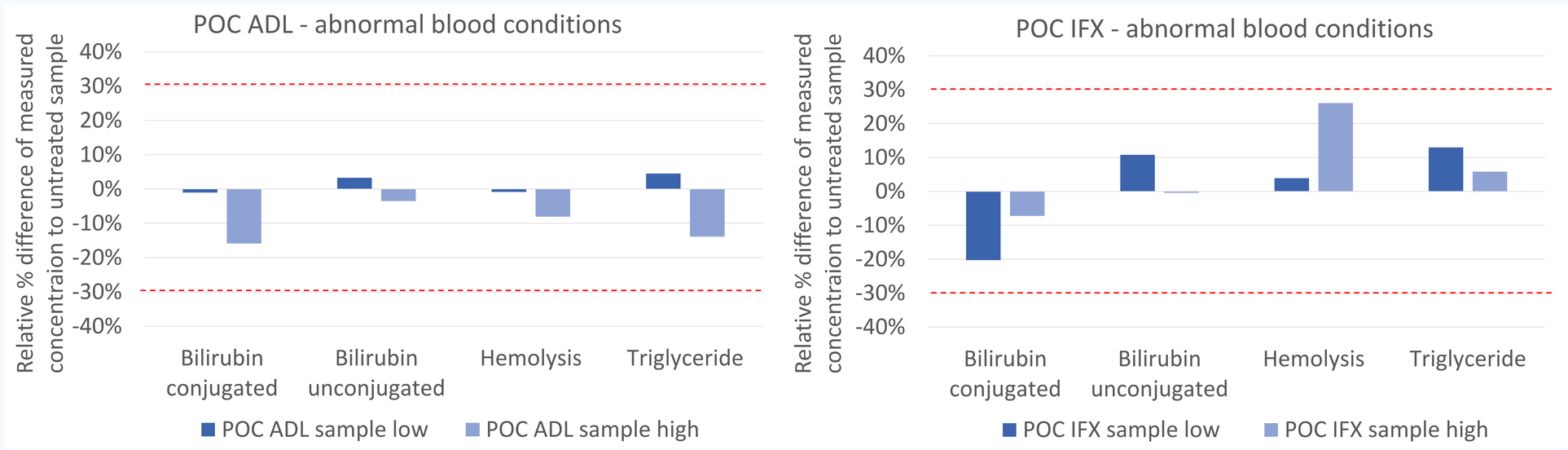

Figure 4: Relative difference between abnormal blood conditions and untreated sample. POC ADL assay left and POC IFX assay right.

Conclusion

Two POC assays for the determination of ADL or IFX in capillary blood or EDTA whole blood samples were successfully developed and can be used by healthcare professionals with time to results of only 15 minutes and without the need for additional laboratory equipment. No systematic interferences were detected with treated EDTA whole blood samples, which could appear when using blood as analyte matrix. The excellent agreement to serum trough levels shows that the POC adalimumab/infliximab whole blood assays are ideal for TDM analysis at a clinician's office or an infusion site.

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