P273 Validation of a smartphone-based patient monitoring system measuring calprotectin as the therapy follow-up marker

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BACKGROUND & OBJECTIVE

The disease course of Inflammatory Bowel Diseases (IBD) can be followed by calprotectin which is measured in patients' feces. One of the IBD therapy goals ("mucosal healing") is to achieve and keep calprotectin values as low as possible, at least below 250 µg/g. We have developed IB*Doc*® which allows the patient to perform a calprotectin test at home. The objective was to validate the IB*Doc*® home testing system and to compare its performance with laboratory-based methods.

METHODS

IB*Doc*® consists of a fecal collection and extraction device (CALEX® Valve), an immunochromatographic rapid test which is measured by a smartphone app (CalApp®) controlling the phone's camera. Results are automatically calculated by the app, sent to and stored in a secure webserver (IB*Doc*® Portal; please refer to P452 for details). Leftover fecal samples (kindly provided by Labor ROTHEN, Basel) were extracted either with CALEX® Valve or by conventional laboratory methods. The CALEX® extracts were then loaded onto immunochromatograhic test cassettes, whereas the manually prepared extracts from the same fecal samples were analyzed with the BÜHLMANN fCAL® ELISA. The test cassettes were read (scanned) with different iPhones and Android phones. Precision, reproducibility and between-smartphone comparability of the IB*Doc*® system was determined. The quantitative IB*Doc*® results were compared to the results obtained by the laboratory-based ELISA method. All statistical analyses were carried out with Analyse-it for Microsoft Excel.

RESULTS

Standardisation of IB*Doc*®

Test cassettes (TCs) were measured with the BÜHLMANN Quantum Blue® Reader using fecal samples calibrated by the BÜHLMANN fCAL® ELISA. The same TCs were measured with the different smartphones and the raw data were transposed using the Quantum Blue® curve parameters in a way that the recalculated IB*Doc*® calprotectin concs. were equal to Quantum Blue® and original fCAL® ELISA concs.

Reproducibility, precision and accuracy of IB*Doc*®

The mean reproducibility CVs (coefficient of variation) of 3 TCs with normal, moderate and high calprotectin values measured (scanned) 20-times with iPhone 5 and Samsung Galaxy S4 were calculated to be 4.6% and 7.8%, respectively (Tab. 1A). 20 TCs each were loaded with 7 stool extracts containing fCAL® ELISA calprotectin target levels of 50 to 829 µg/g and measured with the iPhone 5S. The mean conc. CV was calculated to be 16.6% with perfect accuracy (Tab. 1B).

Tab. 1A: Reproducibility of smartphone reader (smartphone optics).

Reproducibility (20 scans each)	iPhone 5			Samsung Galaxy S4		
	Normal	Moderate	High	Normal	Moderate	High
Mean [µg/g]	53	127	548	48	110	503
Median [µg/g]	55	126	549	50	110	496
SD [µg/g]	3.2	4.1	25.5	4.5	5.7	44.8
CV	6.0%	3.2%	4.7%	9.2%	5.2%	8.9%

Tab. 1B: Precision and accuracy of IB*Doc*® system (smartphone reader & TC variability).

Precision (20 replicates each)	IB*Doc*® (with iPhone 5S)						
	N1	N2	M1	M2	H1	H2	H3
fCAL® ELISA [µg/g]	50	76	134	229	456	634	829
iPhone 5S [µg/g]	51	92	144	232	507	629	856
Conc. CV IB*Doc*®	11.4%	11.4%	16.3%	21.6%	19.8%	14.5%	20.9%

Fig. 1: Comparison of iPhones 4S, 5, 5S, 5C and 3 Android phones to the Quantum Blue® Reader before (red lines) and after (blue lines) correction. Grey line, identity line ; bold orange line, mean of 7 smartphones before correction; bold light blue line, mean of 7 smartphones after correction.

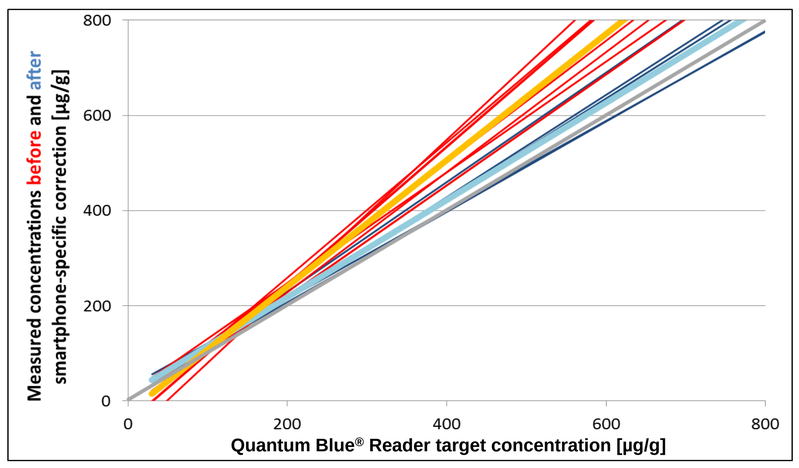
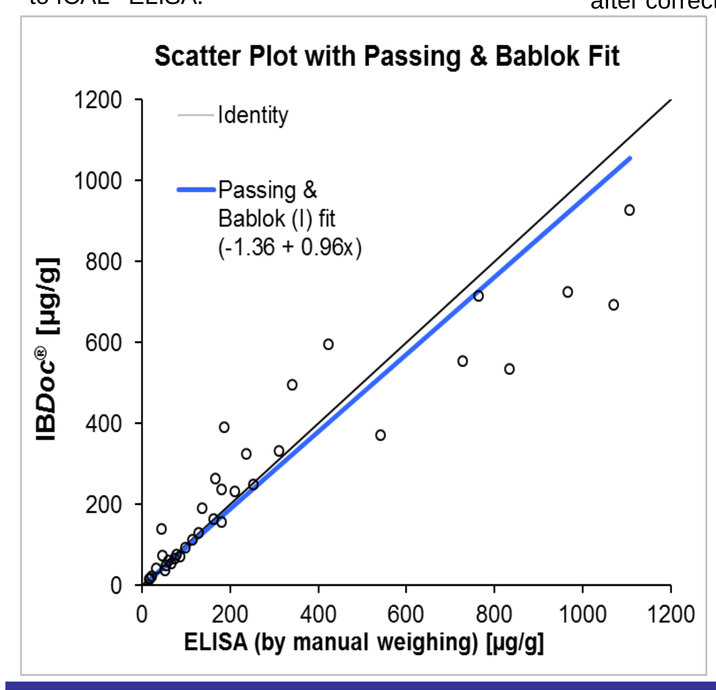


Fig. 2: Quantitative comparison of IB*Doc*® system to fCAL® ELISA.



Tab. 2: Agreement of IB*Doc*® system (using iPhone 5C) with fCAL® reference ELISA.

IB*Doc*® \ ELISA Weigh-in (Reference)	Normal <100	Moderate 100-300	High >300	
Normal <100	91	5	0	96
Moderate 100-300	8	54	1	63
High >300	0	7	108	115
	99	66	109	274

Between-smartphone comparability

The various smartphone optics yielded quite different raw signals when reading the same TCs (Fig. 1, red lines). These raw data were analyzed and then parameterized. Smartphone-specific parameters were then applied to correct the raw data in a way that the calculated final calprotection concs. ranged within ±15% among the various smartphones (Fig. 1, blue lines).

Comparison of IB*Doc*® with reference ELISA

Mean IB*Doc*® values of 35 fecal samples with target concs. <1000 µg/g were compared to fCAL® ELISA by Passing-Bablok: slope = 0.96, bias = -1.4 µg/g (Fig. 2). Linear regression testing yielded R^2 = 0.882. 44 fecal samples with fCAL® ELISA target values ranging from 17 to 2094 µg/g were measured up to 9-times each with the IB*Doc*® system (using iPhone 5C) and each single result was compared to the ELISA reference result. The total agreement was calculated to be 92.3% (Tab. 2).

CONCLUSIONS

- IB*Doc*® is the first complete and validated test system which allows the IBD patient to monitor and follow his inflammatory status by measuring the IBD biomarker, fecal calprotectin, using his/her own smartphone.
- The performance of the smartphone-based IB*Doc*® home testing system is comparable to professional, laboratory-based methods.
- Currently, following smartphones are validated for the use with IB*Doc*®: iPhone 4S, 5, 5S, 5C, 6; Samsung Galaxy S3, S4; HTC One.

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