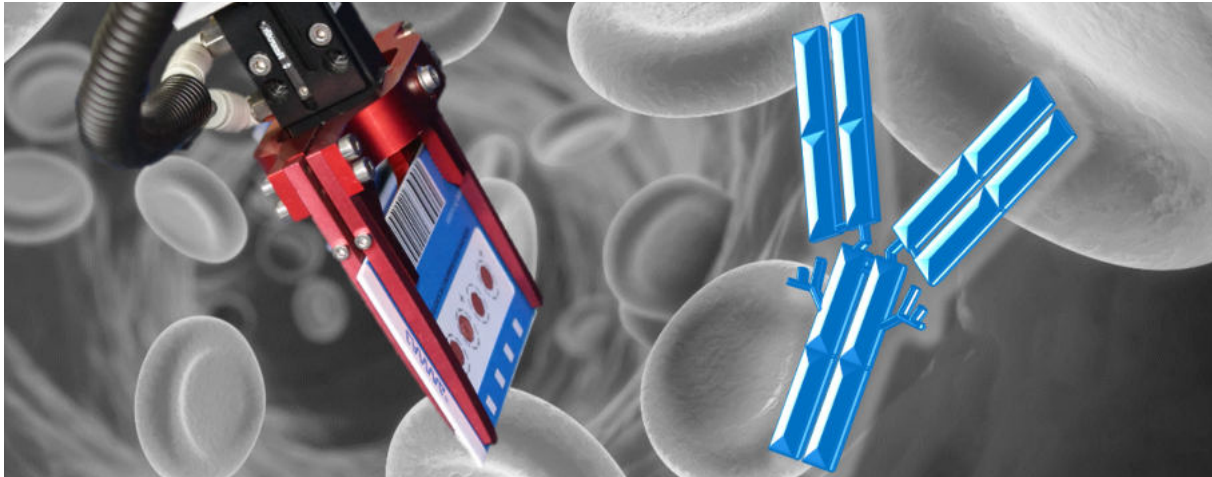


Fully automated Dried Blood Spot sample handling and extraction for serological testing of SARS-CoV-2 antibodies



Keywords

Coronavirus, SARS-CoV-2, pandemy, antibodies, ELISA, serological testing, DBS sample collection

Introduction

The outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has reached unexpected dimensions. All around the globe scientists are researching the immunization process after infection, to develop new and innovative transmission models, vaccines, and therapies. Thereby, the formation and subsequent reduction of human IgG and IgM antibodies against SARS-CoV-2 play a crucial role in epidemiologic studies. Several research groups have demonstrated that dried blood spot (DBS) sampling is a simple and cheap way of performing such serological testing.

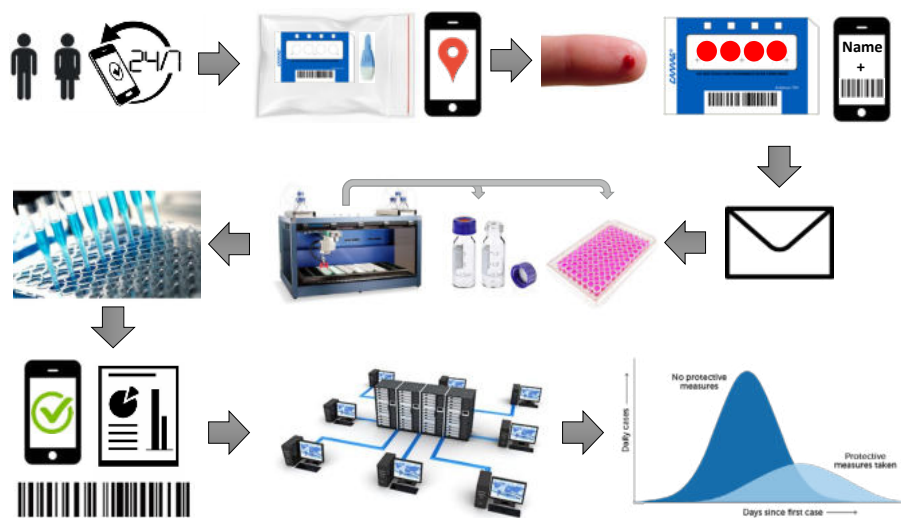


Figure 1: Concept of SARS-CoV-2 antibody analysis using the CAMAG DBS-MS 500 HCT for population screening

NOTE: The presented results are to be regarded as examples only!

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Scope

The presented setup of combining a CAMAG DBS-MS 500 HCT with a CTC PAL module permits to collect DBS extracts in sample vials or microtiter plates (e.g. 96-well plates) for further processing (e.g. ELISA for IgG). It is a valuable tool for diagnostic laboratories to test large populations for SARS-CoV-2 antibodies using a cost-effective, simple, and accurate workflow. The possibility to perform at-home sampling of DBS and sending them to a centralized laboratory is convenient and protects individuals from risking or spreading an infection. The commercially available consumables that are required for a DBS at-home sampling kit are minimal: an alcohol pad for disinfection, a DBS card, a lancet, and instructions. Furthermore, DBS permits the use of standard postal service for the shipment to the lab, without the requirement for sample cooling.

Recommended devices

- CAMAG DBS-MS 500 HCT
- CTC PAL robot for offline sample collection in vials or microtiter plates (e.g. 96-well plate)
- Enzyme-linked immunosorbent assay (ELISA) kits (e.g. KT-1032 from Epitepe Diagnostics)
- Absorbance microplate reader (e.g. Tecan Sunrise)
- Multi-channel pipette

Optional:

- 6 mm Ø extraction head extension kit
- Microplate washer (e.g. Thermo Scientific Wellwash) or an automated ELISA workstation compatible with the KT-1032 from Epitepe Diagnostics

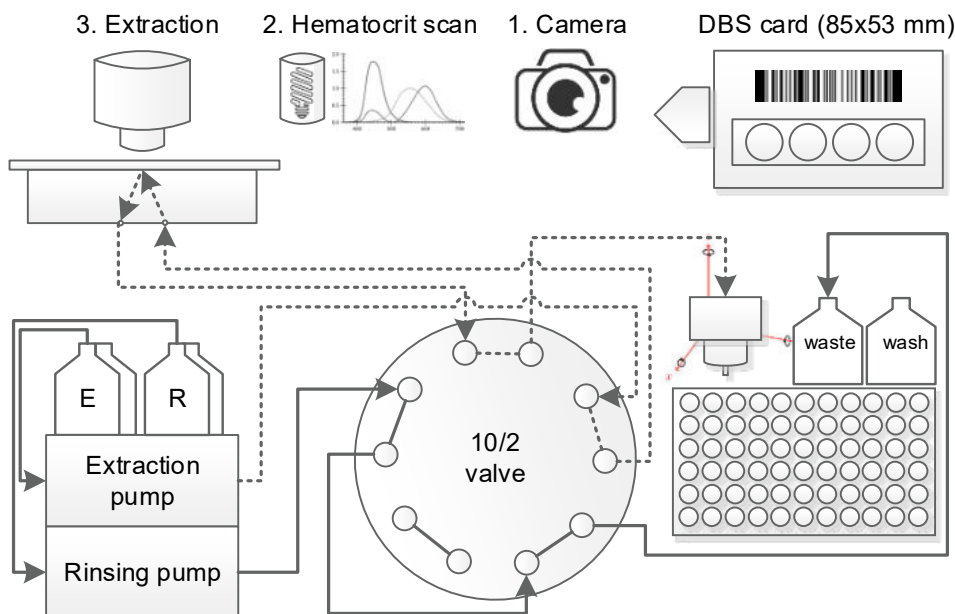


Figure 2: Schematic coupling of a CAMAG DBS-MS 500 HCT with a CTC PAL robot for offline sample collection. Module 1-3 (camera, HCT scan, and extraction) are embedded within the DBS autosampler.

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Samples

Dried blood spot samples with a minimum volume of 10 μL (≥ 6 mm \varnothing) on DBS AutoCollect cards (85 x 53 mm). Volumetric sampling is not required. The exact volume can be compensated using the hematocrit scanner of the CAMAG DBS-MS 500 HCT.

Standards

Negative and positive control samples are required to establish a signal threshold.

Sample extraction workflow

To start a run, DBS cards are loaded into the DBS-MS 500 HCT, and a sample batch is filled within the instrument's software. Afterwards, individual DBS samples are detected within the camera module according to spot quality criteria and barcode or label. Within the next module, the hematocrit is detected to compensate for potential volume bias, prior to the sample extraction (4 mm \varnothing , direct elution from the center of the spot), directly into a 96-well plate. For each extraction, 100 μL buffer solution contained within the Epitope ELISA kit were used. Depending on the automated wash program, the extraction takes 2-3 minutes per sample to deliver a concentrated extract that can be further processed without any other steps involved.

Results

During a proof-of-concept study, 13 authentic samples were analyzed and compared with serological rapid testing. Out of these, 12 (92.3%) were identified correctly using the here reported DBS method. One sample was reported as a false-negative finding. As the immune response is a time-dependent reaction, the duration of 12 days since the onset of symptoms has very likely not been long enough to form a sustainable amount of IgG antibodies based on the applied signal threshold. Overall, the DBS test setup showed a specificity of 100% (6/6) and a sensitivity of 86% (6/7).

The sample's stability was assessed by storing an IgG positive sample in liquid blood for 4 weeks at 4°C in an EDTA blood collection tube, and on a DBS card that was placed in a mini grip plastic bag together with a desiccant. Both conditions gave a positive test result for IgG antibodies after prolonged storage, with a deviation in signal <15% compared with the original sample.

Literature

Gaugler S, Sottas P-E, Blum K, Luginbühl M. Fully automated dried blood spot sample handling and extraction for serological testing of SARS-CoV-2 antibodies. *Drug Testing and Analysis*. 2021. doi:10.1002/dta.2946

Luginbühl M, Fischer Y, Gaugler S. Fully Automated Optical Hematocrit Measurement from Dried Blood Spots, *Journal of Analytical Toxicology*. 2020. doi: 10.1093/jat/bkaa189

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