Heike Weisser*, Katja Steinhagen, Ralf Höcker, Viola Borchardt-Lohölter, Özlem Anvari and Peter M. Kern

Evaluation of dried blood spots as alternative sampling material for serological detection of anti-SARS-CoV-2 antibodies using established ELISAs

https://doi.org/10.1515/cclm-2020-1436
Received September 25, 2020; accepted December 10, 2020; published online January 8, 2021

Abstract

Objectives: During the current pandemic, antibody testing based on venous serum helps to determine whether the tested person has been previously infected with SARS-CoV-2. Alternatively, capillary blood can be taken via a finger prick (dried blood spots, DBS). In this study, paired DBS and venipuncture samples were tested using two serological assays to evaluate the usability of DBS for the detection of anti-SARS-CoV-2 antibodies.

Methods: Paired samples of DBS and venous serum were collected from 389 volunteers, of whom 75 had a recent PCR-confirmed SARS-CoV-2 infection, and tested for anti-SARS-CoV-2 IgG antibodies against both viral S1 and nucleocapsid protein (NCP) antigens using two ELISAs. Degree of agreement and correlation coefficients between ELISA results based on the two sampling methods were calculated.

Results: Results of DBS showed almost perfect agreement and high correlations with results from corresponding serum samples in both the S1-based ELISA and the NCP-based ELISA.

Conclusions: ELISA results derived from DBS showed very high agreement to those obtained with serum, supposing adequate usability and robustness of DBS as sample material for detection of anti-SARS-CoV-2 antibodies. In the near future, large-scale epidemiological screening for antibodies against SARS-CoV-2 will be carried out. Since DBS reduce the strain on healthcare institutions regarding sample collection, they have a potential to facilitate efficient community- and population-based screening in the current SARS-CoV-2 pandemic.

Keywords: antibody detection; COVID-19; dried blood spots; ELISA; SARS-CoV-2.

***Corresponding author: Priv.-Doz. Dr. med. Heike Weisser,** Institute of Laboratory Medicine, University Medicine Marburg – Campus Fulda, Pacelliallee 4, 36043 Fulda, Germany, Phone: +49 (0) 661/84 6370, E-mail: heike.weisser@klinikum-fulda.de
Katja Steinhagen and Viola Borchardt-Lohölter, Institute for Experimental Immunology, affiliated to EUROIMMUN Medizinische Labordiagnostika AG, Lübeck, Germany
Ralf Höcker, Institute of Laboratory Medicine, University Medicine Marburg – Campus Fulda, Fulda, Germany
Özlem Anvari, Hospital St. Josef, Schweinfurth, Germany
Peter M. Kern, Medical Clinic IV, University Medicine Marburg – Campus Fulda, Fulda, Germany

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative pathogen of coronavirus disease 2019 (COVID-19), belongs to the family of coronaviruses and, like SARS-CoV, is classified in the genus Betacoronavirus [1]. The new coronavirus originated in China in the city of Wuhan, Hubei province, and within a few months, the virus spread reached the status of a pandemic [2, 3]. The extent of this virus spread varies both widely nationally and regionally. Epidemiological studies on the specificity, formation rate, dynamics, and persistence of the antibody response are imperative to better understand the further spread of the virus. Serological tests that detect antibodies to SARS-CoV-2 can help to identify people who have already been infected with the virus and help estimate the level of exposure of a population. Thereby, they can support effective strategies to contain the pandemic [4]. However, such large-scale epidemiological studies, especially in less developed countries with limited access to healthcare infrastructure, are hampered by a number of pre-analytical requirements. Usually, serological tests are carried out from plasma or serum and therefore require venous blood collection by trained phlebotomists. Moreover, soon after collection a centrifuge and other supplies to extract the serum from blood specimens are needed. In addition, the samples must be aliquoted,

Open Access. © 2020 Heike Weisser et al., published by De Gruyter. This work is licensed under the Creative Commons Attribution 4.0 International License.

stored and cooled during transport. One approach to circumvent these constraints and thereby to facilitate the large-scale and frequent testing of anti-SARS-CoV-2 antibodies could be the collection of blood samples as dried blood spots (DBS) [5]. These are produced by dripping capillary blood obtained by a finger prick on a filter paper. DBS offer the advantages of optional at-home self-collection without requiring trained phlebotomists and large-scale sample collection in a short period of time.

In addition, DBS samples are highly stable at room temperature and it is not necessary to maintain the cold chain for the sample storage and transport to the laboratory [6]. However, when this study was initiated, the existing commercial SARS-CoV-2 antibody assays had not yet been validated or received regulatory approval with this method of sample collection and transport. The aim of this study was to determine whether DBS are a useful sampling material for detection of IgG antibodies against the S1 domain of the spike protein and nucleocapsid protein (NCP) using the Anti-SARS-CoV-2 enzyme-linked immunosorbent assay (ELISA) and the Anti-SARS-CoV-2 NCP ELISA, respectively.

Materials and methods

Collection of sample material

Between 28 May and 5 June 2020, blood samples were taken from 389 volunteers, of whom 75 had a recent PCR-confirmed SARS-CoV-2 infection. We expected that some of the volunteers had not come into contact with SARS-CoV-2, while others might have had an asymptomatic or symptomatic, unrecognized infection with SARS-CoV-2. This method comparison was conducted in the framework of a longitudinal study on the humoral response to SARS-CoV-2 in a closed cohort. Collection of blood samples was carried out with informed consent of the participants and was approved by the Ethics Committee of the regional medical council Bavaria. Privacy protection was guaranteed by anonymization of blood samples. The study complies with the Declaration of Helsinki.

From each individual, blood samples were collected via both finger prick and venipuncture by a healthcare professional. Venous blood was collected from the median cubital vein using S-Monovette 7.5 mL Z-Gel tubes (Sarstedt, Germany). Capillary blood was collected using the EUROIMMUN Blood Collection Card. First, the side of the disinfected fingertip was punctured by a sterile lancet. Then, the hand was massaged several times from the wrist in the direction of the puncture site, resulting in the formation of a blood drop. One large drop of blood (approximate volume: 30 µL) was placed in each of the five circles on the blood collection card (dried blood spots, DBS). In a sample of ideal quality, the droplets were neither smeared on the surface nor applied repeatedly and the circle was filled with blood to at least two thirds, saturating the filter membrane. If these conditions were not met or only met in parts, the sample did not fully comply with standardized pre-analytical requirements. Hence, such a sample was categorized as being of limited quality. This terminology is used hereafter. The blood collection card dried for 2 to 3 h before it was closed and placed in a sealable plastic pouch with a desiccant sachet. When stored in this manner, the DBS are stable for up to three weeks after sample collection at 2–8 °C and for up to two weeks at room temperature (18–25 °C). Blood collection cards can be transported via standard mail if special packaging requirements are met and the appropriate labeling is provided. The blood collection cards were stored in the fridge and shipped via courier service to the laboratory. Samples were processed in the labs 6–14 (mean 12.2) days after blood collection.

Detection of anti-SARS-CoV-2 antibodies

Before analysis, each DBS was assessed in terms of its quality and degree of saturation. Of the 389 blood collection cards, 215 contained DBS of ideal quality.

The DBS to be analyzed were cut from the membrane of the blood collection card using a 3/16 inch puncher. A circular piece from the center of each DBS was transferred into the well of an empty uncoated 96-well plate and 250 µL extraction buffer was added. After the 96-well plate was covered and incubated at 37 ± 1 °C for 1 h, the extract solution was mixed thoroughly and 100 µL of the extract solution was used as sample material for detection of antibodies against SARS-CoV-2. Extracted samples must be incubated on the same working day.

DBS extracts and serum samples were tested for human SARS-CoV-2 antibodies of the immunoglobulin class IgG against both the S1 domain of the spike protein including the immunologically relevant receptor binding domain using the Anti-SARS-CoV-2 ELISA (IgG) as well as against the nucleocapsid protein (NCP) using the Anti-SARS-CoV-2 NCP ELISA (IgG) from EUROIMMUN. Hence, blood from each individual (n=389) was tested four times, producing 1556 results of serological tests.

The serological tests were performed according to the manufacturer's instructions. Results were evaluated semiquantitatively by calculating a ratio of the extinction of the sample over the extinction of the calibrator. A ratio <0.8 was interpreted as negative, ratio ≥ 0.8 to <1.1 as borderline and a ratio ≥ 1.1 as positive. Analysis of DBS and serum samples were performed at the laboratories of the Institute for Experimental Immunology, EUROIMMUN AG, Lübeck and the Institute of Laboratory Medicine, Fulda, respectively.

Evaluation and statistics

Results obtained by each sampling method were compared between each other. The diagnostic accuracy was calculated as the sum of samples that were positive and samples that were negative with both sampling materials divided by the total number of samples. Borderline results were reported but excluded from the calculation of the diagnostic accuracy, since they are subjected to retesting in laboratory practice. The degree of agreement between results based on different sampling methods was quantified using Cohen's κ [7, 8]. Cohen's κ values are categorized as follows: $0<\kappa<0.2$: slight agreement, $0.21<\kappa<0.4$: fair agreement, $0.41<\kappa<0.6$: moderate agreement, $0.61<\kappa<0.8$: substantial/good agreement, $0.81<\kappa<1$: almost perfect/very good agreement. Borderline results were included in the agreement analysis. Correlation coefficients were used to quantify the statistical association between ELISA ratios based on the two blood sampling methods. The comparisons between DBS and serum samples

were performed separately for DBS with ideal as well as limited quality. For evaluation of differences in number of borderline results between DBS and serum samples paired tests were used.

Results

Comparison between ELISA results based on DBS of ideal quality and paired serum samples

In the S1-based Anti-SARS-CoV-2 ELISA, the diagnostic accuracy of DBS of ideal quality was 100% (Table 1). Seven of 215 results were evaluated as borderline (Table 1). The agreement between results of both sampling methods was almost perfect (Table 2). ELISA ratios were strongly correlated (Figure 1A).

In the Anti-SARS-CoV-2 NCP ELISA, the diagnostic accuracy of DBS of ideal quality was 99.5% (Table 3). One sample was evaluated as weakly positive by DBS but as negative by serum. Sixteen of 215 results were evaluated as borderline (Table 3). The results of both sampling methods showed an almost perfect degree of agreement (Table 2). ELISA ratios were strongly correlated (Figure 1B).

Comparison between ELISA results based on DBS of limited quality and paired serum samples

In the S1-based Anti-SARS-CoV-2 ELISA, the diagnostic accuracy of DBS of limited quality was 100% (Table 4). Ten of 174 results were evaluated as borderline (Table 4). The agreement between results of both sampling methods was almost perfect (Table 2). ELISA ratios were strongly correlated (Figure 1C).

In the Anti-SARS-CoV-2 NCP ELISA, the diagnostic accuracy of DBS of limited quality was 100% (Table 5). Thirteen of 174 results were evaluated as borderline (Table 5). The agreement between results of both sampling methods was almost perfect (Table 2). ELISA ratios were strongly correlated (Figure 1D).

Table 1: Contingency table of 215 DBS of ideal quality and paired serum samples in the Anti-SARS-CoV-2 ELISA (IgG).

Antibodies against S1 of SARS-CoV-2 n=215		Venous serum samples		
		positive	borderline	negative
Dried blood spots of ideal quality	positive	61	2	0
	borderline	0	1	4
	negative	0	0	147

Table 2: Degree of agreement of ELISA results based on paired DBS and serum samples.

Sampling materials	Antibodies against S1 of SARS-CoV-2 κ; confidence interval	Antibodies against NCP of SARS-CoV-2 κ; confidence interval
215 DBS of ideal quality and paired serum samples	0.94; [0.89, 0.99]	0.89; [0.82, 0.95]
174 DBS of limited quality and paired serum samples	0.89; [0.82, 0.97]	0.90; [0.83, 0.97]
389 DBS and paired serum samples	0.92; [0.87, 0.96]	0.89; [0.85, 0.94]

Detection of borderline results

When comparing ELISA results of paired DBS and serum samples with regard to the sampling material, the number of borderline results obtained from DBS and serum were comparable in both the S1 assay (DBS: n=12; serum: n=8; t(388)=1.07, p=0.29) and the NCP assay (DBS: n=20; serum: n=19; t(388)=0.47, p=0.64).

Discussion

The present study was designed to determine whether DBS are a useful sampling material for detection of antibodies against SARS-CoV-2.

Although it has been demonstrated that an abundance of chemical substances differs between capillary and venous systems [9, 10], DBS testing has been used successfully for the screening of newborns and diagnostics for infectious diseases [5]. Nevertheless, for every new diagnostic test it has to be validated whether results based on differing sampling materials (e.g., serum, heparin or citrate plasma, DBS) lead to concordant results or whether the use of one specific sampling material is a source of significant variability [11]. In the latter case, their interchangeable use is not recommended for the new serological test. A potential impact of such a variability on test results is likely to be amplified in case of low-abundant analytes, because the smaller volumes of blood collected via DBS entail an increased probability of false-negative results [12]. A highly sensitive testing strategy is of particular relevance for the

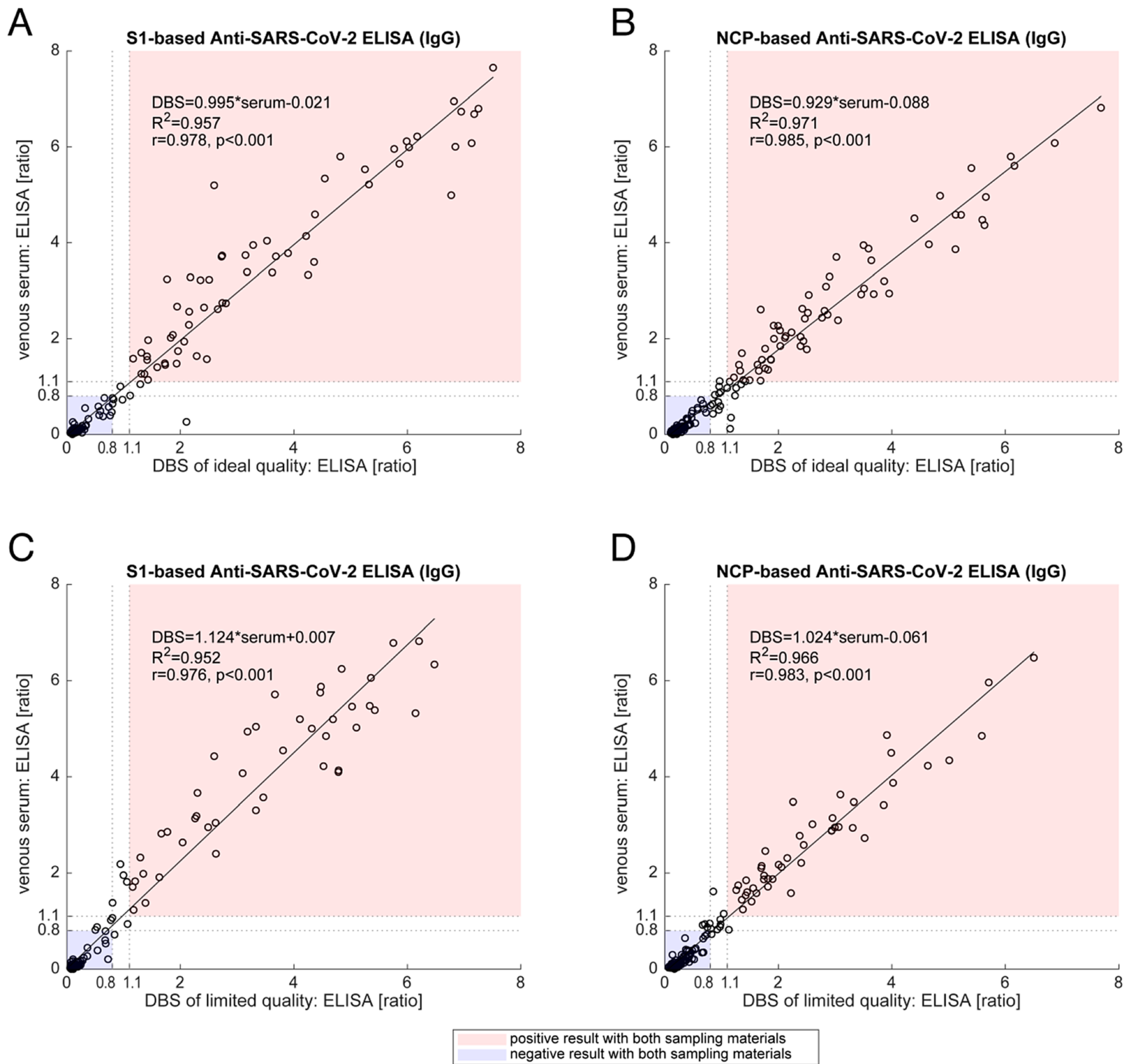

Figure 1: Correlation of ELISA ratios for detection of IgG antibodies against SARS-CoV-2 (S1: left panels, NCP: right panels) based on paired DBS (ideal quality: upper panels, limited quality: lower panels) and serum samples.
Each plot includes the linear regression relation in the form of $Y=\beta_1x + \beta_0$, the coefficient of determination R^2, the correlation coefficient r and the corresponding p-value.

Table 3: Contingency table of 215 DBS of ideal quality and paired serum samples in the Anti-SARS-CoV-2 NCP ELISA (IgG).

Antibodies against NCP of SARS-CoV-2 n=215		Venous serum samples		
		Positive	Borderline	Negative
Dried blood spots of ideal quality	Positive	63	4	1
	Borderline	1	5	6
	Negative	0	0	135

Table 4: Contingency table of 174 DBS of limited quality and paired serum samples in the Anti-SARS-CoV-2 ELISA (IgG).

Antibodies against S1 of SARS-CoV-2 n=174		Venous serum samples		
		Positive	Borderline	Negative
Dried blood spots of limited quality	Positive	43	0	0
	Borderline	4	2	1
	Negative	0	3	121

purpose of epidemiological surveillance. Moreover, minimizing the rate of false negative results is of utmost importance for circumstances in which follow-up testing is difficult, as false negative results would have more severe consequences than false positives. Although a negative serological test result does not exclude a SARS-CoV-2

Table 5: Contingency table of 174 DBS of limited quality and paired serum samples in the Anti-SARS-CoV-2 NCP ELISA (IgG).

Antibodies against NCP of SARS-CoV-2 n=174		Venous serum samples		
		Positive	Borderline	Negative
Dried blood spots of limited quality	Positive	45	1	0
	Borderline	2	5	1
	Negative	0	4	116

infection, follow-up testing of such negatively tested samples is typically not performed in the context of seroprevalence studies. In a similar vein, a maximally specific testing strategy is equally relevant when screening populations with low prevalence, as it is the case for infection with SARS-CoV-2. Positive test results can indicate a SARS-CoV-2 infection and are confirmed by a significant increase in the specific IgG antibody activity and/or seroconversion in a follow-up sample taken after at least seven to 10 days [13–15]. False positive test results must be avoided, since they might be misinterpreted as an indication of immunity to SARS-CoV-2 infection. Orthogonal testing strategies including a primary screening test and a secondary confirmation test can be used to improve the specificity of the combined tests [16]. In the case of a borderline test result however, a secure evaluation is not possible and clarification by means of other diagnostic methods and/or the serological investigation of a follow-up sample is usually performed.

DBS have been established as sampling material for serological detection of antibodies against e.g., hepatitis B and C viruses [17–19], human immunodeficiency virus [20–22], dengue virus [23], and malaria [24, 25]. However, only a few studies on the applicability of DBS for the detection of anti-SARS-CoV-2 antibodies are currently available and their significance is limited by a relatively small sample size.

Recently, a pilot study was conducted which assessed the suitability of DBS obtained by self-collection for use in diagnostic tests of SARS-CoV-2 [26]. The 145 DBS investigated had been collected by the participants themselves, accompanied by a telehealth video session for documentation purposes. 93% of the DBS samples were of sufficient and suitable quality for submission for SARS-CoV-2 RNA detection and serology. The authors concluded that specimens collected and posted by the participants are useful for SARS-CoV-2 testing.

McDade et al. developed an ELISA for detection of anti-SARS-CoV-2 IgG antibodies that requires only a drop of capillary whole blood [27]. The authors demonstrated the feasibility of using DBS samples for SARS-CoV-2 IgG antibody detection in this ELISA based on 18 samples and observed that OD values of DBS samples from PCR-confirmed COVID-19 cases were significantly higher in comparison with presumptive negatives samples [27].

In another study, the same authors assessed the use of the self-collected DBS samples from a community sample of 232 participants including healthcare workers and 30 known COVID-19 cases and their household members [28]. As part of the analysis, a tight agreement between matched DBS and serum samples was shown based on a small number of samples.

A study by Amendola et al. analyzed paired DBS (collected via DBS cards using 266 filter paper from Perkin Elmer) and serum samples from 52 healthcare workers and found high correlation and almost perfect agreement between both sampling methods in detection of specific anti-SARS-CoV-2 antibodies using the Anti-SARS-CoV-2 ELISA (IgG) from EUROIMMUN [29].

In contrast to the small sample sizes reported in previous publications, our study samples were collected via DBS and in parallel via venipuncture from a total of 389 individuals. Based on both sampling materials, IgG antibodies against the S1 domain of the spike protein and the modified nucleocapsid protein were detected. The results revealed that DBS showed almost perfect agreement and high correlation with results from corresponding venous serum samples in both ELISAs reflecting adequate usability of DBS as sample material for detection of anti-SARS-CoV-2 antibodies. Importantly, none of the tests yielded false negative results using DBS compared to serum. Only one sample was evaluated as weakly positive by DBS but as negative by serum, which was a false positive result by DBS (Table 3). Regarding the rate of borderline results, there was neither a difference between DBS and serum samples in the NCP assay nor in the S1 assay.

The applicability of an ELISA (IgM/IgG) and a lateral flow-based rapid test (IgM, IgG) for the analysis of paired DBS and blood plasma samples obtained from 26 individuals was assessed in a proof-of-principle study by Thevis et al. [30]. The results from paired plasma/serum and DBS demonstrated the principle applicability of DBS to the selected anti-SARS-CoV-2 antibody assays when applying moderate modifications to sample preparation protocols of the manufacturers. Interestingly, the authors assessed the effect of modifying parameters such as the blood volume used to produce DBS and sample/buffer dilution ratios and found that prolonged extraction periods were not found to affect the comparability of the test results, whereas the blood volume resulting in DBS and dilution factors were critical to reaching test results similar

to those obtained from plasma and serum analyses with the considered assays [30].

With consideration of such pre-analytical pitfalls like blood volume, we evaluated the pre-analytical quality of the DBS samples. Based on this evaluation, 174 of 389 samples were classified as being of limited pre-analytical quality. A likely explanation for this high share (44.7%) is that the instructions provided for collection of DBS had probably not yet been perfected. Meanwhile, a video and a descriptive tutorial including stepwise illustrations have been added to the DBS collection set to ensure its correct use.

Our analysis was stratified by DBS pre-analytical quality to examine whether differences in their applicability for antibody detection exist. Remarkably, based on the κ values and their overlapping confidence intervals, we observed that DBS samples of limited pre-analytical quality performed equally well as DBS samples of ideal pre-analytical quality (Table 2). Thus, the DBS collecting system is characterized by a relative robustness, which makes it usable in the field of self-collecting. Nevertheless, because low-quality DBS samples might be a source of uncertainty, DBS of high quality should be used whenever possible.

In near future, large-scale epidemiological screening for antibodies against SARS-CoV-2 will be used to determine the proportion of a population previously infected with SARS-CoV-2, revealing the share of asymptomatic and mild infections, which could be a major source of disease transmission. In fact, using DBS, samples could be self-collected and mailed-in on a daily basis e.g., in the framework of a clinical study investigating antibody kinetics on a close-meshed operating schedule or during lockdown and quarantine. Especially in the latter conditions, participants of serological studies may not be able to leave home and hence samples collection is likely to be biased if it relies on clinic-based blood collection. Seroprevalence studies that minimize close contact between participants and health care providers limit the risk of exposure and may encourage participation. For seroprevalence studies in remote, resource-constrained regions, DBS kits could be distributed centrally and transported away on another day without the need for medical personnel being present. Using self-collected DBS allows assessment of seroprevalence in cohorts of meaningful size in short time. Moreover, being able to collect blood samples without the need for phlebotomists reduces the consumption of scarce personal protective equipment. Future studies to assess the long-term stability of DBS cards with respect to storage and archiving conditions are required.

In summary, DBS are an adequate sample material and can be used as a valid alternative for serum or plasma for detection of anti-SARS-CoV-2 IgG antibodies with the S1-based Anti-SARS-CoV-2 ELISA and the Anti-SARS-CoV-2 NCP ELISA. Evidence from the present study adds to a body of research confirming the usability of DBS for serological testing of COVID-19 patients.

Because DBS samples enable decentralized sample collection and thereby reduce the strain on healthcare institutions, they will facilitate efficient community- and population-based screening in the current SARS-CoV-2 pandemic. Moreover, DBS samples can help alleviate costs and logistical constraints associated with collecting, transporting and processing blood for large-scale anti-SARS-CoV-2 antibody testing.

Acknowledgments: The authors thank the volunteers for participating in the study and Tina Bude and Tanja Rützel for their excellent technical assistance. KS and VBL are employees of EUROIMMUN Medizinische Labordiagnostika AG. EUROIMMUN provided reagents used in this study and bore the expenses for logistic costs and volunteers' allowances.
Research funding: None declared.
Author contributions: HW: Project administration, Investigation, Validation, Writing – original draft. KS: Resources, Project administration, Writing – review and editing. RH: Investigation, Data curation, Writing – review and editing. VBL: Formal analysis, Visualization, Writing – original draft. ÖA: Project administration, Investigation, Writing – review and editing. PMK: Funding acquisition, Supervision, Conceptualization, Writing – review and editing.
Competing interests: HW, RH, ÖA, PMK declare no conflicts of interest. KS and VBL are employees of EUROIMMUN Medizinische Labordiagnostika AG.
Informed consent: Informed consent was obtained from all individuals included in this study.
Ethical approval: The study complies with the Declaration of Helsinki.

References

1. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol 2020;5:536–44.
2. Wang G, Jin X. The progress of 2019 novel coronavirus event in China. J Med Virol 2020;92:468–72.
3. Gralinski LE, Menachery VD. Return of the coronavirus: 2019-nCoV. Viruses 2020;12:1–8.
4. WHO. R&D Blueprint and COVID-19; n d. Available from: https://www.who.int/teams/blueprint/covid-19 (Accessed 5 August 2020).

5. Lim MD. Dried blood spots for global health diagnostics and surveillance: opportunities and challenges. Am J Trop Med Hyg 2018;99:256–65.
6. Trifonova OP, Maslov DL, Balashova EE, Lokhov PG. Evaluation of dried blood spot sampling for clinical metabolomics: effects of different papers and sample storage stability. Metabolites 2019; 9:277.
7. Watson PF, Petrie A. Method agreement analysis: a review of correct methodology. Theriogenology 2010;73:1167–79.
8. Kwiecien R, Kopp-Schneider A, Blettner M. Concordance analysis – part 16 of a series on evaluation of scientific publications. Dtsch Ärztebl 2011;108:515–21.
9. Kupke IR, Kather B, Zeugner S. On the composition of capillary and venous blood serum. Clin Chim Acta 1981;112:177–85.
10. Tang R, Yang H, Choi JR, Gong Y, You ML, Wen T, et al. Capillary blood for point-of-care testing. Crit Rev Clin Lab Sci 2017;54: 294–308.
11. Bond MM, Richards-Kortum RR. Drop-to-drop variation in the cellular components of fingerprick blood: implications for point-of-care diagnostic development. Am J Clin Pathol 2015;144: 885–94.
12. Aylward LL, Hays SM, Smolders R, Koch HM, Cocker J, Jones K, et al. Sources of variability in biomarker concentrations. J Toxicol Environ Health B Crit Rev 2014;17:45–61.
13. WHO. Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases: interim guidance; 2020. Available from: https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117 (Accessed 18 November 2020).
14. Udugama B, Kadhiresan P, Kozlowski HN, Malekjahani A, Osborne M, Li VYC, et al. Diagnosing COVID-19: the disease and tools for detection. ACS Nano 2020;14:3822–35.
15. Okba NMA, Müller MA, Li W, Wang C, GeurtsvanKessel CH, Corman VM, et al. Severe acute respiratory syndrome coronavirus 2 – specific antibody responses in coronavirus disease 2019 patients. Emerg Infect Dis 2020;26:1478–88.
16. Xu G, Emanuel AJ, Nadig S, Mehrotra S, Caddell B, Curry SR, et al. Evaluation of orthogonal testing algorithm for detection of SARS-CoV-2 IgG antibodies. Clin Chem 2020;66:1531–7.
17. Lange B, Roberts T, Cohn J, Greenman J, Camp J, Ishizaki A, et al. Diagnostic accuracy of detection and quantification of HBV-DNA and HCV-RNA using dried blood spot (DBS) samples – a systematic review and meta-analysis. BMC Infect Dis 2017; 17:693.
18. Muzembo BA, Mbendi NC, Nakayama SF. Systematic review with meta-analysis: performance of dried blood spots for hepatitis C antibodies detection. Publ Health 2017;153:128–36.
19. Mössner BK, Staugaard B, Jensen J, Lillevang ST, Christensen PB, Holm DK. Dried blood spots, valid screening for viral hepatitis and human immunodeficiency virus in real-life. World J Gastroenterol 2016;22:7604–12.
20. Bertagnolio S, Parkin NT, Jordan M, Brooks J, García-Lerma JG. Dried blood spots for HIV-1 drug resistance and viral load testing: a review of current knowledge and WHO efforts for global HIV drug resistance surveillance. AIDS Rev 2010;12:195–208.
21. Smit PW, Sollis KA, Fiscus S, Ford N, Vitoria M, Essajee S, et al. Systematic review of the use of dried blood spots for monitoring HIV viral load and for early infant diagnosis. PloS One 2014;9: e86461.
22. Adawaye C, Kamangu E, Moussa AM, Tchoumbou B, Vaira D, Moutschen M. Use of Dried Blood Spot to improve the diagnosis and management of HIV in resource-limited settings. World J AIDS 2013;03:251–6.
23. Descloux E, La Fuentez C, Roca Y, De Lamballerie X. Clinical significance of intra-host variability of dengue-1 virus in venous and capillary blood. Clin Microbiol Infect 2014;20:O167–75.
24. Taneja I, Erukala M, Raju KSR, Singh SP, Wahajuddin. Dried blood spots in bioanalysis of antimalarials: relevance and challenges in quantitative assessment of antimalarial drugs. Bioanalysis 2013; 5:2171–86.
25. Canier L, Khim N, Kim S, Eam R, Khean C, Loch K, et al. Malaria PCR detection in Cambodian low-transmission settings: dried blood spots versus venous blood samples. Am J Trop Med Hyg 2015;92: 573–7.
26. Guest JL, Sullivan PS, Valentine-Graves M, Valencia R, Adam E, Luisi N, et al. Suitability and sufficiency of telehealth clinician-observed, participant-collected samples for SARS-CoV-2 testing: the iCollect cohort pilot study. JMIR Public Heal Surveill 2020;6: e19731.
27. McDade TW, McNally E, D'Aquila RT, Mustanski B, Miller A, Vaught L, et al. Enzyme immunoassay for SARS-CoV-2 antibodies in dried blood spot samples: a minimally-invasive approach to facilitate community- and population-based screening. MedRxiv 2020:2020.04.28.20081844. https://doi.org/10.1101/2020.04.28.20081844.
28. McDade TW, McNally E, Zelikovich A, D'Aquila R, Mustanski B, Miller A, et al. High seroprevalence for SARS-CoV-2 among household members of essential workers detected using a dried blood spot assay. PloS One 2020;15:e0237833.
29. Amendola A, Bianchi S, Gori M, Barcellini L, Colzani D, Canuti M, et al. Dried blood spot as an alternative to plasma/serum for SARS-CoV-2 IgG detection, an opportunity to be sized to facilitate COVID-19 surveillance among schoolchildren. Pediatr Infect Dis J 2020;40:e46–7.
30. Thevis M, Knoop A, Schaefer MS, Dufaux B, Schrader Y, Thomas A, et al. Can dried blood spots (DBS) contribute to conducting comprehensive SARS-CoV-2 antibody tests? Drug Test Anal 2020; 12:994–7.