Low sensitivity of SARS-CoV-2 rapid antigen self-tests under laboratory conditions

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Abstract

SARS-CoV-2-antigen-testing has been proposed as a 'game-changing' tool to interrupt infection chains. Thereby European strategies focused on two pillars, namely rapid antigen tests conducted by health care experts and/or trained personal and so-called self-tests. Here, evidence is provided that these assays have a weak performance even under laboratory conditions.

Keywords: Rapid antigen assays, SARS-CoV-2, self-testing
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Brief report

With the broad usage of rapid antigen tests (RAT) as part of the German national SARS-CoV-2 test strategy, the question of their reliability arises. Thereby, it should be noted that different application types ranging from RATs performed in official test centres by qualified medical staff to supervise the usage of RATs in schools and enterprises up to RATs carried out privately are implemented. Having reported a debatable performance of various professional RATs [1], which was independently confirmed [2–5], we evaluated the performance of three assays (Novel Coronavirus (COVID-19) Antigen Test Kit (Colloidal Gold) (Lyher, Hangzhou, Zhejiang, People's Republic of China), the SARS-CoV-2 Rapid Antigen Test (Roche, Mannheim, Germany), and the Clinitest Rapid Covid-19 Antigen Test (Siemens, Cologne, Germany) that received the official approval for self-testing in Germany.

All lateral flow tests were performed strictly following the manufacturers recommendations. The readout was also done as recommended by the manufacturers and done by trained laboratory staff.

In order to address this issue, a cohort of 40 SARS-CoV-2 positive throat washes, three cell-culture derived round-robin-trial specimens, and 10 SARS-CoV-2 RNA negative controls were tested.

Two independent observers analysed the lateral flow assays within the permitted time slot and recorded their results. The overall agreement among the observers was 100%.

The specimens were collected during the screening of hospital staff members. The throat washes were performed with sterile 10 ml NaCl solution (0.9%) at a 30-second gargling interval [6]. RT-PCR was performed using the dual-target RealStar SARS-CoV-2 assay according to the manufacturers protocol. The entire sampling procedure was supervised by trained medical staff members from and within the hospital, while all pathogen testing (RT-PCR, lateral flow assays) were performed by a highly experienced laboratory team (i.e. molecular biologists, technicians). Lateral flow assays were considered as 'valid' if the internal control band was visible according to the manufacturer's protocols.

Thereby, positive samples displayed the SARS-CoV-2 wild type, as well as the variants UK B.1.1.7 and ZA B.1.351. As summarized in Table 1, only 6 of 43 previously RT-PCR (Altona, Hamburg, Germany) positive samples also tested positive for SARS-CoV-2 antigen, which resulted in a false-negative rate of 86% and was true for all RATs used. Moreover, positivity was independent of the respective variant of concern.

This finding, in line with the above-mentioned studies [1–5], shows that people must still comply with basic hygiene rules regardless of the RAT result, but in reality, the risk increases that false-negative tested people will behave more carelessly as public media have already reported that a false-negative index patient has induced a local outbreak in a nursing facility [7]. In this setting, the index patient infected 13 fully vaccinated residents.

Based on the data obtained in this pilot study, we consequently decided not to increase the number of positive samples but to maintain laboratory-based RT-PCR testing, also for economic reasons. Even if other studies demonstrated better

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TABLE 1. A total number of 43 positive PCR samples was analyzed by different RATs. Of these, three samples originate from a round-robin trial. As controls, 10 samples tested negative by PCR were used. Although the congruence of RATs was 100%, only 6 out of 43 PCR positive samples (14%) were detected as positive, independent of VOCs. In addition, 10 PCR-negative samples were tested, all with negative lateral flow test results

Variant	LYHER	Roche	Siemens
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	+	+	+
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	+	+	+
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	—	—	—
ZA B.1.351	+	+	+
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	—	—	—
WT	—	—	—
UK B.1.1.7	+	+	+
WT	—	—	—
UK B.1.1.7	—	—	—
UK B.1.1.7	—	—	—
UK B.1.1.7	—	—	—
UK B.1.1.7	—	—	—
UK B.1.1.7	—	—	—
UK B.1.1.7	+	+	+
UK B.1.1.7	—	—	—
UK B.1.1.7	—	—	—
UK B.1.1.7	—	—	—
UK B.1.1.7	—	—	—
UK B.1.1.7	+	+	+
UK B.1.1.7	—	—	—
n.d.	—	—	—
ZA B.1.351	—	—	—
WT	—	—	—
UK B.1.1.7	—	—	—
PCR–NC–1	—	—	—
PCR–NC–2	—	—	—
PCR–NC–3	—	—	—
PCR–NC–4	—	—	—
PCR–NC–5	—	—	—
PCR–NC–6	—	—	—
PCR–NC–7	—	—	—
PCR–NC–8	—	—	—
PCR–NC–9	—	—	—
PCR–NC–10	—	—	—

WT = wild type, VOC = variant of concern.

performance of RATs [8–10], it has to be taken into account that sensitivities and/or specificities of 85% mean that at least 15% of positive samples are not detected at all or are falsely declared. Instead of being a tool for infection chain interruption, an overestimated impact of RATs may become a silent driver of the pandemic situation due to high false-negative rates in combination with SARS-CoV-2 permissive vaccinated individuals who should get exemptions from pandemic restrictions.

Transparency declaration

The authors declare that no conflicts of interest exist. This included that none of the authors has any positive and/or negative conflict of interest with any of the companies supplying lateral flow assays and/or RT-PCR assays used in the study.

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