Application Report

Method Comparison (Charité PST study)

Version 1

SARS-CoV-2 Rapid Antigen Test
Patient Self Testing (Nasal sample)

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Method Comparison

Introduction

The clinical performance of the Rapid Antigen Test by patient self-testing was evaluated at Charité – Universitätsmedizin Berlin (Berlin, Germany), as an manufacturer independent prospective study with support from the Foundation for Innovative Diagnostics (FIND), Charité University Hospital internal funds, and a grant of the Ministry of Science, Research and the Arts of Baden-Württemberg, Germany[1].

Clinical performance of the Standard™ Q COVID-19 Ag kit (SD Biosensor®, Chuncheongbuk-do, Republic of Korea) was evaluated against the RT-PCR tests Roche cobas® SARS-CoV-2 and TibMolbiol SARS-CoV-2 E-gene assay as the comparator methods. Ethical approval was given by the ethics committee of Charité - Universitätsmedizin (EA1/371/20). Data exchange agreements were signed between study sponsor, SD Biosensor, and Roche as appropriate allowing the usage of the shared data for the Instruction for Use for both the SDB- and Roche-branded products.

Data analyses reported in this document were performed based on the shared line data. In this analysis the test will be referred to by the Roche branded test name "SARS-CoV-2 Rapid Antigen Test Nasal".

Data and Study details

Clinical performance of the SARS-CoV-2 Rapid Antigen Test Nasal wasevaluated using nasal swab samples from 146 subjects in a prospective study at Charité – Universitätsmedizin Berlin. The study cohort included symptomatic adults with high suspicion of SARS-CoV-2 infection. This was based on either 1) reported contact with a confirmed case and any compatible symptom, or 2) fever or impaired taste or smell irrespective of exposure. Participants had to be proficient in German or English in order to understand the written instructions. The enrolled patient cohort included adults aged from 18 - 68 years (median, 32 years; IQR, 13 years), and a majority (59.6%) of the participants had a higher education degree.

Study participants followed written and illustrated instructions to obtain a nasal swab sample and perform the testing by themselves in a separate

[1] Lindner, Andreas K., et al. "SARS-CoV-2 patient self-testing with an antigen-detecting rapid test: a head-to-head comparison with professional testing." *medRxiv* (2021).
https://www.medrxiv.org/content/10.1101/2021.01.06.20249009v1

room. Self-collection and self-testing were observed by health care workers without any intervention*. RT-PCR tests (Roche cobas® SARS-CoV-2 and TibMolbiol SARS-CoV-2 E-gene assay) using combined nasopharyngeal/ oropharyngeal swab (NP/OP) samples were used as the comparator methods as per institutional standard. Nasal sampling always preceded the combined NP/OP sampling. 27.4% of the participants tested positive by RT-PCR.

*One intervention by the study physician was necessary because of a possible risk of injury when the patient tried to insert the swab upside down into the nose.

Sample Size

The SARS-CoV-2 Rapid Antigen Test Nasal test is fully validated and obtained the CE mark for professional use and patient self-sampling under supervision. The aim of the study was to assess the performance of the test for patient self-testing against the comparator method.
The study was continued until 30 positive rapid antigen tests were obtained, which is the minimum sample number recommended by the WHO Emergency Use Listing[2] Procedure to demonstrate sample type equivalency. With an estimated SARS-CoV-2 prevalence of 20% at testing site at the time of the study, the target sample size for this study was set to 150 individuals. The final data collection had 40 PCR positive sample. Thus, the recommended number of samples from CLSI Guideline EP09c[3] for the comparison of two conditions within an already validated measurement procedure was fulfilled.

[2] WHO. Instructions and requirements for Emergency Use Listing (EUL) submission: In vitro diagnostics detecting SARS-CoV-2 nucleic acid and rapid diagnostics tests detecting SARS-CoV-2 antigens. https://extranet.who.int/pqweb/sites/default/files/documents/PQDx_347_NAT-antigen_instructions.pdf. Version 4, June 2020. Date last accessed February 05 2021.
[3] CLSI. Measurement Procedure Comparison and Bias Estimation Using Patient Samples. 3rd ed. CLSI guideline EP09c. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.

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Data analysis

Data analysis was performed on the line data by the Algorithms group in R&D PoC of Roche Diagnostics in Mannheim.
In the line data the information about the donor (age, sex, presence of symptoms, days post symptom onset (DPSO), date of symptom onset, and enrollment date), the specimen (specimen type for PCR and rapid antigen test), and the measurements (information of used reference method, qualitative result of the RT-PCR reference and the SARS-CoV-2 Rapid Antigen Test Nasal; for the RT-PCR positive samples the quantitative Ct-values for the E-gene are also provided) were listed.

Statistical analysis included calculation of positive percentage agreement (PPA), negative percentage agreement (NPA) and two-sided 95% exact (Clopper Pearson) confidence limits.
Further analyses were done dependent on the Ct-value for the E-gene and dependent on DPSO.
Individual results are stated for samples with Ct-value ≤ 24, Ct-value ≤ 27, Ct-value ≤ 30, and Ct-value ≤ 33 as well as for samples with known DPSO ≤ 5 days.

All analyses were done using R v3.6.3, independent verification of the results was performed.
All results are given with 3 significant digits.

Conclusion

In this study and for this study population the relative sensitivity of patient self-testing using the SARS-CoV-2 Rapid Antigen Test Nasal was 82.5% (95% CI: 67.2% - 92.7%). The relative specificity of patient self-testing in this study was 100% (95% CI: 96.5% - 100%).
For samples with Ct-values ≤ 24 the positive percent agreement compared to RT-PCR results was 96.4%, with Ct-values ≤ 27 the positive percent agreement was 93.5%, with Ct-values ≤ 30 the positive percent agreement was 91.2%, and with Ct-values ≤ 33 the positive percent agreement was 91.7%. There were 4 samples measured with a Ct-value >33.

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Results

Sample Description

The number of samples is summarized in the following table.
One sample (Subject ID "T67") was excluded from the analysis as an invalid antigen result was obtained after spilling the buffer solution. This patient had a negative result with the PCR test.

Table 1 – Overview of sample size and sample type for the study

Sample Type	# negative samples	# positive samples
Nasal PST	105	40

The following tables give a description of the age distribution of the study population.

Table 2 – Age distribution for the study population

Age	Frequency	Proportion (%)
[18-30]	62	43
[31-40]	47	32
[41-50]	16	11
[51-60]	14	10
61 and above	6	4
Total	145	100

Table 3 – Characteristics for the variable Age for the study population

	Minimum	25% Quantile	Median	Mean	75% Quantile	Maximum
Age	18	27	32	35.1	40	68

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Method Comparison - overall result

The overall result of the method comparison in this study can be found in the following table:

Table 2 – Cross table for the method comparison of SARS-CoV-2 Rapid Antigen Test Nasal against RT-PCR reference

		RT-PCR reference		
		pos	**neg**	**Σ**
SARS-CoV-2 Rapid Antigen Test Nasal	**pos**	105	7	112
	neg	0	33	33
	Σ	105	40	145

NPA, 95% CI	100%	96.5%	100%
PPA, 95% CI	82.5%	67.2%	92.7%

Method Comparison – results by Ct-values

Additional analysis was performed stratifying the data by Ct-values. Results can be found in the following table:

Table 4 – Positive percent agreement results of SARS-CoV-2 Rapid Antigen Test Nasal against RT-PCR reference by Ct-value

Analyzed group	# positive samples	# true positive samples	# false negative samples	PPA	95%CI lower bound	95%CI upper bound
Ct ≤ 24	28	27	1	96.4%	81.7%	99.9%
Ct ≤ 27	31	29	2	93.6%	78.6%	99.2%
Ct ≤ 30	34	31	3	91.2%	76.3%	98.1%
Ct ≤ 33	36	33	3	91.7%	77.5%	98.2%
all	40	33	7	82.5%	67.2%	92.7%

Additional analysis was also performed stratifying the data by DPSO for the positive samples where this information is known. Results can be found in the following table:

Table 5 – Positive percent agreement results of SARS-CoV-2 Rapid Antigen Test Nasal against RT-PCR reference by DPSO for the positive samples where this information is known

Analyzed group	# positive samples	# true positive samples	# false negative samples	PPA	95%CI lower bound	95%CI upper bound
DPSO ≤ 5 days	29	25	4	86.2%	68.3%	96.1%

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Line Data and attached files

The line data are provided as an attachment of this document as excel file:
"LineListing_AG_Nasal_PST.xlsx"

Table 6 – Change history of document versions

Version	Author	Date	Comment
1	5.1.2e	05-Feb-2021	Initial Version