Rapid Mass spectrometry for COVID-19 detection

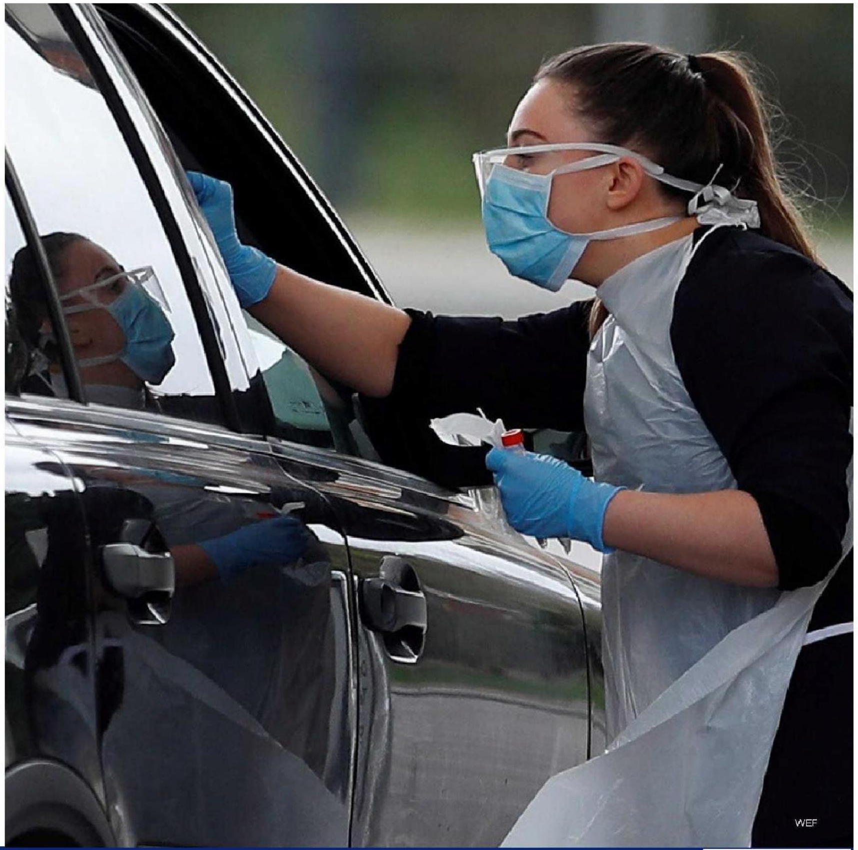
5.1.2e 5.1.2e

LACDR, Leiden University

In collaboration with:

Corona TEAM GGD Amsterdam

Erasmus MC/Viroscience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About this document

Background:
Peptide-MS is a rapid SARS-CoV-2 mass spectrometry (MS) test that targets SARS-CoV-2 derived peptides.
The underlying technology has been developed at the LACDR at Leiden University.

An external validation of the Peptide-MS method was performed in the public testing facility (December 2020 – January 2021) in an independent group of 1292 participants of 18 years or older at GGD Amsterdam.

Study design:
A prospective, real-world study at GGD Amsterdam.

Definition SARS-CoV-2 infection (reference):
RT-qPCR.

Aim:
This report discusses the results of the validation study.
A more detailed text document is available.

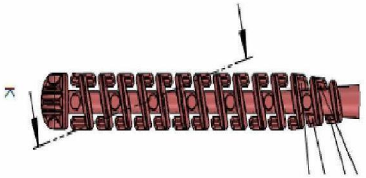
Rapid COVID-19 MS diagnostic test

Peptide-MS method of SARS-CoV-2 proteins: targeted analysis of NCAP peptides after digestion

Advantages:

1. Results within 40-60 minutes
2. Flexible platform that can be modified upon needs
3. Cost efficient: ca. 5-6 € for reagents and consumables, 2-3 € depreciation for instrumentation
4. High throughput (> 100 samples per hour per MS machine) & scalable
5. High degree of automation possible
6. Insensitive for mutations

Dry swab sampling using Comfort-ZZwab-Fast:
New swab for MS based on polyester (co-development with DSM, NL)

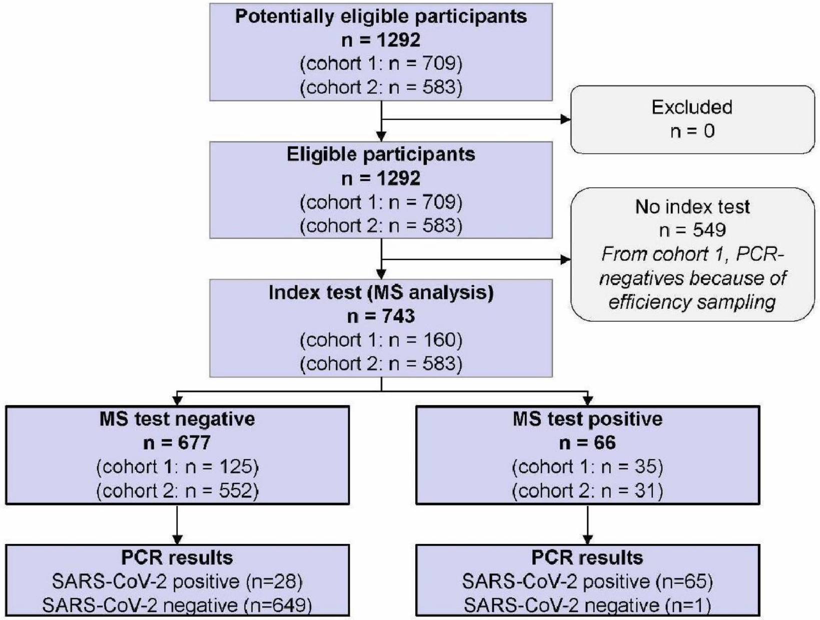


Implementation of automated Peptide-MS workflow in a trailer

Study design

- Additional (second) nasopharyngeal swab samples were collected at the testing site of the GGD Amsterdam in two successive cohorts:
  1. Nested case control design study; sample collection 17 December 2020 – 2 January 2021
  2. Cohort design study; sample collection 3 January 2021 – 10 January 2021
- Both studies were performed under the same conditions and with the same population (>18 years and appointment for testing at GGD: symptomatic or BCO/Coronamelder)
- Reference standard for all samples: RT-qPCR analysis by InBiome on first swab[1]
- 93 RT-qPCR-positive samples were included

Participant enrolment



Potentially eligible participants
n = 1292
(cohort 1: n = 709)
(cohort 2: n = 583)

Excluded
n = 0

Eligible participants
n = 1292
(cohort 1: n = 709)
(cohort 2: n = 583)

No index test
n = 549
From cohort 1, PCR-negatives because of efficiency sampling

Index test (MS analysis)
n = 743
(cohort 1: n = 160)
(cohort 2: n = 583)

MS test negative
n = 677
(cohort 1: n = 125)
(cohort 2: n = 552)

MS test positive
n = 66
(cohort 1: n = 35)
(cohort 2: n = 31)

PCR results
SARS-CoV-2 positive (n=28)
SARS-CoV-2 negative (n=649)

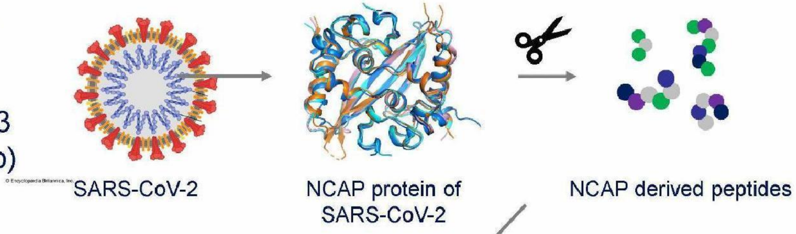
PCR results
SARS-CoV-2 positive (n=65)
SARS-CoV-2 negative (n=1)

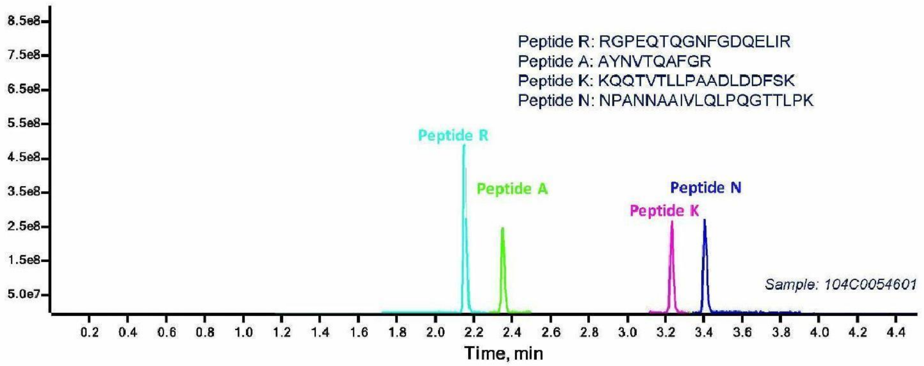
The routine GGD swab was transferred in a vial with buffer and sent for RT-qPCR analysis by the lab of InBiome (Amsterdam). InBiome used a PerkinElmer SARS-CoV-2 Real-Time RT PCR Assay targeting the N-gene and Orf1ab, and an internal control using a human RNA target

Peptide-MS analysis of nasal swab

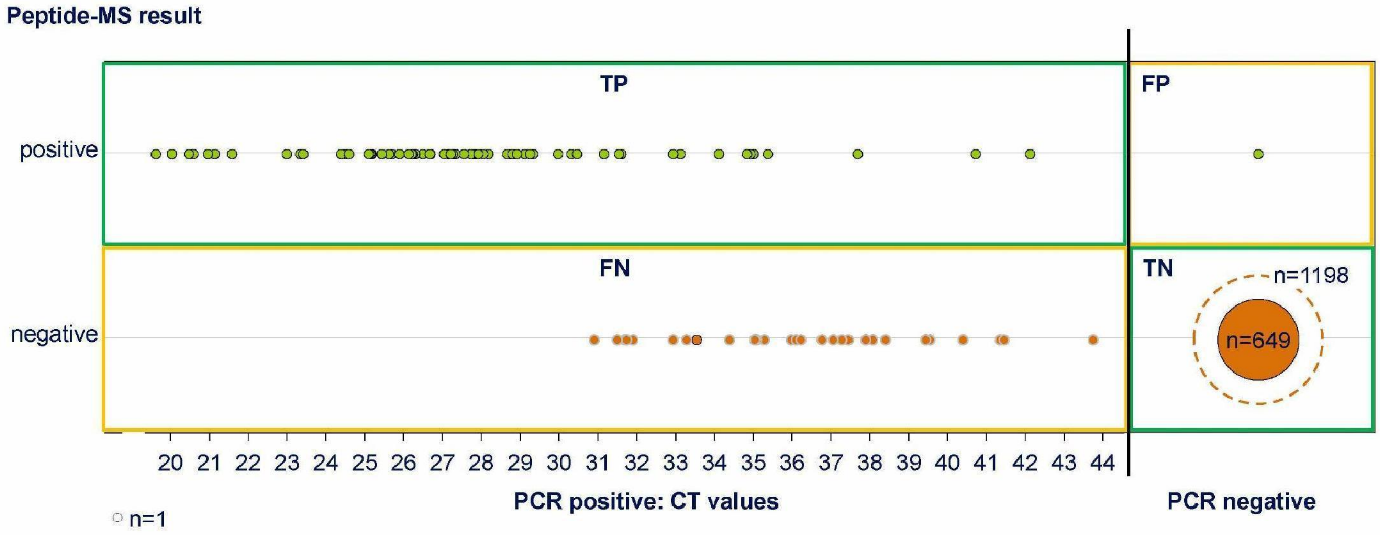
Four unambiguous peptides of NCAP are measured after digestion with LC-MS

Sample shown: swab from patient with Ct-value of 33 (as determined by PCR using first routine GGD swab)




Peptide R: RGPEQTQGNFGDQELIR
Peptide A: AYNVTQAFGR
Peptide K: KQQTVTLLPAADLDDFSK
Peptide N: NPANNAAIVLQLPQGTTLPK

Results of Peptide-MS of nasal swabs



Reference standard: RT-qPCR of second routine GGD swab

Results

		PCR results			
		Positive (all Cts)	**Positive (Ct < 32)**	**Positive (Ct < 30)**	**Negative**
	N	93	60	50	1199
MS results	**Positive**	65	55	50	1
	Negative (measured)	28	5	0	649
	Negative (calculated)				549
	Sensitivity (95% CI)	0.73 (0.63-0.82)	0.92 (0.82-0.97)	1.00 (0.93-1.00)	
	Specificity (95% CI)[1]				1.00 (1.00-1.00)

A higher number of samples (especially PCR-positives) would have resulted in smaller confidence intervals, but we believe the conclusion would be the same. After a discussion with professor 5.1.2e we decided not to start a new sample collection campaign

Statistics are corrected for efficiency sampling in cohort 1

Summary for Peptide MS

- Highly accurate test for COVID-19 with high sensitivity (100% for Ct <30) and specificity (100%)
- High speed and throughput
- Independent from scarce and/or expensive reagents
- Insensitive for mutations
- Able to include epidemiologically important mutations
- Monitor future viral infections; platform can be easily adapted
- Currently developing complementary direct MS profiling method of swab to very rapidly (< 3 mins) detect virus infection with metabolite and lipid fingerprint

Acknowledgement

Analytical BioSciences Group @ LACDR/Leiden University

Corona TEAM @ GGD Amsterdam

Erasmus MC, Viroscience group & ICU team

St Antonius Nieuwegein

Imperial College, London

Many scientists and clinicians (Amsterdam UMC, UMCU & LUMC)

Ministerie van VWS

See complete validation report for more details on method, validation study design and results

For questions reach out to: 5.1.2e 5.1.2e (5.1.2e@lacdr.leidenuniv.nl)