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Short Communication

Do fully automated immunoassays for the evaluation of the immune response to SARS-CoV-2 are commutable?

A. Mairesse [a,*], D. Gruson [a], A. Scohy [b], B. Kabamba [b], H. Rodriguez-Villalobos [b]

[a] Department of Clinical Biochemistry, Cliniques Universitaires Saint-Luc - Université Catholique de Louvain, Avenue Hippocrate 10, Brussels, Belgium

[b] Department of Microbiology, Cliniques Universitaires Saint-Luc - Université Catholique de Louvain, Avenue Hippocrate 10, Brussels, Belgium

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ABSTRACT

On December 30, 2019, the city of Wuhan, China, experienced an outbreak of unexplained pneumonia. From January 7, 2020, a new betacoronavirus, severe acute respiratory syndrome coronavirus was identified (SARS-CoV-2). The World Health Organization (WHO) has since declared a pandemic with millions of confirmed cases worldwide. As part of the fight against the epidemic, laboratories have a critical role in assessing the reliability of new serological assays before taking part of diagnostic protocols or made available broader to the community and to evaluate commutability between assays.

The aim of this study was to perform a comparison between two automated assays for SARS-CoV-2 IgG testing, the MAGLUMI ® 800 and the LIAISON ® XL.

Among the patients confirmed positive for COVID-19, the two automated assays were significantly correlated ($r = 0.811$; $p < 0.0001$). The overall concordance made for MAGLUMI 2019-nCoV IgG positive/negative vs. LIAISON® SARS-CoV-2 IgG positive/negative results was 79% (Index Kappa of Cohen). We list the discrepancies between the two analyzers among the 44 tested patients.

In conclusion, the overall agreement between the two automated assays for SARS-CoV-2 was good. However, the MAGLUMI assay might be more sensitive at the early stages of antibody development and there is a lack of specificity with LIAISON XL.

On December 30, 2019, the city of Wuhan, China, experienced an outbreak of unexplained pneumonia. From January 7, 2020, a new betacoronavirus, severe acute respiratory syndrome coronavirus was identified (SARS-CoV-2). The World Health Organization (WHO) has since declared a pandemic with millions of confirmed cases worldwide. The viral gene was sequenced and the virus was identified for the first time in bronchoalveolar fluid using a real-time reverse transcription polymerase chain reaction (qRT-PCR) assay [1]. Afterward the WHO and US Centers for Disease Control and Prevention (CDC) have recommended for etiological diagnosis of COVID-19 identification of the microorganism (SARS-CoV-2) in the respiratory tract using molecular techniques.

In addition to these techniques, serology could now offer other perspectives. Recently French health authorities have recommended a series of indications for serological tests [2]. On one hand, serology may be a valuable tool for sero-epidemiological investigations. On the other hand, antibodies detection could confirm diagnose symptomatic patients in whom the PCR was negative or not

* Corresponding author.
E-mail addresses: mairesseantoine@gmail.com (A. Mairesse), damien.gruson@uclouvain.be (D. Gruson), anais.scohy@uclouvain.be (A. Scohy), benoit.kabamba@uclouvain.be (B. Kabamba), hector.rodriguez@uclouvail.be (H. Rodriguez-Villalobos).

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Table 1
Positivity rates of the different methods in the 44 patients in whom the date of symptom onset was available.

Symptom onset	COVID IgG (AU/mL) Liaison	COVID IgG (AU/mL) Maglumi
≤5 days	1/5 (20%)	1/5 (20%)
>5–10 days	3/9 (33%)	7/9 (78%)
>10–21 days	25/30 (83%)	25/30 (83%)

Table 2
Discrepancies between the two fully automated serology tests to detect IgG antibodies.

Patients	*COVID IgG (AU/mL) Liaison XL*	*COVID IgG (AU/mL) Maglumi*	Date of symptom onset	Serology	Onset symptoms
1	8,2	9238	21-03-20	29-03-20	D-8
2	6,93	3434	19-03-20	26-03-20	D-7
3	6,12	7131	15-03-20	27-03-20	D-12
4	7,59	96,14	20-03-20	29-03-20	D-9
5	<3,8	1624	17-03-20	24-03-20	D-7
6	56	0,827	25-03-20	05-04-20	D-11

D: day of serology after symptom onset.

performed.. [2]. Moreover, if the neutralizing capacities of the antibodies are proven, their assessment could help health care institutions to know which of their health care workers have already been in contact with the virus and if they can be mobilized if required [3].

Laboratories have a critical role in assessing the reliability of new serological assays before taking part of diagnostic protocols or made available broader to the community and to evaluate commutability between assays [4]. Serological tests could be used to measure vaccine immunity from the perspective of a vaccine. For these reasons, knowing the performance of the available tests seems to be essential.

Our objective was to perform a comparison between two automated assays for SARS-CoV-2 IgG testing, the MAGLUMI ® 800 and the LIAISON ® XL. The MAGLUMI® 800 SARS-CoV-2 IgG (SNIBE - Shenzhen New Industries Biomedical Engineering Co.,Ltd, Shenzhen, China) is a fully automated chemiluminescence immunoassay (CLIA) [5,6]. A test result above 1.0 AU/mL is considered positive. According the manufacturer, antibodies detected by this test directly target the CoV–S (spike – S1 and S2) and the CoV–N (nucleocapsid) antigens. The LIAISON® SARS-CoV-2 (Diasorin, Saluggia, Italy), uses magnetic beads coated with S1 and S2 antigens derived from the SARS-Cov-2 spike protein which is responsible for binding and fusion of the virus with the host cell membrane, these antigens are the primary target of neutralizing antibodies [3]. Using both proteins as targets, the firm has shown that the likelihood of concordance to a neutralization assay is increased significantly. A test result of <12 AU/mL is considered non-reactive, 12–15 AU/mL is equivocal and ≥15 AU/mL is a reactive result.

The results of both techniques were compared in relation to the appearance of antibodies according to the date of symptom onset.

Our comparison study included four groups: healthy volunteers asymptomatic who have been collect during the pandemic (n = 12) (1); healthy volunteers who collect before 2019 (n = 17) (2); samples COVID-19 free with confounding factors selected from January 2018 to August 2019 (n = 10), the samples included with potential cross-reaction to the SARS-CoV-2 immunoassay, such as, EBV infection, parvovirus infection, HBV infection, *Bartonella henselae* infection, *Brucella* spp infection and various autoimmune diseases (3); and samples of patients infected by SARS-CoV-2 confirmed by RT-PCR (n = 44) (4).

Blood sampling was done according with the recent guidelines [7]. The statistical analysis was performed with the software XLSTAT (version 2019.2.2 by Addinsoft). The study has been cleared by the local Ethical Committee 2020/06avr/203).

Among the 12 healthy volunteers sampled during the epidemic, no one developed antibodies and results were negative for both methods. For the samples of healthy volunteers collected before the pandemic, one was tested positive for IgG with LIAISON XL analyzer (15,4 AU/mL) and was negative for MAGLUMI. We can consider this value as false positive because the disease was not present before 2019. Within the samples with confounding factors, a sample was reported as suspicious (13,3 AU/mL) when tested by the LIAISON XL analyzer and negative with MAGLUMI and can also be considered as a false positive result (see Table 1).

In patients confirmed positive for COVID-19, the two automated assays were significantly correlated ($r = 0.811$; $p < 0.0001$). This positive correlation potentially reflects a good agreement between the two automated assays for the assessment of the intensity of antibody titer. The overall concordance made for MAGLUMI 2019-nCoV IgG positive/negative vs. LIAISON® SARS-CoV-2 IgG positive/negative results was 79% (Index Kappa of Cohen) [8]. The discrepancies between the two analyzers among the 44 tested patients are summarized in Table 2.

After 10 days of symptoms onset, the concordance between the two assays was excellent. These data are in line with the most recent literature showing a mean seroconversion of IgG/IgM at 13 days [9]. Discrepant cases between the two assays occurred at the early stage of the disease, between 5 and 10 days after symptom onset. We showed that for five patients the MAGLUMI detects antibodies and the LIAISON XL analyzer does not. For these patients the test was performed between 7 and 12 days after the onset of symptoms which is below the currently reported average rate of seroconversion. It may be hypothesized that the MAGLUMI assay sensitivity could be higher than the LIAISON XL because of the assay format as the MAGLUMI assay is also targeting antibodies against the nucleocapsid in addition to CoV–S (spike – S1 and S2). These preliminary data need to be confirmed by larger studies. Moreover,

MAGLUMI has the advantage of accessing anti-SARS CoV-2 IgM which increases sensitivity to 93.75% and is not available on LIAISON XL [10].

In conclusion, the overall agreement between the two automated assays for SARS-CoV-2 was good. However, the MAGLUMI assay might be more sensitive at the early stages of antibody development and there is a lack of specificity with LIAISON XL.

Author statement

Mairesse Antoine: Conceptualization, Data curation, Writing, Ressources. **Gruson Damien**: Conceptualization, Original draft preparation. **Scohy Anais**: Visualization, Investigation. **Kabamba Benoit:** Supervision.: **Rodriguez-Villalobos Hector**: Software, Validation, Project administration.

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