Clinical Validation of Handheld Thermo-Photonic Device for Rapid Detection and Quantification of Anti-SARS-CoV-2 Antibodies

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Rapid, on-site, and sensitive detection and quantification of anti-SARS-CoV-2 antibodies is an effective and scalable approach for minimizing the burdens of COVID-19 pandemic. Such capability not only opens the door for better and more effective vaccination, but also enables population-wide serological studies focused on answering pressing questions about COVID-19 infection (e.g., correlation of antibody titers with degree of immunity). Here we report on design, development, and clinical validation of a low-cost and portable thermo-photonic innovation that enables sensitive detection and quantification of COVID-19 antibodies. At the core, this patented technology relies on thermo-photonic lock-in imaging of COVID-19 rapid tests. Our clinical results from $COVID^+$ and $COVID^-$ patients suggest ability of developed technology in quantifying antibody titres within the clinically relevant range and with a limit of detection of 90 ng/ml.

Background – Immunological tests play an important role in the management of COVID-19 pandemic and monitoring the effectiveness of vaccines over time at a population level. Existing immunological solution, such as neutralization assay, chemiluminescent assay (CLIA), and enzyme-linked immunosorbent assay (ELISA) are expensive, time-consuming and requires laboratory facilities and trained personnel, therefore they are not deemed suitable for large-scale serodiagnosis and vaccine evaluation. Lateral flow immunoassays (aka Rapid Tests) are fast, low-cost, and point-of-care approaches to antibody testing; however, these convenient and scalable solutions provide essentially binary information about the presence of antibodies and cannot quantify the antibody level of infected and/or vaccinated individuals.

Method – We have developed a low-cost and portable thermo-photonic lock-in imaging device using a cell phone attachment infrared camera, low-cost control electronics, and a 808nm low-cost laser diode (Fig. 1)[1]. Device is essentially a reader of COVID-19 antibody rapid tests. Sensing mechanism is based on measurement of amplitude of photothermal responses from gold nanoparticles immobilized on rapid test control and test lines. Through calibration, device maps the amplitude of thermal-wave responses (aka amplitude metric) to COVID-19 antibody concentrations. Performance of device was tested on n=28 longitudinal

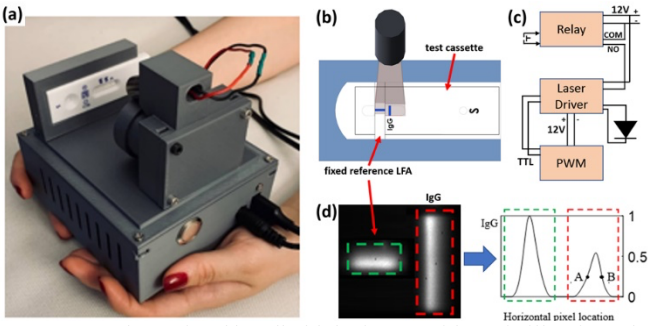

Fig. 1. (a) Schematic of handheld device. Rapid test is illuminated with laser **(b)** controlled by low-cost electronics (c). Themo-photonic lock-in amplitude images are used for prediction of antibody concentrations.

human serum samples from $COVID^+$ and $COVID^-$ patients and compared to results obtained from standard quantitative enzyme-linked immunoassay (qELISA).

Results and Discussion – Figure 2(a) shows the variation of IgG antibodies with respect to the days of ICU admission for representative COVID− patients (patient IDs 85 and 92) and COVID+ patients (patient IDs 94 and 99). The y1 axis represents the standard ELISA test and the y2 axis represents the thermo-photonic amplitude metric. These plots demonstrate that IgG measurements from ELISA and thermo-photonic device are highly correlated. The bar diagrams in Fig. 2(b) show the mean amplitude metrics between COVID+ and COVID− patients and ELISA+ and ELISA− patients. Statistical analysis (t-test) shows that the mean values are significantly different between the groups (t-test, $p>0.001$). The left panel in Fig. 2(c) shows a best-fit line (regression line) to scattered data points; the high value of R-squared ($R^2=0.92$) suggest produced calibration line can be used to predict the concentration of IgG in serum using a thermo-photonic device, albeit at much lower cost and much faster than laboratory-based quantitative ELISA. To determine the sensitivity of the thermo-photonic system to differentiate IgG+ and IgG− samples, a receiver operating characteristic (ROC) curve was drawn, right panel in Fig. 3c. Ture positive and true negative samples were determined based on the IgG+ and IgG− by ELISA. A high value of area under the ROC curve (AUC=0.99) indicates the high predictive ability of the thermo-photonic device in distinguishing IgG+ from IgG− sera.

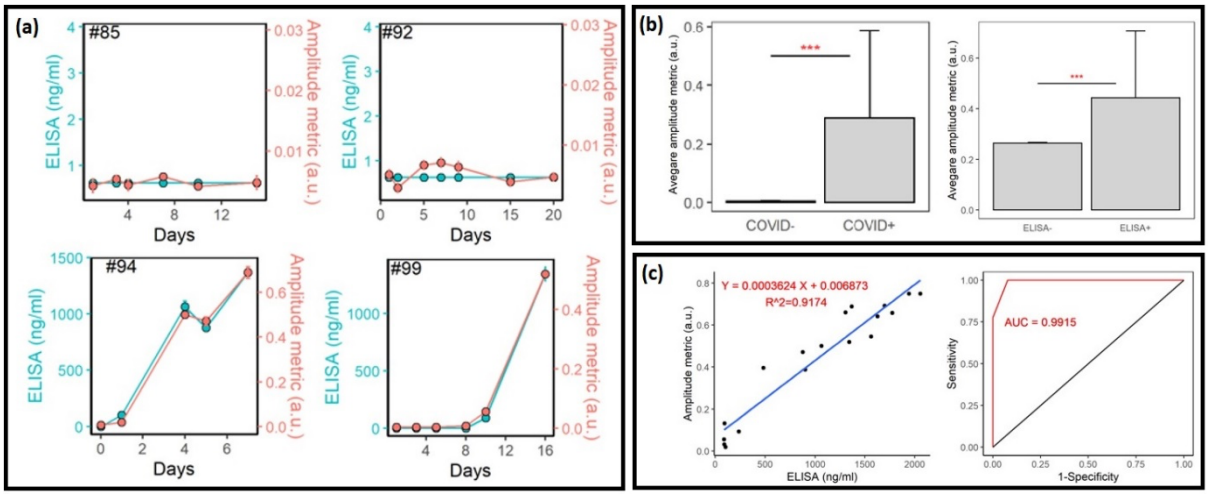

Fig. 2. (a) Representative quantification results of longitudinal human samples using thermo-photonic device and qELISA. **(b)** Bar diagrams showing average amplitude metrics between the COVID− and COVID+ participants and ELISA− and ELISA+ samples. **(c)** Linear regression plot between thermo-photonic device readings and ELISA quantifications as well as the ROC curve that shows the performance of our device for detecting ELISA− and ELISA+ samples.

Conclusions – In this study, we designed, developed, and clinically validated a portable thermo-photonic device for rapid detection and quantification of COVID-19 antibodies. Sensing mechanism of device is based on interrogation of thermo-photonic lock-in responses for gold nanoparticles immobilized on test and control lines of rapid tests. Human serum experiments suggest the developed innovation can detect and quantify COVID-19 antibodies with a performance comparable to that of quantitative ELISA, albeit at much lower cost and significantly faster.

References

[1] D. Thapa, N. Samadi, N. Tabatabaei, Handheld Thermo-Photonic Device for Rapid, Low-Cost, and On-Site Detection and Quantification of Anti-SARS-CoV-2 Antibody. IEEE Sensors Journal. 21:17 (2021) 18504-18511.