EBioMedicine 37 (2018) 11–12

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

EBioMedicine
Published by THE LANCET

Commentary

Calling in the test: Smartphone-based urinary sepsis diagnostics

Michael G. Mauk

Department of Mechanical Engineering and Applied Mechanics, School of Engineering and Applied Science, University of Pennsylvania, 216 Towne Building, 220 S 33rd St., Philadelphia, PA 19104, USA

The tremendous potential of medical diagnostics performed at the point of care (POC), yielding a test result in a time frame of one to a few hours, has been recognized for several decades. Such tests will enable new paradigms for healthcare, including diagnostics testing in non-traditional venues such as pharmacies and storefront clinics, as well as home testing and companion diagnostics to guide and monitor the efficacy of treatments for chronic diseases. Infectious disease tests present an especially important opportunity since a fast test that can identify the causative pathogen(s) may be the key difference between drastically different outcomes. In the developing world where medical laboratory infrastructure is often lacking, and transport of labile specimens may be problematic, such simplified, portable medical tests can fill a crucial need for appropriate, sustainable technology. While the feasibility of POC tests is well-established, and many near-term applications have been identified, the widescale adoption of such tests remains elusive. On the one hand, simple immunoassays in the form of lateral flow strips are common, however, more complicated—and more powerful—molecular diagnostics (nucleic acid based tests) are not yet prevalent. Several technological developments may accelerate introduction of POC molecular tests. These include isothermal nucleic acid amplification processes as alternatives to PCR, that do not require precise temperature cycling, thus considerably simplifying the instrumentation; and the use of smartphone cameras for fluorescence detection. The smartphone also brings many useful features to the POC test platform including connectivity, GPS, and data acquisition, processing, and archiving [1–4].

Sepsis is a serious health problem, registering over 30 million cases per year throughout the world, and with 17% mortality [5]. A rapid, reliable test for sepsis would be a significant advance. Sepsis diagnosis is challenging since there are as-yet no definitive signaling biomarkers identified for assay [6–8]. One approach is to perform a multiplex NAAT (nucleic acid amplification test) for a panel of Sepsis-associated bacterial pathogens in blood or urine. This could avoid the several-day delay incurred with culturing methods of detection.

Much of the prior work in POC diagnostics has focused on engineering aspects such as materials, instrumentation, prototyping, fluid actuation and flow control, and packaging. Prototypes are tested with contrived samples (e.g., DNA in buffer or plasma spiked with a known amount pathogen) under controlled conditions. As POC technology moves from the lab to the clinic, validation of devices and methods with patient samples is needed.

In *EBioMedicine*, Barnes et al. describe one of the most comprehensive assessments to date for a smartphone-based POC system [9]. The test (*smaRT-LAMP*, smartphone-based real-time loop-mediated isothermal amplification) uses a smartphone and blue LED to detect the green fluorescence from an array of tube-based isothermal LAMP reactions. The Barnes et al. work is noteworthy in the extensive validation of a smartphone-based platform for multiplex NAAT for eight Gram-negative and Gram-positive bacteria in urine. The study affirmed that 1) the isothermal LAMP assay can deliver the same performance as real-time PCR performed in a commercial benchtop thermocycler instrument, 2) a consumer-grade smartphone can quantify the fluorescence in real-time from multiple reaction tubes, and 3) a simple lysis procedure is adequate for sample preparation. The device relies on a heating block on a hotplate, uses a consumer-grade smartphone (Samsung Galaxy), and operates with a freeware App, Bacticount, that performs the data acquisition and processing. The system has a total cost of under $100 in parts (not including the smartphone). In urine samples from sepsis patients, excellent concordance in sensitivity and specificity between the smaRT-LAMP system and conventional hospital culture testing was demonstrated. The smaRT-LAMP system provided test results within about 1 h, compared to the 18 to 28 h required for culture-based tests. Further, pathogen identification in urine samples matched those based on blood tests, and the researchers suggest a sensitivity of 1 to 10 CFUs could be feasible in 1 ml blood samples.

It should be noted that the technology described here is not particularly innovative from the engineering side. There is no microfluidics: samples are processed in 0.2 ml tubes with manual pipetting. Still, sample preparation for LAMP detection of bacterial targets in urine specimens is relatively simple. Moreover, it is this commentary author's estimation that this process, including smartphone detection, would be amenable to a chip-based implementation for automated operation and better confinement to avoid risks of cross contamination. Nevertheless, the format described here as-is would no doubt be workable and welcome in resource-limited settings, providing acutely-need diagnostics capabilities.

Disclosure

The author declared no conflicts of interest.

DOI of original article: https://doi.org/10.1016/j.ebiom.2018.09.001.
E-mail address: mmauk@seas.upenn.edu.

https://doi.org/10.1016/j.ebiom.2018.10.047

References

[1] Bates M, Zumla A. Rapid infectious diseases diagnostics using Smartphones. Ann Trans Med 2015;3(15):215.

[2] Song J, Pandian V, Mauk MG, Bau HH, Cherry S, Tisi LC, et al. Smartphone-based mobile detection platform for molecular diagnostics and spatiotemporal disease mapping. Anal Chem 2018;90:4823–31.

[3] X Xu, Akay A, Wei H, Wang SQ, Pingguan-Murphy B, Erlandsson B-E, et al. Advances in Smartphone-based point-of-care diagnostics. Proc IEEE 2015;102(2):236–47.

[4] Laksanasopin T, Guo TW, Nayak S, Sridhara AA, Xie S, Olowookere OO, et al. A smartphone dongle for diagnosis of infectious diseases at the point of care. Sci Transl Med 2015;7(273):273re1.

[5] Fleishmann C, Scherag A, Adhikari NK, Hartog CS, Tsaganos T, Schlattman P, et al. Assessment of global incidence and mortality of hospital-treated sepsis: Current estimates and limitations. Am J Respir Crit Care Med 2016;193:259–72.

[6] Reinhart K, Bauer M, Riedemann NC, Hartog CS. New approaches to Sepsis: Molecular diagnostics and biomarkers. Clin Microbiol Rev 2012;25(4):609–34.

[7] M Sinha J, Jupe H, Mack H, Coleman TP, Lawrence SM, Fraley SI. Emerging technologies for molecular diagnosis of sepsis. Clin Microbiol Rev 2018;31(2) [e00089-17].

[8] Fan S-L, Miller NS, Lee J, Remick DG. Diagnosing sepsis—the role of laboratory medicine. Clin Chim Acta 2016;460:203–10.

[9] Barnes L, Heithoff DM, Mahan SP, Fox GN, Zambrano A, Choe J, et al. Smartphone-based pathogen diagnosis in urinary sepsis patients. EBioMedicine 2018. https://doi.org/10.1016/j.ebiom.2018.09.001.