



Next-Generation Microfluidic Point-of-Care Diagnostics

Alphonsus H.C. Ng^{1,2,3*} and Aaron R. Wheeler^{1,2,3*}

Microfluidics or lab-on-a-chip (LOC)⁴ diagnostic devices have the potential to provide fast, laboratory-quality results to expedite clinical decisions at various point-of-care (POC) settings, including outpatient clinics, emergency rooms, and intensive care units (1). Unfortunately, these technologies remain out of reach in the developing world, where lack of access to quality diagnoses contributes to the enormous burden of disease (2).

An obvious obstacle to translating the success of microfluidic POC devices to the developing world is the challenge of designing instruments and methods appropriate for resource-limited settings. For example, the WHO coined the ASSURED criteria for the ideal POC test: affordable, sensitive, specific, user-friendly, rapid and robust, equipment-free, and deliverable to users (2). This is a daunting array of requirements, and some believe that the criterion of “equipment-free” may artificially restrict POC testing to inherently low-performance, equipment-free assay formats (e.g., lateral flow tests) (3) and hinder the use of newer technologies such as cartridge-based POC tests and technologies relying on smartphones. In the right context, these devices can still be cost-effective and impactful.

Despite this and other obstacles, there is great optimism that LOC diagnostic devices will eventually save lives in the developing world. The miniaturization of diagnostic tests and systems integration are bounded engineering problems that can be solved by leveraging existing technologies. With the emergence of the “maker movement” and the availability of inexpensive electronic components such as microcontrollers, do-it-yourself tools such as 3D printers, and consumer electronics such as smartphones, a new generation of researchers have emerged to tackle the challenges of developing diagnostic tests for resource-limited settings.

The Smartphone Dongle

In an exemplary demonstration of the new generation of POC diagnostic tools, Laksanasopin et al. (4) described an LOC-based smartphone accessory (“dongle”) that is tailor-made for resource-limited settings (Fig. 1). The dongle is capable of carrying out immunoassays on disposable plastic cassettes preloaded with plugs of reagents and wash buffer and immobilized with disease-specific antigens. Through immunorecognition, antibody markers in the sample are captured by the antigens on the plastic surface and then detected using secondary antibodies labeled with gold nanoparticles. Finally, analyte binding events are transduced and amplified through silver reduction onto the nanoparticles. The fluid handling in the cassette relies on a hand-powered “1-push vacuum” mechanism, which generates the negative pressure required to move the sample and reagents through the device. The other components of the dongle, including light-emitting diodes, photodiodes, and microcontroller, are powered through the audio jack (from the smartphone), which also serves as the conduit for data transmission. Because the dongle consumes very little power, an audio jack interface with a smartphone is sufficient to provide power for at least 41 assays on a single charge. The manufacturing cost of the dongle is US \$34.

The new device was evaluated in Rwanda by a team of healthcare workers who were previously unfamiliar with the technology. To guide the workers through each test, the smartphone used to control the device is equipped with an app that provides step-by-step directions and built-in timers. After an initial training period of 30 min, the healthcare workers tested fresh fingerprick whole blood from 96 patients whose disease status was not revealed until the conclusion of the test. The cassettes were prepackaged with reagents appropriate to detect anti-HIV as well as treponemal and nontreponemal (i.e., cardiolipin) tests for syphilis, and each triplex test required 15 min and US \$1.44 in materials. The performance of the dongle rivaled laboratory-based testing, with sensitivity and specificity of 100% and 87% for HIV, 92% and 92% for treponemal syphilis, and 100% and 79% for nontreponemal syphilis. In a survey carried out after the tests, the vast majority (97%) of the participants preferred the dongle method to conventional laboratory tests (requiring venous blood draw) because of

¹ Institute of Biomaterials and Biomedical Engineering and ² Department of Chemistry, University of Toronto, Toronto, ON, Canada; ³ Donnelly Centre for Cellular and Biomolecular Research, Toronto, ON, Canada.

* Address correspondence to this author at: 80 St. George St., Toronto, ON, Canada M5S 3H6. E-mail: a.l.ng@mail.utoronto.ca; aaron.wheeler@utoronto.ca.

Received April 14, 2015; accepted April 15, 2015.

Previously published online at DOI: 10.1373/clinchem.2015.240226

© 2015 American Association for Clinical Chemistry

⁴ Nonstandard abbreviations: LOC, lab-on-a-chip; POC, point-of-care.

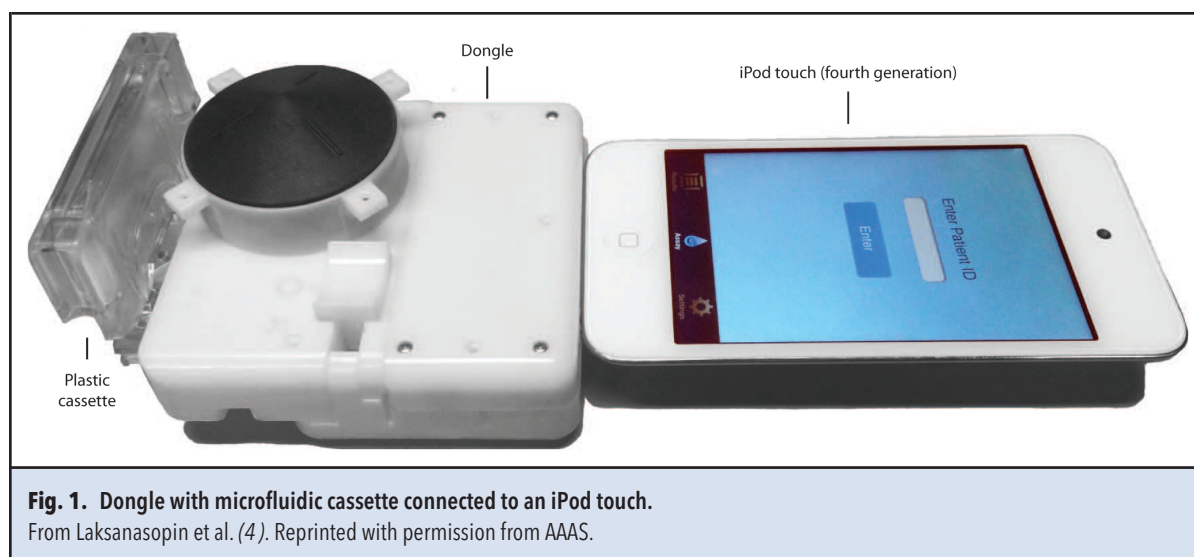


Fig. 1. Dongle with microfluidic cassette connected to an iPod touch.
From Laksanasopin et al. (4). Reprinted with permission from AAAS.

the fast turnaround time, multiplexing capability, lower amount of blood required, and simplicity of the method.

Laksanasopin et al. (4) demonstrate, quite convincingly, that smartphone technology and thoughtful system integration can help improve diagnosis, making it faster and cheaper without compromising the quality of the test. We believe that this study sets the pace for the next generation of diagnostic devices for the developing world.

Implications for the Practice of Clinical Chemistry

Peer-reviewed publications about new diagnostic devices are exciting, but these innovations will not have impact unless they can be widely distributed and used (3). With the increasing adoption of smartphones in the developing world, leveraging their capabilities for POC testing may be a game-changing strategy to deliver laboratory-quality LOC diagnostics in resource-limited settings. The cost and complexity of LOC diagnostic devices can be substantially reduced when functions such as detection, power source, and data processing are outsourced to a smartphone (4). A smartphone interface can provide users with a familiar platform to acquire, visualize, and upload diagnostic data. In addition, the marriage of smartphones and diagnostics may be able to expand the reach of existing healthcare delivery systems, making it

straightforward to give wireless counseling, conduct disease surveillance, receive external quality assurance, and provide decision support to healthcare workers in remote locations (3).

Not surprisingly, more researchers are beginning to use smartphones in their next-generation LOC diagnostic prototypes. The new devices often include a 3D-printed enclosure that houses a smartphone, off-the-shelf electronic/optical components, and microfabricated assay elements. For example, by use of a smartphone for detection, along with micropatterning (5) for multiplexing, multiple disease biomarkers for hepatitis C virus can be detected in a resource-limited setting. As LOC diagnostic tests mature and become more widely used, their adoption in the developing world will increase (as with the mobile phone), and ultimately, the next generation of tests may help reduce the enormous burden caused by infectious and noncommunicable diseases every year.

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

Authors' Disclosures or Potential Conflicts of Interest: No authors declared any potential conflicts of interest.

References

1. Chin CD, Linder V, Sia SK. Commercialization of microfluidic point-of-care diagnostic devices. *Lab Chip* 2012;12:2118–34.
2. Peeling RW, Mabey D. Point-of-care tests for diagnosing infections in the developing world. *Clin Microbiol Infect* 2010;16:1062–9.
3. Pai NP, Vadnais C, Denkinger C, Engel N, Pai M. Point-of-care testing for infectious diseases: diversity, complexity, and barriers in low- and middle-income countries. *PLoS Med* 2012;9:e1001306.
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;7:273re1.
5. Lin R, Skandarajah A, Gerver RE, Neira HD, Fletcher DA, Herr AE. A lateral electrophoretic flow diagnostic assay. *Lab Chip* 2015;15:1488–96.