



“Smart Diagnosis” of Parasitic Diseases by Use of Smartphones

Muhammad A. Saeed,^a Abdul Jabbar^a

^aDepartment of Veterinary Biosciences, Faculty of Veterinary and Agricultural Sciences, University of Melbourne, Werribee, Victoria, Australia

ABSTRACT Accurate and rapid diagnosis is crucial in combating parasitic diseases that cause millions of deaths worldwide. However, the scarcity of specialized diagnostic equipment in low- and middle-income countries is one of the barriers to effective management of parasitic diseases and warrants the need for alternative, inexpensive, point-of-care diagnostic tools. Due to their multiple built-in sensors, smartphones offer cost-effective alternative to expensive diagnostic devices. However, the use of smartphones in parasitic diagnoses remains in its infancy. This minireview describes various smartphone-based devices applied specifically for the diagnosis of parasitic diseases and discusses challenges and potential implications for their use in future.

KEYWORDS smartphones, parasitic diseases, diagnosis, microscopy, lab-on-a-chip

Parasitic diseases cause millions of morbidities and mortalities per annum and impose serious health and socioeconomic consequences, mainly in developing countries of the world (1). According to the Centers for Disease Control and Prevention, malaria alone causes approximately 660,000 casualties per annum, and neglected tropical diseases (NTDs), including Chagas disease, echinococcosis, schistosomiasis, soil-transmitted helminthiases, African trypanosomiasis, cysticercosis, lymphatic filariasis, scabies, etc. affect millions of people worldwide (<https://www.cdc.gov/parasites/about.html>). Accurate and rapid diagnosis is of paramount importance in the effective clinical management of such parasitic diseases. However, the diagnosis of parasitic diseases is severely compromised due to the scarcity of trained personnel and lack of specialized diagnostic equipment in developing countries. For instance, the utility of many commonly used diagnostic methods for parasitic diseases, such as microscopy and nucleic acid amplification, is hindered by the unavailability of a skilled workforce and expensive instruments, reagents, and electricity costs in developing countries (1, 2). This situation results in the inadequacy of these diagnostic tools for the neediest communities, leading to a compromise in the management of parasitic diseases.

Mobile phones and smartphones have brought enormous convenience and sizable impact to modern society, as depicted by a wide range of smartphone users worldwide. Smartphones are a more advanced form of mobile phones, with fully functional computing capabilities and user-friendly features such as personal information management applications, compact digital cameras, Global Positioning System (GPS) navigation, internet access etc. Most smartphones are designed to have multiple sensors such as an imaging camera, vibration sensor, GPS sensor, light level sensor, etc. (3). Due to these powerful built-in sensors, smartphones are setting their roots into the medical field as an alternative to expensive laboratory instruments for various diagnostic purposes (3), and they are of particular interest in regions with limited resources (4). However, the use of smartphones and mobile devices in the diagnosis of parasitic diseases remains in its infancy and limited information is available on the topic. This

Accepted manuscript posted online 18 October 2017

Citation Saeed MA, Jabbar A. 2018. “Smart diagnosis” of parasitic diseases by use of smartphones. *J Clin Microbiol* 56:e01469-17. <https://doi.org/10.1128/JCM.01469-17>.

Editor Colleen Suzanne Kraft, Emory University

Copyright © 2017 American Society for Microbiology. All Rights Reserved.

Address correspondence to Abdul Jabbar, jabbara@unimelb.edu.au.

article aims to review all available studies (as of 16 June 2017) on hardware or software components of smartphones as applied specifically to address the diagnosis of parasites of medical or veterinary importance. Furthermore, the review discusses future implications and challenges with reference to parasitic diseases.

LITERATURE SEARCH

Using ISI Web of Knowledge, all databases were searched from 1900 to 2017 (accessed on June 16, 2017) with multiple search terms and filters (see Table S1 in the supplemental material). The same terms were used to search for articles on PubMed and Google Scholar. Additional relevant articles were identified from the references cited in the articles found in the primary search. Twenty-four studies (Table 1) related to the smartphone-based diagnosis of parasites were finally included in this review.

PARASITE DIAGNOSIS USING SMARTPHONES

This section provides the designs and applications of various smartphone-based diagnostic methods and devices used for the diagnosis of parasites. For the convenience of readers, we have created various categories for different devices; however, some of them may fall under more than one category (see Tables 1 and 2).

Standalone smartphone technology. Owing to high-magnification lenses and powerful image processors, a standalone smartphone (i.e., without use of any external enhancement such as a lens or a microscope) presents a useful tool for the diagnosis of parasitic diseases. For example, Meena and Bhatia used a smartphone for the first time to diagnose a cestode parasite in tomographic images (see Table 1) and they used the smartphone to examine images of a small cysticercus (a larval stage of a cestode) that was otherwise invisible to the clinicians on visual examination (5).

Smartphone applications (apps) and algorithms present another use of smartphones as a standalone tool in the diagnosis of parasitic diseases, such as the interpretation of the rapid diagnostic test (RDT) results for malaria (6, 7). Although RDTs present an inexpensive point-of-care (POC) tool, their effective application in the diagnosis of malarial parasites could be impeded by an incorrect analysis of the results by a poorly trained end user (6). To avoid visual interpretation, a smartphone was used to image and transfer the results of the RDTs of malaria to a globally accessible Research Electronic Data Capture (REDCap) database for analysis using a specialized algorithm. Despite its slightly lower sensitivity (see Table 1), this method significantly reduced reporting errors and false-negative diagnoses compared to a method of visual interpretation (6). In another study, the control line on an RDT for malaria was converted into a smartphone-readable quick response (QR) code (7). A smartphone was deployed to capture RDT images and an associated app was used to perform image processing and recognition of QR codes to determine the concentration of histidine-rich protein 2 (a *Plasmodium falciparum*-specific protein). The detection limit of the assay was 0.966 nM (~543 parasites per μl) compared to that of the World Health Organization (WHO) benchmark testing for an RDT (500 parasites per μl) for low parasitemia, suggesting that this method needs modification to increase its sensitivity. Overall, these smartphone-based diagnostic techniques allow automated identification, secured record keeping, and quality assurance that could be highly useful in malaria surveillance programs.

Although thousands of smartphone apps are currently being used in the health care industry, there is limited information available on apps for the diagnosis of parasites. TickID (NC State University) is an example of one such a freely downloadable app for smartphones (8). This app provides basic information on identification (pictures of male, female, and juvenile ticks) and management (disease biology, personal protection, tick removal, etc.) of selected ticks and tick-borne diseases for a common user. Similar smartphone apps could be developed regionally as well as globally for socio-economically important parasites and could present great assistance for the diagnosis and management of parasitic diseases.

TABLE 1 Smartphone-based devices for the diagnosis of parasites

Category	Parasite or vector	Stage	Study location	Study type	Sample size(s)	Sensitivity or detection limit ^b	Specificity ^b	Reference
Standalone smartphone technology	<i>Taenia solium</i>	Cyst	India	Field	1	NA	NA	5
	<i>Plasmodium falciparum</i>	NA ^c	USA	Lab	NA	21 parasites/ μ l	NA	6
	<i>P. falciparum</i>	NA	USA	Lab	NA	1 nM (543 parasites/ μ l)	NA	7
	Human tick	NA	USA	NA	NA	NA	NA	8
Lens-mounted smartphone microscopy	<i>Ascaris lumbricoides</i>	Egg	Tanzania	Field	199	81%	87%	9
	Hookworm	Egg				14%	89%	9
	<i>Trichuris trichiura</i>	Egg				54%	63%	9
	<i>T. trichiura</i>	Egg	Côte d'Ivoire	Field	164, 180	31%	71%	10
	<i>Schistosoma mansoni</i>	Egg				68%	64%	10
	<i>A. lumbricoides</i>	Egg	USA	Lab	NA	NA	NA	11
Smartphone-assisted manual microscopy	<i>A. lumbricoides</i>	Egg	New Zealand	Lab	NA	NA	NA	12
	<i>Schistosoma hematobium</i>	Egg	Ghana	Field	49	56%	93%	13
	<i>S. hematobium</i>	Egg				68%	100%	13
	<i>S. hematobium</i>	Egg	Côte d'Ivoire	Field	226	36%	100%	14
	<i>S. mansoni</i>	Egg				50%	100%	14
	<i>Giardia lamblia</i>	Cyst	USA	Lab	NA	NA	NA	15
	<i>G. lamblia</i>	Cyst	USA	Lab	NA	NA	NA	16
	<i>P. falciparum</i>	NA	USA	Lab	NA	NA	NA	17
	<i>P. falciparum</i>	NA	Côte d'Ivoire	Field	223	80%	100%	18
	<i>P. falciparum</i>	Mixed	Uganda	Lab	NA	NA	NA	4
	<i>P. chabaudi</i>	Hemozoin	USA	Lab	NA	NA	NA	19
	Smartphone-assisted automated microscopy	<i>S. hematobium</i>	Egg	Sweden	Lab	NA	79%	100%
Animal parasites		Egg	USA	Lab	NA	NA	NA	21
<i>G. lamblia</i>		Cyst	USA	Lab	NA	12 cysts/10 ml	94 (50 cysts/10 ml)	22
<i>P. falciparum</i>		Trophozoite	Portugal	Lab	6	81%	94%	23
<i>Trypanosoma cruzi</i>		DNA	USA	Lab	NA			24
<i>Loa loa</i>		Microfilaria	Cameroon	Field	33	100%	94%	25
Smartphone-assisted microfluidic technology	<i>P. falciparum</i>	NA	USA	Lab	NA	1 pg/ml	NA	26
	<i>Anopheles arabiensis</i>	DNA	USA	Lab	NA	NA	NA	27
	<i>A. gambiae</i>	DNA				NA	NA	27

^aNA, not available/applicable.
^bSensitivity and specificity percentages are given in comparison to a conventional method, e.g., a standard microscope or manual identification; decimal points of these figures were rounded off.

TABLE 2 A comparison of smartphone-based devices used in the diagnosis of parasites

Category	Main device and technology	Advantage(s)	Limitation(s)	Reference
Standalone smartphone technology	iPhone	Rapid; avoids false-negative diagnosis	Validated with only one study	5
	iPhone 5S + algorithm	Automated; reduces reporting errors; avoids false-negative diagnosis	Lower sensitivity than visual method	6
	iPhone 6S + smartphone application (app)	Automated; reduces reporting errors; avoids false-negative diagnosis	Lower sensitivity than visual method	7
Lens-mounted smartphone microscopy	iPhone 4s + ball lens	Low cost; portable	Small FOV; low sensitivity	9, 10
	iPhone 4S + reversed camera lens	Low cost; portable; relatively larger FOV ^a	Illumination and vignetting issues; field validation required	11
Smartphone-assisted manual microscopy	Nokia Lumia 1020 + double convex objective lens + ImageJ	Composite imaging of eggs scattered on different focal planes	Lower resolution; field validation required	12
	iPhone 5S + Foldscope	Low-cost; portable; high specificity	Limited sensitivity; manual slide navigation issue	13
	iPhone 5S + CellScope	Low-cost; portable; high specificity	Low sensitivity; manual slide navigation issue	13, 14
	Motorola ZN5 + LED + aperture	Lens-free and lightweight; avoids undesired artifacts caused by mosaicing algorithms	Powerful smartphone required to image holograms; field validation required	15
	Sony-Erickson U10i Aino + external lens + color filter	Fluorescent microscopy; large FOV; large depth-of-field	Field validation required	16
	Nokia N73 + lens assembly	Wide-field imaging; allows both bright-field and fluorescent imaging	Field validation required	17
	iPhone 5S + Newton NM1 microscope	Handheld; portable; high specificity	Limited sensitivity; relatively expensive; slide navigation issues	18
	Nokia candy bar models + light microscope	High quality imaging; image sharing facility	Heavy microscope	4
	iPhone 5S + polarized microscopic assembly	Improved contrast; time-saving; operable by less-skilled personnel	Field validation required; high-resolution lens required	19
	Smartphone-assisted automated microscopy	Nokia E71 or Sony Ericsson C905 + algorithms	Automated; time-saving; high specificity	Images from each device need separate validation
Smartphone-assisted microfluidic technology	iPhone 5s or Sony Xperia Z3 or Nokia Lumia 1020 + ImageJ	Automated; yields superior results to McMaster method	Field validation required; fluorescent-labeling required	21
	Nokia Lumia 1020 + algorithm	Large FOV and sample load; automated; portable	Field-validation required	22
	HTC 1S or LG Nexus 5 + algorithm + app	Automated; high specificity	Limited sensitivity	23
	Samsung Galaxy S + thermal cycler + MATLAB + ImageJ	Automated; no need for sample preparation	Complex data analysis; thermal cycler required	24
	iPhone 5S + reversed lens cell scope + algorithm + app	Automated video imaging; high sensitivity and specificity; no need for sample preparation	Relatively complex design	25
	iPhone 4 + Optofluidic device + Photoshop CS5	Rapid; portable; high sensitivity	Expertise required for data analysis; field validation required; fluorescent labeling required	26
	iPhone 4 + microfluidic device	Rapid; portable; small sample size required	Field validation required; DNA amplification required; relatively expensive	27

^aFOV, field-of-view.

Lens-mounted smartphone “microscopy”. Mounting a simple, portable lens on a smartphone camera can provide a powerful handheld microscope for the identification of parasites. The lens size determines the spatial resolution and field of view (FOV), as smaller lenses have a smaller FOV but greater spatial resolution and vice versa (28). Bogoch et al. constructed a handheld microscope by mounting a 3-mm ball lens to a smartphone camera, and used it for the identification of soil-transmitted helminths (STH) and *Schistosoma* eggs in urine and stool samples of school-aged children (9, 10). Although this device showed low to moderate sensitivities and specificities (see Table 1) and had a small FOV that produced inferior quality images (see Table 2), this is an inexpensive and portable microscope. With improved sensitivity, this could be invaluable in the field diagnosis of STH infection in developing countries.

In order to increase the resolution of lens-mounted smartphone microscopy, Switz et al. applied a reversed camera lens to a smartphone to produce a large FOV (~10 mm²) with a resolution of $\leq 5 \mu\text{m}$ for better quality images of STH eggs in stool samples (11). A major issue in imaging parasitic eggs is their scattering at different focal depths in a three dimensional (3D) plane. Sowerby et al. addressed this issue by mounting a 12-mm double convex objective lens on a smartphone camera to image *Ascaris lumbricoides* eggs and create composite images using a software program, ImageJ (12). Overall, external lens-mounted smartphone microscopes are portable, inexpensive, and operate without constant electricity needs, which make them a field-deployable tool in parasitic diagnosis in resource-constrained regions of the world.

Smartphone-assisted manual microscopy. Smartphones have recently been applied in conjunction with various microscopic assemblies for the diagnosis of parasites. Ephraim et al. used smartphone-assisted Foldscope and reversed-lens CellScope for the diagnosis of *Schistosoma haematobium* eggs in urine samples of school-aged children (13). The handheld Foldscope was made of paper, consisting of a 2.38-mm ball lens and a light-emitting diode (LED) secured to a smartphone camera. The reversed-lens CellScope was constructed with a lens embedded in a 3D-printed plastic and secured to a smartphone camera. Despite their low to moderate sensitivities (see Table 1), both “microscopes” showed high specificities. In another field study, the CellScope consistently demonstrated high specificity, despite low sensitivity, for the diagnosis of *Schistosoma* eggs in urine and stool samples (14), indicating that with enhanced sensitivity, these devices could be deployed in the field for large-scale screening of schistosomes.

In an attempt to design a compact microscope, Tseng et al. introduced a lens-free microscope for the identification of *Giardia lamblia* cysts (15). The sample of interest was illuminated using an incoherent LED light (shone vertically). The scattered light interfered with unscattered LED light to create a hologram of each cell, which was detected by a smartphone camera. Depending on the power of the smartphone, extremely rich information in the hologram allowed rapid reconstruction of the microscopic images. In another study, *G. lamblia* cysts were identified using a smartphone-based fluorescence microscope (16), where an LED light was used to excite the sample and the emitted fluorescent light was detected with an external lens placed in front of a smartphone camera. For fluorescent imaging in this study, a dark-field background was created using an inexpensive color filter (16).

Smartphone-assisted microscopes have also been applied for the diagnosis of *Plasmodium* spp. For instance, a bright-field microscope was constructed using objective and wide-field eyepiece lenses to produce 28 \times magnification onto a smartphone camera sensor for the identification of *P. falciparum* in blood smears (17). In another field study, *P. falciparum* was identified in Giemsa-stained blood films using a handheld Newton Nm1 light microscope attached to a smartphone (18). The system achieved a moderate sensitivity and a high specificity (see Table 1), suggesting that this could be invaluable in large-scale malaria screening programs. Other malarial biomarkers, such as hemozoin, have also been detected in blood smears, using a low-cost and high-fidelity smartphone-assisted polarized microscope (19). However, this system requires

adequate lens resolution to differentiate the presence of hemozoin within an infected blood smear.

Smartphone-assisted automated microscopy. Manual microscopic examination of parasitic eggs is considered laborious and time-consuming, as it requires a microscope as well as a trained person, which limits its use in the field in developing countries. A possible solution to this problem could be the use of a dedicated smartphone app or algorithm for automated detection of parasites. For instance, Linder et al. introduced two pattern-recognition algorithms for the identification of *S. haematobium* eggs in images acquired by a smartphone or a webcam (20). This method achieved a high specificity and a moderate sensitivity, compared to a visual identification method (see Table 1). In another study, Slusarewicz et al. introduced a smartphone-based fecal egg-counting technique for animal parasites (21). The eggs were stained with a fluorescent chitin-binding protein and photographed using a smartphone, followed by automated egg-counting with ImageJ. For strongyle eggs, a significant linear correlation ($R^2 = 0.98$) and coefficient of variation were found between the automated counts and manual McMaster counts, indicating that the automated system performed better than the most commonly used traditional method in veterinary parasitology.

Smartphone-assisted automated microscopy is not confined only to egg identification, as a smartphone-based fluorescence microscopy technique has recently been applied to quantify DNA from *Trypanosoma cruzi* (24). PCR was performed inside a central processing unit (CPU) by controlling the heating/cooling cycles with computer software. PCR products were exposed to UV light and imaged by a smartphone, using a low-cost filter. A histogram of the pixel intensities of the patient sample was compared to that of a control sample for detecting target pathogenic DNA (24). Similarly, Koydemir et al. designed a smartphone-based fluorescence microscope with a large FOV ($\sim 0.8 \text{ cm}^2$) to detect *G. lamblia* cysts (22). In this method, a smartphone was used to image fluorescently labeled cysts captured on a membrane, and the images were transferred to a remote processing system for automatic detection and counting of cysts in large volumes of water (e.g., 10 to 20 ml) with an algorithm in a short time (22). Rosado et al. have recently introduced a smartphone-based image processing and analysis methodology for identification of *P. falciparum* trophozoites in Giemsa-stained blood smears (23). The system automatically identified the parasite based on preannotated characters and achieved a moderate sensitivity and a high specificity (see Table 1).

Smartphone-assisted microscopy is not confined to still imaging only, as the use of smartphone video microscopy has been demonstrated recently for the quantification of *Loa loa* microfilariae (a larval stage of the parasite that has a serpentine movement) (25). The device (CellScope Loa) used a smartphone to perform video imaging of an unprocessed blood sample, which was analyzed using an algorithm for automatic quantification of microfilariae. The final result was displayed through an app in less than 2 min. The device showed high sensitivity and specificity (see Table 1) compared to manual counts in thick blood smears from 33 potentially *Loa*-infected patients, suggesting the potential implications of this device in the field screening of the parasite (25). Such smartphone-assisted video imaging could be applicable for the diagnosis of other blood parasites and motile parasitic stages in body fluids or excreta.

Smartphone-assisted microfluidic technology. Due to their high throughput, easy handling, parallelism, and sensitivity, the use of microfluidic lab-on-a-chip devices (LOCDs) has greatly increased in medical diagnostics (26). Smartphones offer tremendous potential for *in vitro* measurements of biochemical reactions in LOCDs. For instance, Stemple et al. recently introduced a handheld smartphone-assisted LOCD for the detection of a *P. falciparum*-specific protein, HRP-2 (26). Anti-HRP-2-conjugated submicrobeads were mixed with 10% whole blood sample in a microfluidic LOCD. A smartphone was deployed for illumination of the sample followed by the detection of the scattered light. Using scattering/absorption characteristics of the sample, the system was able to measure as low as 1 pg/ml of HRP-2 from blood in 10 min (26).

In another study, Liu et al. described an integrated microfluidic chip with a smartphone recorder for the identification of *Anopheles* spp. (27). The microfluidic device allowed DNA extraction followed by target DNA amplification using loop-mediated isothermal amplification (LAMP). The amplified products were excited with a DNA-intercalating dye and the fluorescence signal was detected with a smartphone camera. This multiplex system could be used for parallel identification of several mosquito species. Such a sophisticated smartphone-based LOCD could be highly useful not only in the onsite diagnosis of parasites but also in the quick recording of test results and geographic location for quality control.

CONCLUSIONS AND FUTURE IMPLICATIONS

Smartphone microscopy is one of the most common applications of smartphones for the diagnosis of parasitic diseases. A smartphone allows the direct transfer of images (by Multimedia Messaging Service [MMS], Bluetooth, etc.) to a reference laboratory for quick assessment, feedback, and quality assurance by an expert parasitologist (4, 28). Traditionally, the Kato-Katz is the commonly used method for the diagnosis of intestinal helminths. However, it involves laborious manual microscopy and the hookworm ova are rapidly cleared in this method, resulting in false-negative diagnoses. As an alternative, an inexpensive and portable ball-lens-mounted smartphone microscope presents a simple POC tool for the identification of STHs in community surveys (9, 10). However, the use of this device is limited due to various issues such as specimen orientation, hygiene, manual slide navigation, low sensitivity, and small FOV (see Table 2). Some of these issues have been addressed by applying other lens settings, such as a reversed lens (11) and a double convex lens (12), although these devices require field validation.

The smartphone-assisted Foldscope and CellScope tools present attractive POC tools for the diagnosis of schistosomes, as they have been tested in the field, are lightweight, and cost less than \$1 and \$6, respectively (13). Despite their high specificity, a major limitation of these devices is their low sensitivity. This could be explained by their small FOV (2) or by irregular distribution of *Schistosoma* eggs in the excreta. To detect *Schistosoma* eggs in large field surveys with improved sensitivity, these devices could be trialed in conjunction with a specialized algorithm for automated identification (20). The Newton NM1 microscope had higher sensitivity than the Foldscope or CellScope for the diagnosis of *Schistosoma* (14). A combination of the NM1 with the smartphone algorithm method (20) could further enhance the sensitivity of this device for field diagnosis of schistosomes. However, the NM1 can be much more expensive than the Foldscope or CellScope microscopes. Another way to enhance the sensitivity of smartphone-assisted microscopic devices could be the use of fluorescently labeled egg-binding dyes, which produces superior results to the commonly used McMaster method for the identification of strongyle eggs (21). A similar system could be trialed for the diagnosis of human helminths. The recent application of smartphone microscopy for the detection of pathogenic DNA (24, 27) presents a multiplex potential for parallel identification of several parasitic species in a high-throughput and short-time format.

Smartphone-assisted video microscopy is a recent advancement in parasite diagnostics. For instance, the CellScope Loa allowed the quantification of *L. loa* microfilariae in less than 2 min with a high sensitivity (100%) (25). Such a device could potentially be applied for rapid field diagnosis of other blood-borne parasites, such as *Leishmania* and *Trypanosoma*. Furthermore, video microscopes have the ability to characterize motility patterns of parasites, which could be applied for the diagnosis of flagellate parasites and parasitic larval stages (29).

One of the advantages for using smartphone-based diagnostic tools is the use of dedicated algorithms and softwares for automated identification of parasites. For instance, the utilization of a specialized algorithm facilitated smartphone-assisted automatic detection of *G. lamblia* in large volumes of water in only 1 h compared to the conventional methods which may take 1 to 2 days (22). Since waterborne parasitic

diseases remain the second leading cause of death in children under age five in developing countries, this technology could be applicable for large-scale water testing in these regions. Similar to pattern-recognition algorithms used for human face recognition in biometric analysis, algorithms could be developed for the identification of parasites and parasitic eggs. The introduction of pattern-recognition algorithms for the identification of *Schistosoma* eggs and *P. falciparum* is a recent advancement in this context (20, 23). Smartphone apps are also finding use in parasite diagnostics, for instance, TickID (8). Similar apps are required for diagnosis and self-management of other parasitic infections, especially in resource-constrained regions where people may own a smartphone despite the inadequacy of basic health care facilities (2, 17). An ideal diagnostic app should work both for iOS and Android systems. Developing dedicated algorithms and freely downloadable apps for automated diagnosis of parasites offers great potential for future parasitology research.

Smartphone-assisted microfluidic LOCDs have the potential for high-throughput diagnosis of parasites. For instance, a smartphone-assisted LOCD enabled the detection of *P. falciparum* from whole blood in ~10 min compared to the conventional blood smear method, which may take 1 to 3 h (26). Such devices require testing in large-scale field trials for the diagnosis of important blood-borne parasites. Despite the high robustness of microfluidic LOCDs, they could be more expensive than conventional diagnostic tools, which warrants the need for studies exploring ways to reduce the cost of such devices for rapid processing of a large number of samples.

Most smartphone-based diagnostic devices have been tested in well-controlled laboratory conditions and only for tropical parasitic diseases. Further studies are required to explore the usefulness of such devices for the diagnosis of other important parasitic diseases in field conditions and on clinical specimens. Despite the portability of smartphone-based diagnostic tools, issues such as need for manual processing of samples and preparation of microscopic slides remain to be addressed. Limited battery capacity of smartphones is a major bottleneck for their field deployability in remote health care facilities, which can be solved by applying mobile charging devices with a car battery or solar power (28). Internet prices can be high in low-income regions, which may hinder transfer of the diagnostic data to a reference laboratory. Lack of awareness and a tangible commercial market are the other major challenges for smartphone-based diagnostic devices, which could be addressed through integrated training and practical business plans. Sustained research and strong collaboration among researchers, clinicians, and the public sector are required in this context. Currently, there are no set standards and regulatory approval methods in place for commercialization of smartphone-based diagnostic devices, which warrants the urgent need for developing standard guidelines by professional associations/societies such as the World Federation of Parasitology, the World Association for the Advancement of Veterinary Parasitology, and the American Society for Microbiology. Moreover, these technologies require rigorous quality control and adequate field validation before deploying them in clinics. A consortium of experts could be of great help for quality assurance and enhanced usability of such technologies. Despite all these challenges, these devices have the technical capacity to meet the enormous diagnostic needs of developing countries with high prevalences of parasitic diseases.

The combined use of smartphones with inexpensive handheld microscopes and microfluidic devices offers a great opportunity for the advancement of portable diagnostic technologies to overcome the burden of many parasitic diseases in resource-constrained regions and offers researchers opportunities to develop similar technologies at affordable prices. Despite lower sensitivity than an established laboratory test, a smartphone-assisted onsite diagnostic test could be more useful to provide onsite "sample-to-answer" treatment to a patient infected with a parasitic disease, as this patient may not return to the clinic for the results of a laboratory test (1, 2). The future of smartphone-assisted diagnostic technologies is very promising and the widespread adoption of such technologies is anticipated in the near future for the accurate and rapid diagnosis of parasitic diseases in an easy-to-use format.

SUMMARY

In this minireview, we have described various smartphone-based devices, applied specifically for the diagnosis of parasitic diseases of medical and veterinary importance, and discussed challenges, potential implications, and needs for future development. Smartphones have been used as a standalone tool or in combination with other microscopic and microfluidic devices for the identification of various stages of parasites, such as eggs, cysts, and microfilariae. When used with a dedicated algorithm, app, or software, smartphones allow automated and rapid diagnosis of parasites that make them a powerful tool in large field surveys for disease surveillance and outbreak containment. Major strengths of smartphone-based microscopic devices is their low cost, widespread availability, and onsite diagnostic potential, which can be highly applicable in resource-constrained regions for effective management of a parasitic disease. As an emerging technology, smartphone-based diagnostic devices face challenges such as a lack of set standards and guidelines, awareness, and a tangible commercial market. Despite these challenges, these devices hold the potential to fulfill the enormous diagnostic needs of developing countries with high prevalences of parasitic diseases. Further studies are warranted to explore the usefulness of such devices, especially in field conditions and in clinical settings, not only for parasitic but also for other microbial diseases. The widespread adoption of smartphone-based diagnostic devices is anticipated in the near future for rapid diagnosis of parasitic diseases.

SUPPLEMENTAL MATERIAL

Supplemental material for this article may be found at <https://doi.org/10.1128/JCM.01469-17>.

SUPPLEMENTAL FILE 1, PDF file, 0.1 MB.

ACKNOWLEDGMENTS

The 2016 Learning and Teaching Initiative Grants Scheme from The University of Melbourne supported this study.

We declare no conflict of interest.

REFERENCES

- Drain PK, Hyle EP, Noubary F, Freedberg KA, Wilson D, Bishai W, Rodriguez W, Bassett IV. 2014. Evaluating diagnostic point-of-care tests in resource-limited settings. *Lancet Infect Dis* 14:239–249. [https://doi.org/10.1016/S1473-3099\(13\)70250-0](https://doi.org/10.1016/S1473-3099(13)70250-0).
- Rajchgot J, Coulibaly JT, Keiser J, Utzinger J, Lo NC, Mondry MK, Andrews JR, Bogoch II. 2017. Mobile-phone and handheld microscopy for neglected tropical diseases. *PLoS Negl Trop Dis* 11:e0005550. <https://doi.org/10.1371/journal.pntd.0005550>.
- Kwon L, Long K, Wan Y, Yu H, Cunningham B. 2016. Medical diagnostics with mobile devices: comparison of intrinsic and extrinsic sensing. *Bio-technol Adv* 34:291–304. <https://doi.org/10.1016/j.biotechadv.2016.02.010>.
- Tuijn CJ, Hoefman BJ, Van Beijma H, Oskam L, Chevrollier N. 2011. Data and image transfer using mobile phones to strengthen microscopy-based diagnostic services in low and middle income country laboratories. *PLoS One* 6:e28348. <https://doi.org/10.1371/journal.pone.0028348>.
- Meena M, Bhatia K. 2013. Smart phone as an adjunctive imaging tool to visualize scolex in orbital myocysticercosis. *Int Ophthalmol* 33:319–321. <https://doi.org/10.1007/s10792-012-9666-6>.
- Scherr TF, Gupta S, Wright DW, Haselton FR. 2016. Mobile phone imaging and cloud-based analysis for standardized malaria detection and reporting. *Sci Rep* 6:28645. <https://doi.org/10.1038/srep28645>.
- Scherr TF, Gupta S, Wright DW, Haselton FR. 2017. An embedded barcode for “connected” malaria rapid diagnostic tests. *Lab Chip* 17:1314–1322. <https://doi.org/10.1039/C6LC01580H>.
- Pérez de León AA, Teel PD, Li A, Ponnusamy L, Roe RM. 2014. Advancing integrated tick management to mitigate burden of tick-borne diseases. *Outlooks Pest Manage* 25:382–389.
- Bogoch II, Andrews JR, Speich B, Utzinger J, Ame SM, Ali SM, Keiser J. 2013. mobile phone microscopy for the diagnosis of soil-transmitted helminth infections: a proof-of-concept study. *Am J Trop Med Hyg* 88:626–629. <https://doi.org/10.4269/ajtmh.12-0742>.
- Bogoch II, Coulibaly JT, Andrews JR, Speich B, Keiser J, Stothard JR, N’Goran EK, Utzinger J. 2014. Evaluation of portable microscopic devices for the diagnosis of *Schistosoma* and soil-transmitted helminth infection. *Parasitol* 141:1811–1818. <https://doi.org/10.1017/S0031182014000432>.
- Switz NA, D’Ambrosio MV, Fletcher DA. 2014. Low-cost mobile phone microscopy with a reversed mobile phone camera lens. *PLoS One* 9:e95330. <https://doi.org/10.1371/journal.pone.0095330>.
- Sowerby SJ, Crump JA, Johnstone MC, Krause KL, Hill PC. 2016. Smartphone Microscopy of parasite eggs accumulated into a single field of view. *Am J Trop Med Hyg* 94:227–230. <https://doi.org/10.4269/ajtmh.15-0427>.
- Ephraim RKD, Duah E, Cybulski JS, Prakash M, D’Ambrosio MV, Fletcher DA, Keiser J, Andrews JR, Bogoch II. 2015. Diagnosis of *Schistosoma haematobium* infection with a mobile phone-mounted Foldscope and a reversed-lens CellScope in Ghana. *Am J Trop Med Hyg* 92:1253–1256. <https://doi.org/10.4269/ajtmh.14-0741>.
- Coulibaly JT, Ouattara M, D’Ambrosio MV, Fletcher DA, Keiser J, Utzinger J, N’Goran EK, Andrews JR, Bogoch II. 2016. Accuracy of mobile phone and handheld light microscopy for the diagnosis of schistosomiasis and intestinal protozoa infections in Cote d’Ivoire. *PLoS Negl Trop Dis* 10:e0004768. <https://doi.org/10.1371/journal.pntd.0004768>.
- Tseng D, Mudanyali O, Oztoprak C, Isikman SO, Sencan I, Yaglidere O, Ozcan A. 2010. Lensfree microscopy on a cellphone. *Lab Chip* 10:1787–1792. <https://doi.org/10.1039/c003477k>.
- Zhu H, Yaglidere O, Su T-W, Tseng D, Ozcan A. Wide-field fluorescent microscopy on a cell-phone, p 6801–6804. *In* 2011 Annual International

- Conference of the IEEE Engineering in Medicine and Biology Society (EMBC 2011), Boston, MA.
17. Breslauer DN, Maamari RN, Switz NA, Lam WA, Fletcher DA. 2009. Mobile phone based clinical microscopy for global health applications. *PLoS One* 4:e6320. <https://doi.org/10.1371/journal.pone.0006320>.
 18. Coulibaly JT, Ouattara M, Keiser J, Bonfoh B, N'Goran EK, Andrews JR, Bogoch II. 2016. Evaluation of malaria diagnoses using a handheld light microscope in a community-based setting in rural Cote d'Ivoire. *Am J Trop Med Hyg* 95:831–834. <https://doi.org/10.4269/ajtmh.16-0328>.
 19. Pirstill CW, Coté GL. 2015. Malaria diagnosis using a mobile phone polarized microscope. *Sci Reports* 5:13368. <https://doi.org/10.1038/srep13368>.
 20. Linder E, Grote A, Varjo S, Linder N, Lebbad M, Lundin M, Diwan V, Hannuksela J, Lundin J. 2013. On-chip imaging of *Schistosoma haematobium* eggs in urine for diagnosis by computer vision. *PLoS Negl Trop Dis* 7:e2547. <https://doi.org/10.1371/journal.pntd.0002547>.
 21. Slusarewicz P, Pagano S, Mills C, Popa G, Chow KM, Mendenhall M, Rodgers DW, Nielsen MK. 2016. Automated parasite faecal egg counting using fluorescence labelling, smartphone image capture and computational image analysis. *Int J Parasitol* 46:485–493. <https://doi.org/10.1016/j.ijpara.2016.02.004>.
 22. Koydemir HC, Gorocs Z, Tseng D, Cortazar B, Feng S, Chan RYL, Burbano J, McLeod E, Ozcan A. 2015. Rapid imaging, detection and quantification of *Giardia lamblia* cysts using mobile-phone based fluorescent microscopy and machine learning. *Lab Chip* 15:1284–1293. <https://doi.org/10.1039/C4LC01358A>.
 23. Rosado L, da Costa JMC, Elias D, Cardoso JS. 2016. Automated detection of malaria parasites on thick blood smears via mobile devices. *Procedia Comput Sci* 90:138–144. <https://doi.org/10.1016/j.procs.2016.07.024>.
 24. Walker FM, Ahmad KM, Eisenstein M, Soh HT. 2014. Transformation of personal computers and mobile phones into genetic diagnostic systems. *Anal Chem* 86:9236–9241. <https://doi.org/10.1021/ac5022419>.
 25. D'Ambrosio MV, Bakalar M, Bennuru S, Reber C, Skandarajah A, Nilsson L, Switz N, Kamgno J, Pion S, Boussinesq M, Nutman TB, Fletcher DA. 2015. Point-of-care quantification of blood-borne filarial parasites with a mobile phone microscope. *Sci Transl Med* 7:286re4. <https://doi.org/10.1126/scitranslmed.aaa3480>.
 26. Stemple CC, Angus SV, Park TS, Yoon JY. 2014. Smartphone-based optofluidic lab-on-a-chip for detecting pathogens from blood. *J Lab Autom* 19:35–41. <https://doi.org/10.1177/2211068213498241>.
 27. Liu C, Mauk MG, Hart R, Bonizzoni M, Yan G, Bau HH. 2012. A low-cost microfluidic chip for rapid genotyping of malaria-transmitting mosquitoes. *PLoS One* 7:e42222. <https://doi.org/10.1371/journal.pone.0042222>.
 28. Dendere R, Myburg N, Douglas T. 2015. A review of cellphone microscopy for disease detection. *J Microsc* 260:248–259. <https://doi.org/10.1111/jmi.12307>.
 29. Linder E, Varjo S, Thors C. 2016. Mobile diagnostics based on motion? A close look at motility patterns in the schistosome life cycle. *Diagnostics* 6:24. <https://doi.org/10.3390/diagnostics6020024>.