

Supporting information

Engineering Steps for Mobile Point-of-Care Diagnostic Devices

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- 1. List of mobile phone diagnostic studies with references.....Table T1**

Table T1. List of mobile phone diagnostic studies and their application for diagnosis of different diseases. References are made available here

readout	disease	setting	analytical sensitivity	clinical sensitivity	clinical specificity	ref
colorimetric	measles, mumps, HSV-1/2	laboratory	not discussed	100%, 99%, 100%, 100%	97%, 95%, 100%, 100%	¹
	ovarian cancer	laboratory	20 ng/mL	89.5%	90%	²
	ebola	field	200 ng/mL	100%	100%	³
	HIV	laboratory	1 pg/mL	n/a	n/a	⁴
	UTI,	laboratory	10 CFU/mL	n/a	n/a	⁵
	red blood cells	laboratory	50 mg/dL	n/a	n/a	⁶
	zika	laboratory	0.05 ng/mL	n/a	n/a	⁷
	HIV, TB, malaria	laboratory	not discussed	n/a	n/a	⁸
	dengue	laboratory	5 nM	n/a	n/a	⁹
	sepsis	laboratory	22 pg/mL	91%	82%	¹⁰
electrochemical	cervical cancer	laboratory	10 amol	100%	92%	¹¹
	HPV	laboratory	50 amol	83–92%	90–100%	¹²
	HIV	laboratory	48 ng/mL	100%	100%	¹³
	HIV, syphilis	field	2 pg/mL	100%, 77%	91%, 89%	¹⁴
	malaria	laboratory	20 ng/mL	n/a	n/a	¹⁵
	malaria	laboratory	16 ng/mL	n/a	n/a	¹⁶
	HCV	laboratory	12 pM	n/a	n/a	¹⁷
	avian influenza	laboratory	8×10^5 PFU/mL	96%	99%	¹⁸
fluorescence	thrombin	laboratory	18 NIH units/mL	n/a	n/a	¹⁹
	ebola	laboratory	0.2 ng/mL	n/a	n/a	²⁰
	zika	laboratory	3×10^4 PFU/mL	n/a	n/a	²¹
	CMV	laboratory	1×10^3 PFU/mL	n/a	n/a	²²
	HIV	laboratory	17 pg/mL	n/a	n/a	²³
	HIV, dengue	laboratory	100 pM	n/a	n/a	²⁴
	E. coli	laboratory	300 copies/pL	n/a	n/a	²⁵
	zika, dengue, chikungunya	laboratory	22 PFU/mL	n/a	n/a	²⁶
	HSV-2	laboratory	~100 copies/pL	n/a	n/a	²⁷
	HIV, HBV	laboratory	1×10^3 copies/mL	n/a	n/a	²⁸

microscopy	<i>Loa loa</i> filariasis	field	3×10^4 mf/mL	100%	94%	29
	schistosomiasis	field	not discussed	56%	93%	30
	giardiasis	laboratory	1×10^6 cells/mL	n/a	n/a	31
	<i>S. aureus</i>	laboratory	50 cfu/mL	n/a	n/a	32
	malaria, tuberculosis	laboratory	n/a	n/a	n/a	33

References

- (1) Berg, B.; Cortazar, B.; Tseng, D.; Ozkan, H.; Feng, S.; Wei, Q.; Chan, R. Y. L.; Burbano, J.; Farooqui, Q.; Lewinski, M.; et al. Cellphone-Based Hand-Held Microplate Reader for Point-of-Care Testing of Enzyme-Linked Immunosorbent Assays. *ACS Nano* **2015**. <https://doi.org/10.1021/acsnano.5b03203>.
- (2) Wang, S.; Zhao, X.; Khimji, I.; Akbas, R.; Qiu, W.; Edwards, D.; Cramer, D. W.; Ye, B.; Demirci, U. Integration of Cell Phone Imaging with Microchip ELISA to Detect Ovarian Cancer HE4 Biomarker in Urine at the Point-of-Care. *Lab Chip* **2011**. <https://doi.org/10.1039/c1lc20479c>.
- (3) Brangel, P.; Sobarzo, A.; Parolo, C.; Miller, B. S.; Howes, P. D.; Gelkop, S.; Lutwama, J. J.; Dye, J. M.; McKendry, R. A.; Lobel, L.; et al. A Serological Point-of-Care Test for the Detection of IgG Antibodies against Ebola Virus in Human Survivors. *ACS Nano* **2018**, *12* (1), 63–73. <https://doi.org/10.1021/acsnano.7b07021>.
- (4) Loynachan, C. N.; Thomas, M. R.; Gray, E. R.; Richards, D. A.; Kim, J.; Miller, B. S.; Brookes, J. C.; Agarwal, S.; Chudasama, V.; McKendry, R. A.; et al. Platinum Nanocatalyst Amplification: Redefining the Gold Standard for Lateral Flow Immunoassays with Ultrabroad Dynamic Range. *ACS Nano* **2018**, *12* (1), 279–288. <https://doi.org/10.1021/acsnano.7b06229>.
- (5) Cho, S.; Park, T. S.; Nahapetian, T. G.; Yoon, J. Y. Smartphone-Based, Sensitive MPAD Detection of Urinary Tract Infection and Gonorrhea. *Biosens. Bioelectron.* **2015**. <https://doi.org/10.1016/j.bios.2015.07.014>.
- (6) Jalal, U. M.; Jin, G. J.; Shim, J. S. Paper-Plastic Hybrid Microfluidic Device for Smartphone-Based Colorimetric Analysis of Urine. *Anal. Chem.* **2017**, *89* (24), 13160–13166. <https://doi.org/10.1021/acs.analchem.7b02612>.
- (7) Rong, Z.; Wang, Q.; Sun, N.; Jia, X.; Wang, K.; Xiao, R.; Wang, S. Smartphone-Based Fluorescent Lateral Flow Immunoassay Platform for Highly Sensitive Point-of-Care Detection of Zika Virus Nonstructural Protein 1. *Anal. Chim. Acta* **2018**, No. xxxx, 1–8. <https://doi.org/10.1016/J.ACA.2018.12.043>.
- (8) Mudanyali, O.; Dimitrov, S.; Sikora, U.; Padmanabhan, S.; Navruz, I.; Ozcan, A. Integrated Rapid-Diagnostic-Test Reader Platform on a Cellphone. *Lab Chip* **2012**. <https://doi.org/10.1039/c2lc40235a>.
- (9) Choi, J. R.; Hu, J.; Feng, S.; Wan Abas, W. A. B.; Pingguan-Murphy, B.; Xu, F. Sensitive Biomolecule Detection in Lateral Flow Assay with a Portable Temperature-Humidity Control Device. *Biosens. Bioelectron.* **2016**. <https://doi.org/10.1016/j.bios.2015.12.005>.
- (10) Min, J.; Nothing, M.; Coble, B.; Zheng, H.; Park, J.; Im, H.; Weber, G. F.; Castro, C. M.; Swirski, F. K.; Weissleder, R.; et al. Integrated Biosensor for Rapid and Point-of-Care Sepsis Diagnosis. *ACS Nano* **2018**. <https://doi.org/10.1021/acsnano.7b08965>.
- (11) Castro, C. M.; Im, H.; Zurkiya, O.; Fexon, L.; Shao, H.; Pathania, D.; Weissleder, R.; Pivovarov, M.; Rho, J.; Liang, M.; et al. Digital Diffraction Analysis Enables Low-Cost Molecular Diagnostics on a Smartphone. *Proc. Natl. Acad. Sci.* **2015**. <https://doi.org/10.1073/pnas.1501815112>.
- (12) Ho, N. R. Y.; Lim, G. S.; Sundah, N. R.; Lim, D.; Loh, T. P.; Shao, H. Visual and Modular Detection of Pathogen Nucleic Acids with Enzyme–DNA Molecular Complexes. *Nat. Commun.* **2018**. <https://doi.org/10.1038/s41467-018-05733-0>.

- (13) Turbé, V.; Gray, E. R.; Lawson, V. E.; Nastouli, E.; Brookes, J. C.; Weiss, R. A.; Pillay, D.; Emery, V. C.; Verrips, C. T.; Yatsuda, H.; et al. Towards an Ultra-Rapid Smartphone- Connected Test for Infectious Diseases. *Sci. Rep.* **2017**. <https://doi.org/10.1038/s41598-017-11887-6>.
- (14) Laksanasopin, T.; Guo, T. W.; Nayak, S.; Sridhara, A. A.; Xie, S.; Olowookere, O. O.; Cadinu, P.; Meng, F.; Chee, N. H.; Kim, J.; et al. A Smartphone Dongle for Diagnosis of Infectious Diseases at the Point of Care. *Sci. Transl. Med.* **2015**, 7 (273), 273re1. <https://doi.org/10.1126/scitranslmed.aaa0056>.
- (15) Nemiroski, A.; Hennek, J. W.; Christodouleas, D. C.; Fernandez-Abedul, M. T.; Maxwell, E. J.; Whitesides, G. M.; Kumar, A. A. Universal Mobile Electrochemical Detector Designed for Use in Resource-Limited Applications. *Proc. Natl. Acad. Sci.* **2014**. <https://doi.org/10.1073/pnas.1405679111>.
- (16) Lillehoj, P. B.; Huang, M. C.; Truong, N.; Ho, C. M. Rapid Electrochemical Detection on a Mobile Phone. *Lab Chip* **2013**. <https://doi.org/10.1039/c3lc50306b>.
- (17) Aronoff-Spencer, E.; Venkatesh, A. G.; Sun, A.; Brickner, H.; Looney, D.; Hall, D. A. Detection of Hepatitis C Core Antibody by Dual-Affinity Yeast Chimera and Smartphone-Based Electrochemical Sensing. *Biosens. Bioelectron.* **2016**. <https://doi.org/10.1016/j.bios.2016.07.023>.
- (18) Yeo, S. J.; Choi, K.; Cuc, B. T.; Hong, N. N.; Bao, D. T.; Ngoc, N. M.; Le, M. Q.; Hang, N. L. K.; Thach, N. C.; Mallik, S. K.; et al. Smartphone-Based Fluorescent Diagnostic System for Highly Pathogenic H5N1 Viruses. *Theranostics* **2016**. <https://doi.org/10.7150/thno.14023>.
- (19) Petryayeva, E.; Algar, W. R. Single-Step Bioassays in Serum and Whole Blood with a Smartphone, Quantum Dots and Paper-in-PDMS Chips. *Analyst* **2015**. <https://doi.org/10.1039/c5an00475f>.
- (20) Hu, J.; Jiang, Y. Z.; Wu, L. L.; Wu, Z.; Bi, Y.; Wong, G.; Qiu, X.; Chen, J.; Pang, D. W.; Zhang, Z. L. Dual-Signal Readout Nanospheres for Rapid Point-of-Care Detection of Ebola Virus Glycoprotein. *Anal. Chem.* **2017**. <https://doi.org/10.1021/acs.analchem.7b02222>.
- (21) Ganguli, A.; Ornob, A.; Yu, H.; Damhorst, G. L.; Chen, W.; Sun, F.; Bhuiya, A.; Cunningham, B. T.; Bashir, R. Hands-Free Smartphone-Based Diagnostics for Simultaneous Detection of Zika, Chikungunya, and Dengue at Point-of-Care. *Biomed. Microdevices* **2017**. <https://doi.org/10.1007/s10544-017-0209-9>.
- (22) Wei, Q.; Qi, H.; Luo, W.; Tseng, D.; Ki, S. J.; Wan, Z.; Göröcs, Z.; Bentolila, L. A.; Wu, T. T.; Sun, R.; et al. Fluorescent Imaging of Single Nanoparticles and Viruses on a Smart Phone. *ACS Nano* **2013**. <https://doi.org/10.1021/nn4037706>.
- (23) Joh, D. Y.; Hucknall, A. M.; Wei, Q.; Mason, K. A.; Lund, M. L.; Fontes, C. M.; Hill, R. T.; Blair, R.; Zimmers, Z.; Achar, R. K.; et al. Inkjet-Printed Point-of-Care Immunoassay on a Nanoscale Polymer Brush Enables Subpicomolar Detection of Analytes in Blood. *Proc. Natl. Acad. Sci.* **2017**. <https://doi.org/10.1073/pnas.1703200114>.
- (24) Arts, R.; Den Hartog, I.; Zijlema, S. E.; Thijssen, V.; Van Der Beelen, S. H. E.; Merkx, M. Detection of Antibodies in Blood Plasma Using Bioluminescent Sensor Proteins and a Smartphone. *Anal. Chem.* **2016**. <https://doi.org/10.1021/acs.analchem.6b00534>.
- (25) Stedtfeld, R. D.; Tourlousse, D. M.; Seyrig, G.; Stedtfeld, T. M.; Kronlein, M.; Price, S.; Ahmad, F.; Gulari, E.; Tiedje, J. M.; Hashsham, S. A. Gene-Z: A Device for Point of Care Genetic Testing Using a Smartphone. *Lab Chip* **2012**. <https://doi.org/10.1039/c2lc21226a>.

- (26) Priye, A.; Bird, S. W.; Light, Y. K.; Ball, C. S.; Negrete, O. A.; Meagher, R. J. A Smartphone-Based Diagnostic Platform for Rapid Detection of Zika, Chikungunya, and Dengue Viruses. *Sci. Rep.* **2017**. <https://doi.org/10.1038/srep44778>.
- (27) Liao, S. C.; Peng, J.; Mauk, M. G.; Awasthi, S.; Song, J.; Friedman, H.; Bau, H. H.; Liu, C. Smart Cup: A Minimally-Instrumented, Smartphone-Based Point-of-Care Molecular Diagnostic Device. *Sensors Actuators, B Chem.* **2016**. <https://doi.org/10.1016/j.snb.2016.01.073>.
- (28) Ming, K.; Kim, J.; Biondi, M. J.; Syed, A.; Chen, K.; Lam, A.; Ostrowski, M.; Rebbapragada, A.; Feld, J. J.; Chan, W. C. W. Integrated Quantum Dot Barcode Smartphone Optical Device for Wireless Multiplexed Diagnosis of Infected Patients. *ACS Nano* **2015**, *9* (3), 3060–3074. <https://doi.org/10.1021/nn507279z>.
- (29) D'Ambrosio, M. V.; Bakalar, M.; Bennuru, S.; Reber, C.; Skandarajah, A.; Nilsson, L.; Switz, N.; Kamgno, J.; Pion, S.; Boussinesq, M.; et al. Point-of-Care Quantification of Blood-Borne Filarial Parasites with a Mobile Phone Microscope. *Sci. Transl. Med.* **2015**. <https://doi.org/10.1126/scitranslmed.aaa3480>.
- (30) Ephraim, R. K. D.; Cybulski, J. S.; Duah, E.; Prakash, M.; D'Ambrosio, M. V.; Fletcher, D. A.; Keiser, J.; Andrews, J. R.; Bogoch, I. I. Diagnosis of Schistosoma Haematobium Infection with a Mobile Phone-Mounted Foldscope and a Reversed-Lens CellScope in Ghana. *Am. J. Trop. Med. Hyg.* **2015**. <https://doi.org/10.4269/ajtmh.14-0741>.
- (31) Koydemir, H. C.; Gorocs, Z.; Tseng, D.; Cortazar, B.; Feng, S.; Chan, R. Y. L.; Burbano, J.; McLeod, E.; Ozcan, A. Rapid Imaging, Detection and Quantification of Giardia Lamblia Cysts Using Mobile-Phone Based Fluorescent Microscopy and Machine Learning. *Lab Chip* **2015**. <https://doi.org/10.1039/c4lc01358a>.
- (32) Shrivastava, S.; Lee, W. Il; Lee, N. E. Culture-Free, Highly Sensitive, Quantitative Detection of Bacteria from Minimally Processed Samples Using Fluorescence Imaging by Smartphone. *Biosens. Bioelectron.* **2018**. <https://doi.org/10.1016/j.bios.2018.03.006>.
- (33) Breslauer, D. N.; Maamari, R. N.; Switz, N. A.; Lam, W. A.; Fletcher, D. A. Mobile Phone Based Clinical Microscopy for Global Health Applications. *PLoS One* **2009**. <https://doi.org/10.1371/journal.pone.0006320>.