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"Development of Point-of-Care Assays for Disease Diagnostic and Treatment Monitoring for Resource-Constrained Settings"

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ABSTRACT OF DISSERTATION
Dissertation Title: Development of Point-of-Care Assays for Disease Diagnostic and Treatment Monitoring for Resource-Constrained Settings

Abstract.

Human Immunodeficiency Virus-1 (HIV-1) is one of the deadliest pathogens of present times. It still poses a significant threat to global health. As per the most recent available statistics, around 36.9 million people are living with HIV-1 in 2017. HIV-1 virus attacks the CD4+ T cells and can cause acquired immune deficiency syndrome (AIDS). Viral load monitoring and CD4+ T cell enumeration are the two most preferred methods to identify the onset of disease and the effectiveness of treatment respectively.

In this dissertation, we addressed the challenges of the development of cost-effective and rapid assays for the accurate counting of CD4+ T cells and quantification of HIV-1 viral load for resource-constrained settings. The lack of such assays has severely affected people living in disease prevalent areas. CD4+ T cells count information plays a vital role in the effective management of HIV-1 disease. A flow-free magnetic actuation platform was developed that uses antibody-coated magnetic beads to efficiently capture CD4+ T cells from a 30 µL drop of whole blood. On-chip cell lysate electrical impedance spectroscopy has been utilized to quantify the isolated CD4 cells. The developed assay has a limit of detection of 25 cells per µL and provides accurate CD4 counts in the range of 25–800 cells per µL. The whole immunoassay along with the enumeration process is very rapid and provides CD4 quantification results within 5 min time frame. The assay does not require off-chip sample preparation steps and minimizes human involvement to a greater extent. The developed impedance-based immunoassay has the potential to significantly improve the CD4 enumeration process especially for POC settings.

As there are currently no point-of-care (POC) disease diagnostic tests for HIV-1 viral load quantification A simple, portable, cost-effective, user-friendly, and field-deployable imaging platform for the rapid quantification of HIV-1 viral load for POC) settings is presented. The developed system combines microfluidics technology with a wide field of view lensless imaging modality. The detection of viruses and other nanoscale objects is a challenging task due to the weak scattering of light from these small entities. In this work, highly specific antibodies are functionalized to a glass slide inside a microchip to capture HIV-1 virions. These captured virions are tagged with antibody-conjugated microparticles which have a higher index of refraction than these virions. HIV-1 virions captured with these microparticles generate detectable diffraction patterns on a custom-built imaging setup. Computational analysis enables the rapid quantification of the isolated viruses with high accuracy.

There is a dire need to develop strategies to overcome the inherent shortcomings of currently existing microchip devices that often fail to detect virions at very low concentrations. Microfluidic devices can only hold a tiny amount of test samples. Hence, it is of utmost importance to pre-

concentrate HIV-1 virions from a complex sample matrix for further downstream processing. This pre-concentration process can significantly improve the detection limit of microfluidic devices and may play an essential role in the effective management of HIV-1 and other infectious diseases. Integrating pre-concentration of viral samples with microchip-based capture and subsequent lensless imaging can help in the development of highly sensitive assays. We have demonstrated a lab on a chip microdevice for the detection and quantification of HIV-1 viral load. The performance of this developed method was assessed and validated by comparing the results with the current gold standard method reverse transcriptase-polymerase chain reaction (RT-qPCR).This platform technology can reliably detect the presence of the HIV-1 viruses and thus can play a significant role in controlling the spread and management of this infectious disease.

BIOGRAPHICAL SKETCH
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Time in Preparation: 2017 - 2020

Qualifying Examination Passed: Fall 2016

Published Papers:

1) Mazhar Sher, R. Zhuang, U. Demirci, and W. Asghar, "Paper-based Analytical Devices for Clinical Diagnosis: Recent Advances in the Fabrication Techniques and Sensing Mechanisms," Expert Review of Molecular Diagnostics, vol. 17, pp. 351-366, 2017.

2) K. Rappa, J. Samargia, Mazhar Sher, J. S. Pino, H. F. Rodriguez, and W. Asghar, "Quantitative Analysis of Sperm Rheotaxis using a Microfluidic Device," Microfluidics and Nanofluidics, vol. 22, p. 100, 2018.

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8) Mazhar Sher, Benjamin Coleman, and W. Asghar, “ Development of a Point-of-Care Assay for the Rapid Quantification of HIV-1 Viral Load using Higher Refractive Index Antibody-Coated Microparticles”, In Preparation.

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