BioMEMS

Diagnosing drug-resistant TB at Point-of-Need

Problem Statement

Resistant strains of Mycobacterium Tuberculosis (TB) continue to flood regions of Africa, where more 2.5 million people were estimated to have been infected, accounting for more than a quarter of the cases worldwide. One of the leading causes of death in people with TB is co-infection with HIV+ and drug or multi-drug resistant (MDR-TB) strains. Anti-TB medications have been used for decades initially showing great effectiveness but, like many other antibacterial drugs, were administered inappropriately, were of poor quality and/or were not used by the patient as directed by a medical professional, leading to rampant drug resistance.

MDR-TB can be caused by the two most powerful, first-line anti-TB drugs, isoniazid and rifampicin, being rendered ineffective against disease progression. Most MDR-TB is treatable by using second-line drugs. However, those drugs require a lengthy treatment of up to 2 or more years.

Current TB Testing & Treatment

Invariably, this causes a need for patients testing positive for TB to value an accurate, timely, and low-cost testing option to not only identify a positive/negative result but also further identify possible resistance to both first-line and second-line treatments. The World Health Organization (WHO) devotes many resources to the detection and treatment of TB, leading to the development of various testing methodologies. The two most common tests are the skin antigen test and nucleic acid amplification tests (nAAT).

Although very accurate, the skin antigen test takes far too long to provide an opportunity for effective treatment, usually days, which has proven ineffective in most infected regions.

The nAAT, on the other hand, provides a faster, alternative solution that can be deployed in regions most affected by TB. Xpert, for example, is a commonly used nAAT that is administered by a health professional to diagnose TB and, if the result is positive, would indicate if the strain is resistant or not to rifampicin, the first-line defense treatment option.

Similarly, Truenat is another commonly used nAAT designed to be more easily deployed and implemented in areas lacking modern infrastructures such as reliable electricity and communication technologies.[1,2] One of the major disadvantages of nAAT, however, is the time it takes to retrieve a result – it can take more than an hour in many cases. This limits throughput, especially in large-scale public health screening. Additionally, these methodologies require trained professionals to gather the sample from patients, prepare the sample according to the testing protocol, and use the instrumentation to retrieve and interpret a result.

The nAAT tests are also susceptible to cross-contamination and unintended infection of the assisting professional. Both methodologies require potential exposure to biohazardous samples during collection, sample preparation and disposal.

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[1] https://tbfacts.org/truenat/

[2] K.S. Sahana, Anitha S Prabhu, Prakash RM Saldanha, Usage of Cartridge Based Nucleic Acid Amplification Test (CB-NAAT/GeneXpert) test as diagnostic modality for pediatric tuberculosis; case series from Mangalore, South India, Journal of Clinical Tuberculosis and Other Mycobacterial Diseases, Volume 11, 2018, Pages 7-9, ISSN 2405-5794,

BioMEMS

New & Novel Diagnostics Platform

Using the BioMEMS Diagnostics platform, a test panel can be developed within months to detect and quantify MDR-TB strain variants in saliva or sputum. The platform consists of a single-use disposable test cartridge, handheld analyzer and smart device app. The test cartridge is designed to hold up to 10 different biomarker assays and render results in less than 5 minutes. The cartridge can selectively capture and quantify TB cells from an unpurified, complex biofluid sample (i.e., saliva, sputum, etc.) at single-digit picomolar levels of specificity and sensitivity -- well beyond more traditional POC in-vitro diagnostic technologies. And unlike most Point of Care or Point of Need diagnostics, BioMEMS assays provide extraordinarily precise quantitation and metrics. In other words, not just Y/N or Low, Med, High.

The development of such a test panel can be completed and implemented on the BioMEMS Diagnostics platform within a year, and provide a more accurate, affordable and rapid solution than others available on the market today. The platform can be easily deployed in remote areas requiring no medical training whatsoever and no lab environment is necessary. The results are ported wirelessly from the handheld analyzer to any paired smart device. The test cartridges are designed to limit any possible exposure to biofluids and reagents, requiring no sample preparation. Each such sample gathered can be collected to conserve the sample for future testing if needed. All in under 5 minutes.

From an economic perspective, nAAT systems can be deployed for around $12 - $13 USD/test to meet the needs of highly infected regions that tend to have very low GDP. Typically, this is accomplished with a “buydown” by a foundation or NGO to offset the actual cost of the test, which may range up to $45 USD. This includes the cost of overhead and facilities, labor, reagents (e.g. test cartridges or chips) and instrumentation. Each nAAT instrument does require a significant upfront capital outlay estimated at $14,000 - $17,000 USD per instrument, with multiple instruments likely to be required for any mass screening event.[3,4]

These costs would be burdensome to many governments and would likely prompt them to engage non-profit organizations like PEPFAR, TB REACH (Stop TB), TB Care (USAID), World Bank, and others to help fund the deployment and resources necessary to screen populations. Again, this does not include trained lab personnel, a lab setting, however temporary, and lab supplies with attendant logistical issues.

By comparison, the BioMEMS platform solution can be developed and deployed for significantly less than the overall programmatic costs of current solutions and provide a more time-efficient and resource-effecient alternative to help address a world health crisis.

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[3] Lee DJ, Kumarasamy N, Resch SC, Sivaramakrishnan GN, Mayer KH, Tripathy S, Paltiel AD, Freedberg KA, Reddy KP. Rapid, point-of-care diagnosis of tuberculosis with novel Truenat assay: Cost-effectiveness analysis for India's public sector. PLoS One. 2019 Jul 2;14(7):e0218890. doi: 10.1371/journal.pone.0218890. PMID: 31265470; PMCID: PMC6605662.
[4] https://www.newtbdrugs.org/news/who-endorses-new-rapid-diagnostic-test-tb