Exploring the Impact of the Implementation of MALDI-TOF MS in a low-income setting at the MRC in The Gambia

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Background

- Rapid diagnosis of pathogens is important for initiating effective antibiotic administration and improving the outcomes of treatment and care.
- Amongst the many methods and technologies that have developed for rapid pathogen diagnosis, one of the most effective and efficient is Matrix-Assisted Laser Desorption/Ionization-Time Of Flight (MALDI-TOF) mass spectrometry.
- MALDI-TOF MS is used mainly in clinical microbiological labs in high-income countries like the U.S. On the contrary, low-income countries lack infrastructure and resources necessary to support similar technologies
- The purpose of this study is to work with the Medical Research Council (MRC) in Gambia to explore the impact of the introduction of a powerful diagnostic technology such as MALDI-TOF MS in a low-income environment.

About The MRC Gambia

- The MRC is one of two research units established in sub-Saharan Africa by the MRC in the UK through London School of Hygiene and Tropical Medicine (LSHTM).
- Large research portfolio. Spans from basic research to disease surveillance for public health purposes.
- Despite the resources and funding at The MRC, clinical microbiology remains challenging. The Gambia experiences many environmental challenges which complicate even conventional methods of pathogen identification. These challenges significantly impact clinical outcomes and quality of care in these regions.
- Given MALDI-TOF MS's significant impact within our labs at UCLA and within the field of clinical microbiology in general, we expect a similar or even greater impact can be observed in The Gambia through a collaborative effort with UCLA Health's Department of Pathology & Microbiology.
- Through the work at the MRC, we hope to explore the impact unprecedented regional uses for MALDI-TOF MS in the Gambia.

Fig 1: MRC facilities in The Gambia

Fig 2: MRC facilities in The Gambia

What is MALDI-TOF MS?

- MALDI-TOF MS is an extremely effective, robust, rapid and accurate microbial identification technique that uses a laser energy absorbing matrix to create ions from large molecules with minimal fragmentation [2,3].
- Positive specimens are collected and prepared for analysis by MALDI TOF-MS by mixing or coating with solution of an energy-absorbent, organic compound called matrix [2,3].
- Samples are then energized with a laser beam. Desorption and ionization with the laser beam generate singly protonated ions from analytes within the sample. Charged analytes are then detected and analyzed by the time of flight (TOF) mass analyzer [2,3].
- Analyzed particles are then characterized and organisms are identified by comparing their distinct 'analytic fingerprint' to those in a robust database [2,3].

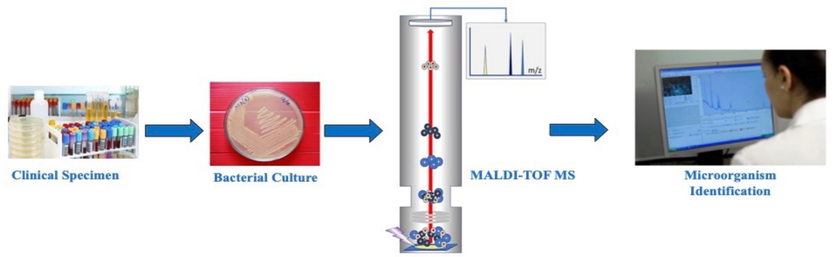

Fig 3: MALDI-TOF MS basic workflow [2]

MALDI-TOF MS at UCLA

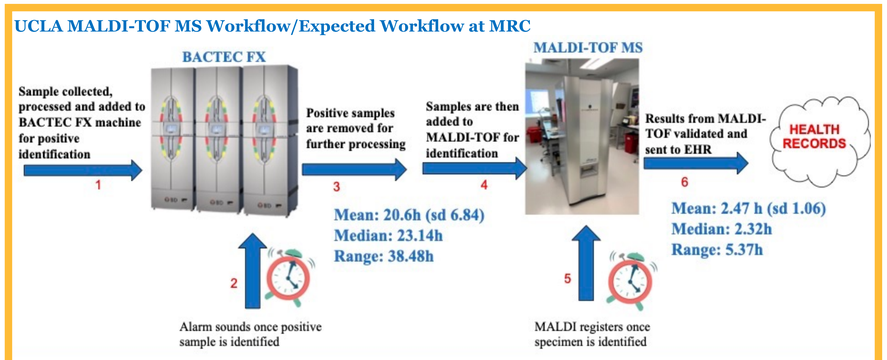

Fig 4: Overview of MALDI workflow at UCLA with values observed at UCLA for E.coli, S.aureus and K.pneumoniae combined (n=101)

- MALDI-TOF MS is one of the most robustly utilized forms of pathogen identification at UCLA. Currently, we run approximately 500 tests per day.
- In order to inform expectations on the impact of MALDI-TOF MS at The MRC, we assessed the impact of MALDI-TOF MS within our labs at UCLA.
- We primarily considered the time to identification (TTI) for 3 bacterial organisms, of similar profile to those found at The MRC. These were gram-negatives: *Escherichia coli; Klebsiella pneumoniae* and gram-positive *Staphylococcus aureus*.
- On average, preliminary results showed that gram-negative organisms, *E.coli* (33±8.6h) *and K.pneumoniae* (42.4±19.1h) were identified faster than gram-positive organisms like *S. aureus (45.1*±16.6h).
- Preliminary results for the 3 organisms combined showed a mean TTI of 40.5±15.9h. In contrast, conventional methods (without MALDI) can take up to 84±70.4h.

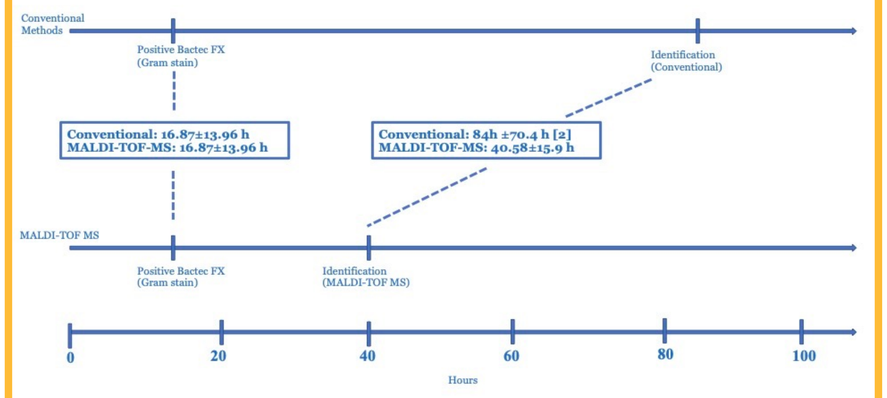

Fig 5: Differences between MALDI-TOF MS (at UCLA) and conventional methods for combined organisms.

State of MALDI

MALDI-TOF MS/Microbial Identification in High-Income Countries:

- Like at UCLA, across The US, and in many other high-income countries MALDI-TOF MS has become one of the most important methods for rapid microbial identification. Additionally, although high in initial cost, MALDI-TOF MS saves costs longitudinally with significant savings (up to 56% [3]) seen as soon as 1-year following implementation [2].
- In high-income countries, the penetrance of MALDI-TOF MS is 30%, highlighting the existing inequity of resources even in these regions.
- Research efforts are currently underway, exploring ways to improve specimen processing and harness MALDI-TOF MS technology to analyze patient specimens directly, eliminating the need for culturing. Additionally, as spectral databases and analysis software continue to improve, the use of MALDI-TOF methods will continue to optimize [2].
- This overall streamlining of diagnostic analysis, coupled with increased accessibility of this technology could result in more rapid organism identification, shorter hospital stays, improved prognoses, more appropriate care and decreased financial burden to both the hospital and patient [2].

MALDI TOF MS/Microbial identification in Africa:

- Low-income countries are still mostly reliant on microbial identification through conventional methods, if at all. Clinical microbiology continues to be an underdeveloped field in these regions. There is very little penetrance of MALDI-TOF MS and technologies alike in these regions (Senegal; Mali; South Africa) [1].
- Conventional methods are long, arduous, costly and especially complicated in low-income settings [1].
- There are also additional challenges to consider when working in lower income countries. The crippling levels of inequity, environmental challenges, general lack of resources and infrastructure affects the functionality of any existing lab in this region [1].
- The clinical impact of failure to promptly identify pathogens can be devastating. It can result in prolonged hospital stays, increased mortality, increased microbial resistance, ineffective/inappropriate treatment and increased costs.

Future work in MRC:

- Moving forward, we will use our results found at UCLA to provide a scope of what to expect at MRC when MALDI-TOF MS is implemented. Additionally, using UCLA expertise and data to develop the necessary SOP's, and enable smooth implementation of MALDI-TOF MS in September.
- In order to realize full clinical impact of MALDI TOF MS, additional support in the form of a stewardship team is strongly encouraged [3].
- Considering all that we know about MALDI-TOF MS from literature and UCLA, we hope that we can successfully assist in its implementation beginning in September 2021; setting a precedent not only for how MALDI-TOF MS should be implemented in The Gambia, but in Africa as a whole.

References

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MRC Unit The Gambia

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