Diagnosis of Respiratory Infections through Human Breath

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WARWICK
INTEGRATE
ANTIMICROBIAL RESISTANCE

1 INTRODUCTION

Antimicrobial resistance and the implications on effective treatment of a wide variety of bacterial infections:

- Overuse of antibiotics in healthcare has contributed to the development of strains of bacterial which are now resistant to a majority of antibiotics.
- This has resulted in untreatable infections or increased mortality in some patients.
- Various studies have demonstrated that VOCs (Volatile Organic Compounds) from breath can be used to identify the presence of bacterial or viral infections.
- **Our concept is to protect remaining antimicrobials via breath based diagnostics – to give confidence to clinicians NOT to prescribe.**

2 DISEASE

- In 2015, there were approximately 251 million cases of lower RTI in the world, leading to 2.74 million deaths, with the two most common types being bronchitis and pneumonia.
- Currently, there is no point of care diagnostic for RTI leading to over prescription of antibiotics.
- For TB, in 2014 there were approximately 480,000[1] cases of multidrug resistant tuberculosis (MDR-TB) worldwide.
- Patients diagnosed with MDR-TB require a different treatment path to those with non multidrug resistant strains of TB. Figure 1 refers to a patient with drug resistant TB.

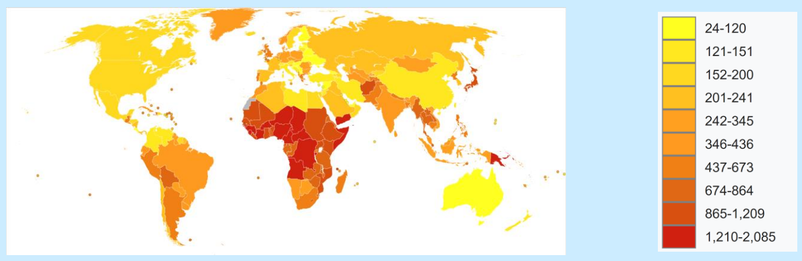
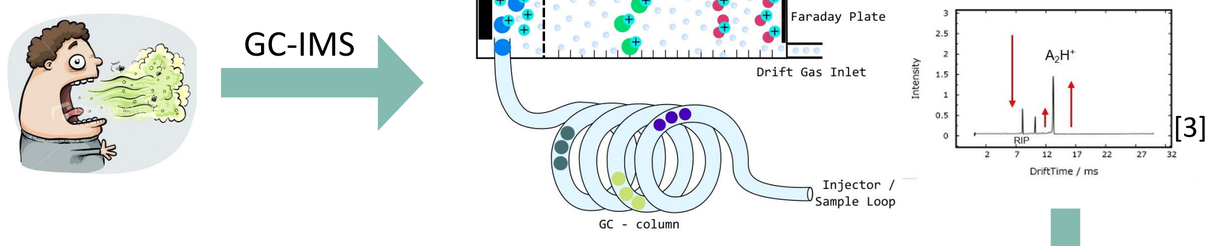


Figure 1: World RTI infection rates per million

3 SOLUTION

The development of a high throughput, non invasive breath test that can determine whether a patient has a bacterial or viral infection would allow patients to be treated in the appropriate care path quickly whilst reducing use of antibiotics in a clinical setting. The work in the Biological Sensors Lab in conjunction with collaborators have focused on answering this questions, with particular focus on tuberculosis, in a clinical setting.



[3]

In the Biological Sensors Laboratory we use equipment to detect and test VOCs present in biological samples. Here, an IMSPEX BreathSpec machine was used. The BreathSpec is a GC-IMS (Gas Chromatography – Ion Mobility Spectrometer) specially adapted to analyse breath samples and can detect compounds at low ppb (parts per billion) to ppt (parts per trillion) range.

Patient Diagnosis

4 CAPABILITY

- The patient simply exhales for 4-6 seconds to give their sample, with results being shown after a few minutes. Figure 2 demonstrates a patient using the BreathSpec.
- This provides a high throughput method, with little inconvenience to the patient and also medical practitioners operating the BreathSpec.
- Due to the low volume of sample needed, even patients with respiratory issues, which can often be the case in patients with suspected RTI and TB, can easily use the BreathSpec. Figure 3 gives an example output. This shows the background signal (straight line) and then individual chemical components

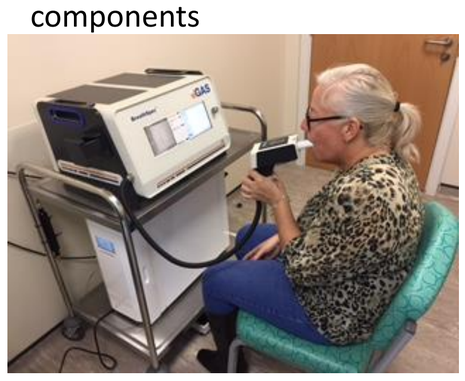


Figure 2: Patient using the BreathSpec

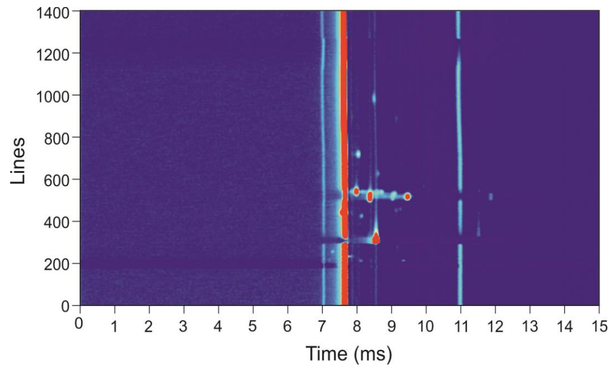
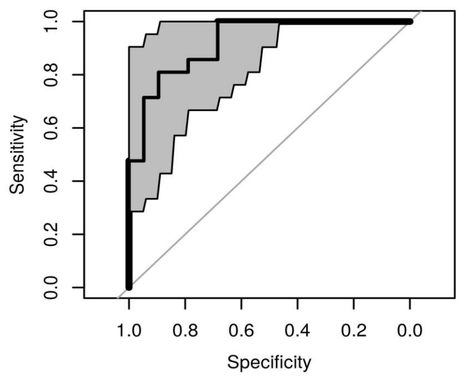
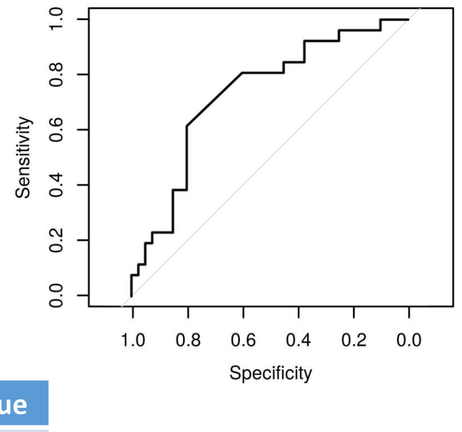


Figure 3: Example of GC-IMS data

- For RTI, 71 patients were recruited from the Royal Liverpool hospital. 28 with confirmed/probably bacterial and 41 confirmed bacterial infection (clinical confirmation). Data was processed using our existing pipeline to calculate sensitivity/specificity, ROC etc.
- For TB, 21 confirmed TB patients were recruited and 19 healthy controls. Samples were collected from the University Hospital Coventry and Warwickshire and Glenfield Hospital Leicester. ROC results given below.





Parameter	TB Value	RTI Value
AUCROC	0.92	0.73
Sensitivity	0.81	0.62
Specificity	0.79	0.8

5 PROJECT OUTPUTS

- TB diagnosis in breath in still on-going – now focussed on monitoring disease progression/remission. We are now attempting to link breath volatiles to TB growth.
- Pilot studies on RTI is completed and has been presented at ECCMID 2017 (infectious disease conference) and the work has been submitted to PlosONE.
- Based on this work, a £3M grant has been awarded by the EU for further developing a breath test bafor TRI based on the IMPSEX platform (with Warwick University as partners).

The *Future?*

References
[1] World Health Organisation http://www.who.int/mediacentre/factsheets/fs194/en/
[2] Cha J, Lee HY, Lee KS, et al. Radiological Findings of Extensively Drug-Resistant Pulmonary Tuberculosis in Non-AIDS Adults: Comparisons with Findings of Multidrug-Resistant and Drug-Sensitive Tuberculosis. *Korean Journal of Radiology*. 2009;10(3):207-216. doi:10.3348/kjr.2009.10.3.207
[3] GAS http://www.gas-dortmund.de/index-gas.php?lan=1&spath=388