Rationale

- Treatment and prevention of further spread of Tuberculosis (TB) in low-income countries is still problematic
- An accurate, cheap and simple to use diagnostic test is lacking
- Especially those patients suspected of TB in whom sputum ZN-smear is negative pose a diagnostic problem
- Exhaled breath analysis showed promising results for diagnosis of active TB (Phillips, Tuberculosis 2012)

Hypothesis

- To investigate whether the breath-print of patients with smear-positive TB and healthy controls, and between smear-negative patients with and without TB could be discriminated by an integrated electronic nose platform and GC-MS.

Aim

- The aim of this study was to investigate whether the breath-print of patients with suspected TB (positive clinical score and/or chest X-ray abnormalities or/and at least 3 of the 5 major criteria listed below) and healthy controls could be discriminated from non-TB patients using an integrated electronic nose platform or GC/MS. Different exhaled biomarkers were measured and analyzed using principal component (PC) analysis followed by linear discriminant analysis providing a cross-validated bootstrap-based ROC curve.
- Diagnosis of TB by eNose and GC-MS could also be established in an intention-to-diagnose population of smear-positive and smear-negative (positive PCR) from non-TB (negative PCR and healthy controls) using a cross validated accuracy of 81%.
- The results of GC-MS analysis could discriminate patients with TB, smear positive and smear negative (positive PCR) from non-TB (negative PCR and healthy controls) with a cross validated accuracy of 81%.

Methods

Design: cross-sectional case-control study, Chittagong Bangladesh

Inclusion criteria:
- Patients with suspected TB: chest X-ray abnormalities and/or positive clinical score (Bangladesh National Guidelines TB, 4th ed.)
- Healthy controls: no suggestive symptoms, negative TB history

Suspected TB:
- Positive sputum smear: TB confirmed (case)
- Negative staining:
  - TB confirmed by positive Xpert PCR on sputum or BAL fluid (case)
  - TB excluded by negative Xpert PCR on sputum or BAL fluid (control)

Breath analysis:
- Exhaled breath was collected by inhalation of VOC filtered air and exhalation of a vital capacity volume into a Nalophan bag
- Breath volatile organic compounds (VOCs) were stored on tenax sorbent tubes and sent for transportation
- Exhaled breath was analyzed by:
  - A platform of electronic noses, with a total of 190 sensors (Brinkman et al. ERS 2012)
  - Gas Chromatography Mass Spectrometry (GC-MS)

Results

- GC-MS analysis could discriminate patients with TB, smear positive and smear negative (positive PCR) from non-TB (negative PCR and healthy controls) with a cross validated accuracy of 81%
- Diagnosis of TB by eNose and GC-MS might be derived from different VOCs

Conclusions

- TB can be accurately diagnosed by exhaled breath measurements using an integrated electronic nose platform or GC-MS
- Diagnosis of TB could also be established in an intention-to-diagnose population of smear-negative patients
- Diagnosis of TB by eNose and GC-MS might be derived from different exhaled biomarkers

Implications

- Exhaled breath analysis is sensitive and specific for smear positive and smear negative TB, confirmed by Xpert PCR
- Exhaled breath analysis is cheap, easy to perform, non invasive and on site available, which makes it a promising solution for the diagnostic difficulties in patients suffering from TB in low income countries
- The results of GC-MS analysis can be used to develop a tailor-made eNose with sensors specific for differentiating VOCs