Background

Active pulmonary tuberculosis (TB) is a leading cause of death from infectious disease throughout the world. Two billion people – one third of the world’s population – are infected with Mycobacterium tuberculosis, and 1.6 million died from the disease in 2005[1]. There has been little progress in detection of TB in recent decades: microscopy and culture remain the mainstay of laboratory diagnosis and there is an urgent need for new diagnostic tools, especially in high-burden countries. An ideal diagnostic test would be sensitive and specific for active pulmonary TB, as well as rapid, cost-effective, non-invasive, and suitable for use in developing countries.

A breath test could potentially detect persons with active pulmonary TB because M. tuberculosis manufactures volatile metabolites in vitro, and a number of these volatile organic compounds (VOCs) can be detected in the breath as apparent biomarkers of infection[2]. In a multicenter international study, breath VOCs identified patients with active pulmonary tuberculosis (TB) with 85% accuracy[3]. Laboratory-based GC/MS has established proof of principle of a breath tests for active pulmonary TB, but this technology is limited by high costs and slow turnaround time. A new point-of-care desktop breath testing system, BreathLink™, has dramatically reduced both the cost and the turnaround time of a breath test. We report here the preliminary findings from a multicenter international study employing BreathLink™ at sites in India, UK, and the Philippines.

The BreathLink™ system

The Breathscanner 3.2 collects and concentrates the VOCs in a sample of alveolar breath, separates them by gas chromatography (GC), and detects them with a surface acoustic wave detector (SAW). A sample of room air VOCs are analyzed in the same way, and the chromatograms are segmented into a series of time slices. A new non-random times slices identified with multiple Monte Carlo simulations. Chromatograms segmented into a series of time slices. Time slices compared in disease group and control group. Significant non-random times slices identified with multiple Monte Carlo simulations. Non-random times slices combined into a predictive algorithm with weighted digital analysis (WDA). Outcome of predictive algorithm displayed in receiver operating characteristic (ROC) curve identified by Monte Carlo analysis.

Results

Human subjects

191 subjects were included in the analysis (TB/controls): Mumbai 39/16, Manila 51/38, Cavite 1/34, London 2/10, Total: 93/98.

Analysis of data

Multiple Monte Carlo simulations identified 10 significant non-random times slices that distinguished TB patients from controls. The accumulated area under curve (AUC) of the ROC curve was 0.80.

Conclusions

The BreathLink™ point-of-care breath test identified pulmonary TB with 80% accuracy. This was a preliminary analysis of data from an ongoing study, and results may improve as more subjects are entered into the analysis of data, and the subset with a positive sputum culture is analyzed separately.

References