Breath-based non-invasive diagnosis of Alzheimer's disease: A pilot study

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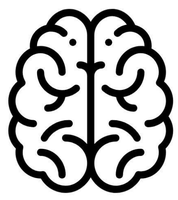
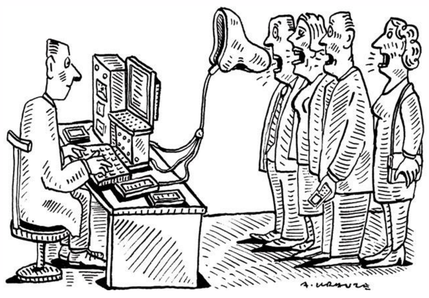
1 INTRODUCTION



- In the UK, there are currently about 860,000 dementia cases [1] costing £26.3 billion annually. Dementia is a progressive neurological disease which affects multiple brain functions, including memory.
- 60-80% of dementia cases are Alzheimer's disease (AD). Early diagnosis is key to disease management of dementia and AD.
- These conditions are progressive, meaning that symptoms develop gradually and become more severe over several years. Existing diagnostic tools are either invasive and painful or expensive and not widely available (e.g. MRI, PET).



Recent studies have shown that exhaled volatile organic compounds (VOCs) can be used to diagnose a range of conditions, including colorectal cancer [2], COPD [3] and many more. In some cases, specific biomarkers are associated with these diseases. Breath testing has the potential to offer new opportunities for the non-invasive diagnosis of AD.

2 AIMS & RECRUIMTNET

- The aim of this study was to investigate the use of breath to diagnose AD. Specifically, whether exhaled breath can be used to distinguish between AC, mild-cognitive impairment (MCI) and controls.
- In total, 100 subjects were recruited. Of these, 25 were classified as AD suffers, 25 with MCI and 50 healthy controls.
- The control group was formed from spouses and partners as an age, gender and diet matched control group.

3 CAPABILITIES

This study utilised the GAS BreathSpec, which is a CE-marked instrument consisting of a gas chromatograph (GC) and ion mobility spectrometer (IMS), known collectively as GC-IMS (Figure. 1). This instrument has been optimised for the sensitive detection of VOCs in human breath with capabilities to measure low ppb substances.

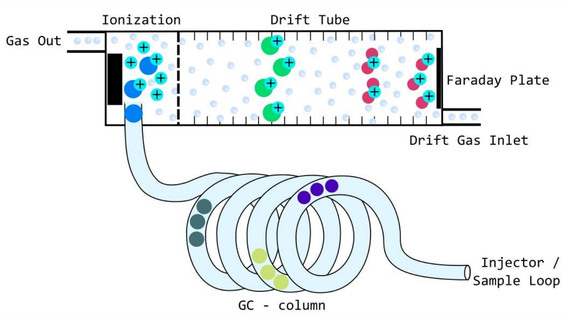


Figure 1: GC-IMS Working Principle

Figure 2: BreathSpec GC-IMS Instrument

The sampling procedure is fast, easy, and suitable for vulnerable subjects, including the elderly. Only 4 seconds of exhaled breath are required and there is no need for samples to be stored or transported. Measurement results are available in less than 10 minutes. The instrument is shown in Figure 2.

4 ANALYSIS & RESULTS

A typical output plot from the BreathSpec GC-IMS instrument is shown in Figure 3. This breath sample is from a confirmed AD patient.

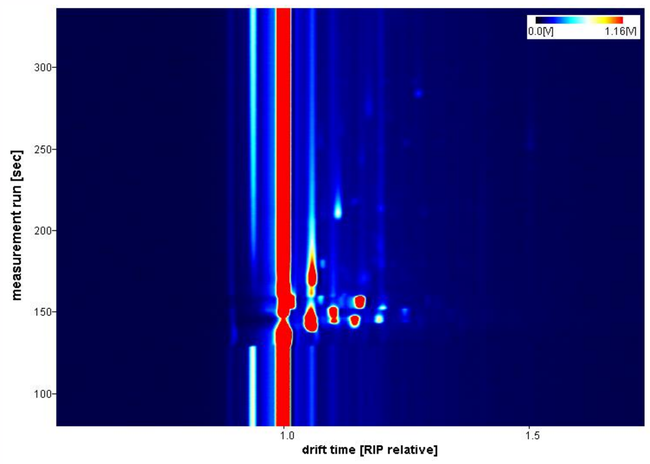


Figure 3: Typical BreathSpec GC-IMS Output

Data analysis was conducted using 5 classification algorithms. The best results were achieved using Random Forest. Statistical analysis of the results for AD vs controls showed an AUC/sensitivity/specificity of 0.82/0.74/0.9 (p-value 0.0003) and AD vs MCI of 0.68/0.84/0.67 (p-value 0.027), shown in Figures 4 and 5, respectively.

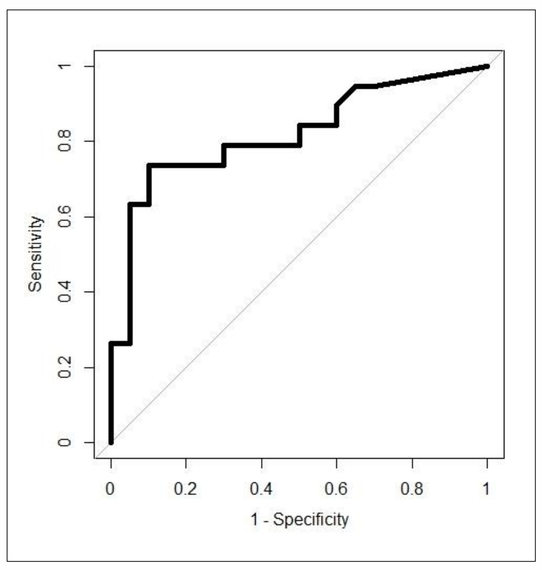


Figure 4: AD vs Controls

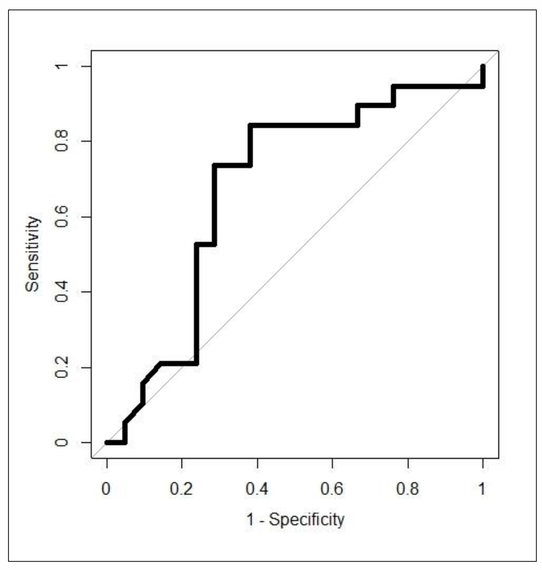


Figure 5: AD vs MCI

The results indicate that there is a significant difference between the breath of AD sufferers versus healthy controls. However, the difference between MCI and AD is smaller.

5 CONCLUSION

Results from this pilot study confirm the utility of breath VOC analysis to distinguish AD from healthy controls, and MCI. In the future, we hope to undertake a larger trial to both identify the key chemical biomarkers and to understand if this approach can be used to monitor disease progression.

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