Breath analysis by ion mobility spectrometry allows to discriminate COPD from lung cancer patients

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BACKGROUND

COPD and lung cancer (LC) are major health concerns caused by **tobacco** smoking. Both diseases are characterized by inflammatory reactions that trigger oxidative stress, liberating **volatile organic compounds** (VOCs) in breath. Hence, breath analysis could hold promise for the diagnosis of LC in at risk COPD patients, since many of the symptoms are non-specific and overlapping.[1]

AIM

We investigated the use of breath analysis to discriminate between healthy smokers, and patients with either COPD, lung cancer or asthma. The goal is to develop a non-invasive screening test for lung cancer.

METHODS

Breath (alveolar air) and background samples were taken from 28 COPD patients, 56 lung cancer (LC) patients, 6 asthma patients and 17 healthy smokers (HS). Samples were analysed by a **Multicapillary Column/Ion Mobility Spectrometer** (MCC/IMS).[2]

After background correction, a lasso regression was performed to select the most important VOCs, followed by receiver operating characteristic (ROC) analysis and estimation of the model characteristics.[2]

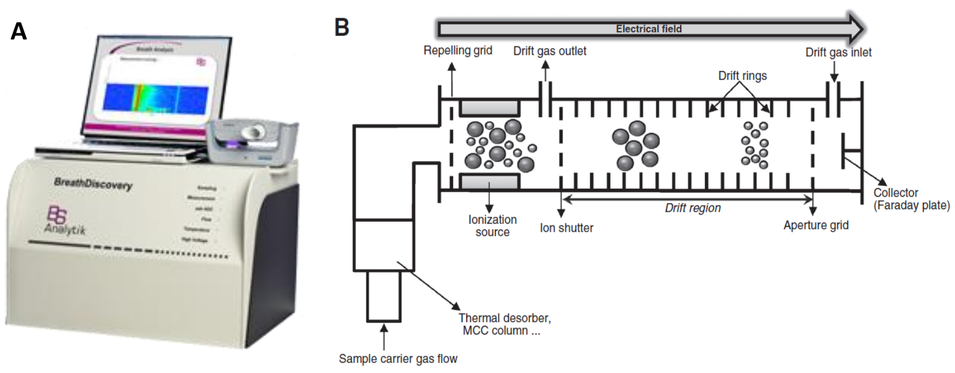

Figure 1: A) Image of the BreathDiscovery (MCC/IMS device). B) Scheme of an MCC/IMS.

RESULTS

A. Patient characteristics

	COPD	HS	LC	Asthma	p-value
N	28	17	56	6	
Gender (M/F)	20/8	14/3	37/19	4/2	0.647[a]
Age (years)*	64.8 (61.7-75.3)	57.2 (53.7-62.1)	69.9 (64.3-72.7)	51.3 (44.6-72.1)	0.001[b]
Smokestatus (never/current/ex)	1/8/19	0/1/16	6/25/25	1/2/3	0.008[a]
Packyears*	36.0 (21.4-60.0)	8.4 (1.6-16.2)	30.0 (14.0-45.0)	8.1 (3.8-33.0)	<0.001[b]

B. Model characteristics

	COPD vs HS	COPD vs LC	COPD vs asthma
Sensitivity	0.821 (0.648-0.931)	0.768 (0.645-0.864)	1.000 (0.607-1.000)
Specificity	0.882 (0.663-0.980)	0.857 (0.691-0.953)	0.429 (0.257-0.614)
PPV	0.920 (0.760-0.986)	0.915 (0.808-0.972)	0.273 (0.119-0.483)
NPV	0.750 (0.530-0.902)	0.649 (0.487-0.789)	1.000 (0.779-1.000)
Accuracy	0.844 (0.717-0.929)	0.798 (0.702-0.873)	0.521 (0.363-0.691)
AUC_{ROC}	0.889 (0.777-0.975)[#]	0.853 (0.753-0.935)[#]	0.429 (0.393-0.750)

C. ROC curves

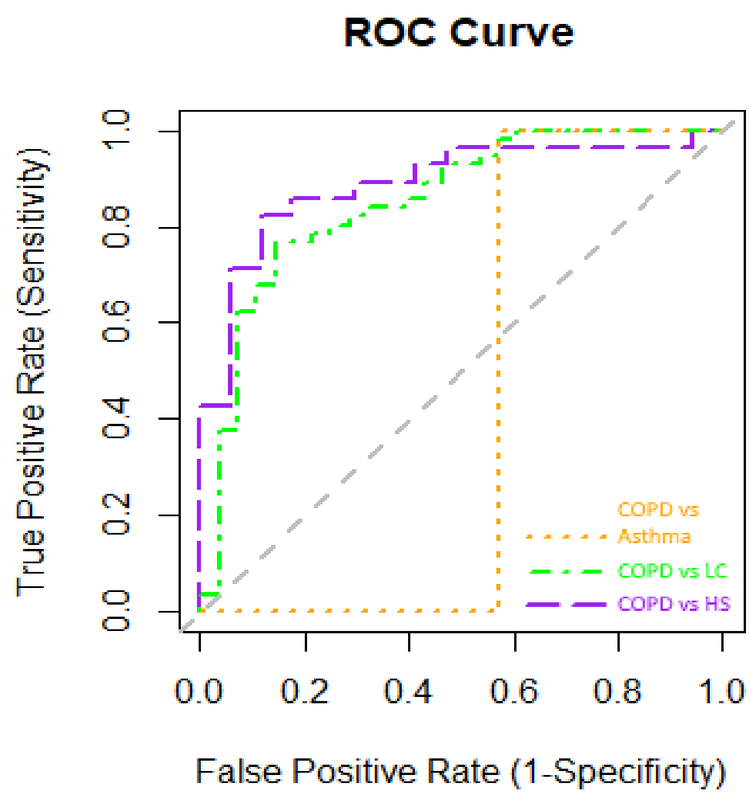

Figure 2: A) Patient characteristics from the different groups. *Median (Q1-Q3); [a]Fisher's Exact test; [b]Kruskal-Wallis test. B) Model characteristics for COPD vs HS, COPD vs LC and COPD vs asthma. [#]AUC_{ROC} significanty different from 0.5. C) ROC curve comparing COPD vs HS (purple, dashed), COPD vs LC (green, dotdash) and COPD vs asthma (orange, dotted). AUC, area under the curve; COPD, Chronic Obstructive Pulmonary Disease; HS, healthy smokers; LC, lung cancer; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic; VOCs, volatile organic compounds.

Using MCC/IMS, each VOC is characterized by a retention time and an ion mobility value, giving them an unique character. Good discrimination was achieved using MCC/IMS between **COPD patients and HS** with 0.844 accuracy, 0.821 sensitivity, 0.882 specificity, 0.920 PPV and 0.750 NPV. The AUC_{ROC} was 0.889. Discrimination between **COPD and LC patients** was also clear, showing 0.798 accuracy, 0.768 sensitivity, 0.857 specificity, 0.915 PPV and 0.649 NPV. The AUC_{ROC} was 0.853. With an AUC_{ROC} of 0.429 and accuracy of 0.521, discrimination of **COPD from asthma patients** was not possible.

These results are in line with Dragonieri *et al.*[3] and de Vries *et al.*[4] describing good discrimination of COPD patients from lung cancer patients and healthy controls using breath analysis. Fens *et al.*[5] and de Vries *et al.*[4] were able to discriminate between COPD and asthma patients with moderate to good accuracy using electronic nose (eNose).

CONCLUSION

The accuracy, sensitivity and NPV of the diagnostic model for COPD vs HS and LC confirms previous research and suggests the possibility to use **breath analysis by MCC/IMS** as a tool in order to **diagnose COPD in smokers and LC in COPD patients**. However, there is a low accuracy in discriminating COPD vs asthmatic patients. Further research should validate these findings and correlate breath VOCs with clinical parameters before being used as a screening test.

References

[1]Van de Kant *et al.*, Respir Res, 2012; [2]Lamote *et al.*, Eur Respir J, 2017; [3]Dragonieri *et al.*, Lung Cancer, 2009; [4]de Vries *et al.*, J Breath Res, 2015; [5]Fens *et al.*, Clin Exp Allergy, 2011

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