Exhaled breath analysis for identifying eosinophilic and neutrophilic inflammation in a mixed population of patients with asthma or COPD

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Rationale

- Asthma and COPD are prevalent and complex diseases including many phenotypes with differences in inflammatory profile and responses to treatment [Agusti ERJ 2016].
- Volatile organic compounds (VOCs) in exhaled air, as obtained by gas-chromatography and mass-spectrometry (GC-MS), are associated with inflammatory profiles in both asthma [Ibrahim Thorax 2011] and COPD [Fens ERJ 2011].

Hypothesis

Inflammatory profiles can be obtained from exhaled air in chronic airway diseases, regardless of the diagnosis of asthma or COPD, and this can be accomplished by an electronic nose (eNose).

Aim

To determine diagnostic accuracy of exhaled breath analysis by electronic nose for neutrophilic and/or eosinophilic inflammation in a mixed patient population.

Methods

Design: Cross-sectional case-control design using the diagnostic and monitoring visits of the day-to-day care in clinical practice.

Fig 1. SpiroNose measurement setup. (1) Bacteria filter, nose clamp and soft bite mouthpiece, (2) Spirometer, (3) SpiroNose.

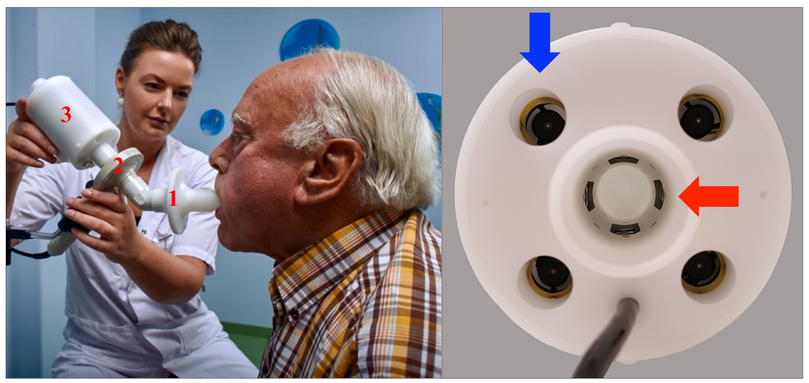


Fig 2. Frontview of the SpiroNose. (De Vries J. Breath Res. 2015)

4 identical sensor arrays monitoring exhaled breath.

4 reference sensor arrays monitoring ambient VOCs.

Subjects:

- Asthma (according GINA-criteria) and COPD (according GOLD-guidelines) patients with different inflammatory phenotypes in peripheral blood:
  1. Eosinophilic (**count>0.3x10^9/L**)
  2. Neutrophilic (**proportion>61%**)
  3. Mixed granulocytic
  4. Pauci-granulocytic

Data collection:

- During spirometry (expiratory vital capacity manoeuvre < 0.4 L/s), fingerprints from exhaled breath were collected in duplicate by the SpiroNose (Academic Medical Center, Amsterdam and Comon Invent BV, Delft) based on 4 identical and exchangeable metal oxide sensor arrays at the rear end of a pneumotachograph.

Data-analysis (Matlab2015) (De Vries J. Breath Res. 2015)

- Signal processing
- Environment correction based on alveolar gradients
- Sensor stability was verified using test gas (Lindegas) as quality control (QC) gas before every session.

Statistics (SPSS20)

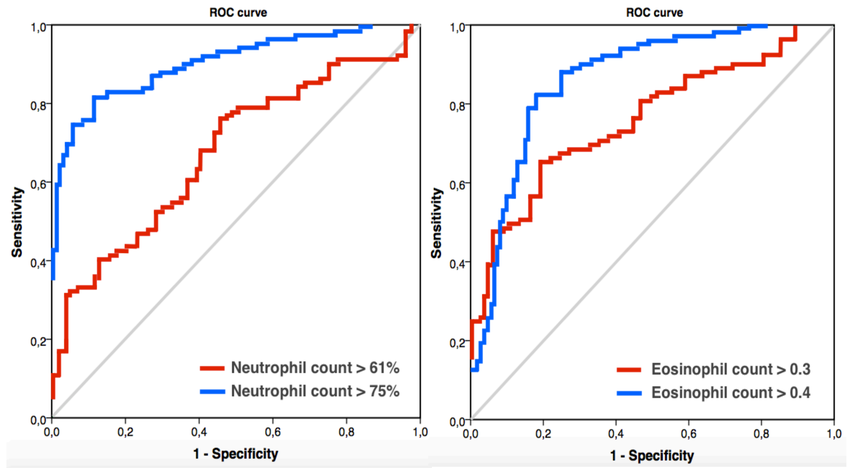
- Principal component analysis (PC 1-4), ANOVA, discriminant analysis and ROC analysis.

Results

Table 1. Patient characteristics

	Asthma	COPD
N	206	115
Age, years (SD)	54.3 (17.1)*	65.2 (13.4)*
Female, % (male, %)	59.6 (40.4)	52.3 (47.7)
FEV1, pb %pred (SD)	83.2 (17.6)*	65.9 (21.6)*
BMI (SD)	27.1 (5.2)	28.2 (6.3)
Smoking (never/ex/current)	124/60/22	1/97/17
Pack years (SD)	8.8 (8.2)*	28.4 (11.7)*
GOLD (II/III/IV)	NA	56/37/22
GINA (mild/moderate/severe)	63/108/35	NA
Eosinophil counts (SD)	0.39 (0.41)*	0.29 (0.28) *
Neutrophil counts (SD)	5.41 (2.98)*	7.15 (3.02)*
ICS-use, n (%)	175 (85)	81 (70)
OCS-use, n (%)	45 (22)	27 (23)

mean(standard deviation) NA: Not applicable *Significant difference (p<0.05)



Patients (n=321; 206 asthma/115 COPD) with different inflammatory phenotypes:

1. Neutrophilic (n=86)
2. Eosinophilic (n=93)
3. Mixed granulocytic (n=31)
4. Pauci-granulocytic (n=111)

- PC1 showed a significant difference (p=0.02) between eosinophilic and neutrophilic inflammation (CVV=80%).
- The ROC-AUC reached 0.67±0.11 for neutrophilia and 0.74±0.09 for eosinophilia.
- With increased cut-off values for neutrophilia (**proportion>75%**) and eosinophilia (**count>0.4x10^9/L**) ROC curves raised to 0.86±0.08 and 0.84±0.09 (blue line).

Conclusion

- Breath analysis by SpiroNose is able to identify neutrophilia and/or eosinophilia amongst patients with chronic airways disease.
- Higher cut-off values for inflammation increased diagnostic accuracy demonstrating a dose-effect relationship for the expired inflammatory signal.

Implication

These results show the value of eNose assessment for point-of-care inflammatory phenotyping of patients with asthma and/or COPD and may facilitate personalized treatment.

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