Using exhaled breath profiles in the discrimination between COPD, lung cancer and their co-morbidity

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Rationale

- Lung cancer is a frequent co-morbidity in COPD patients.
- Exhaled breath profiles by electronic nose (eNose) in the discrimination between COPD and lung cancer have shown definite overlap (Dragonieri Lung Canc. 2009).
- The integration of eNose technology with spirometry (SpiroNose) provides a fast method for exhaled breath analysis at the outpatient clinic.

Hypothesis

The SpiroNose is able to discriminate COPD from lung cancer patients and allocates COPD patients with co-morbid lung cancer in the overlap area.

Aim

To determine diagnostic accuracy of exhaled breath analysis by SpiroNose for COPD vs. lung cancer and to identify those patients who, based on exhaled breath profiles, are allocated in the overlap area between both diseases.

Methods

Subjects:
- COPD (n=55), according GOLD-guidelines
- Lung cancer (n=43), according TNM-staging

Design

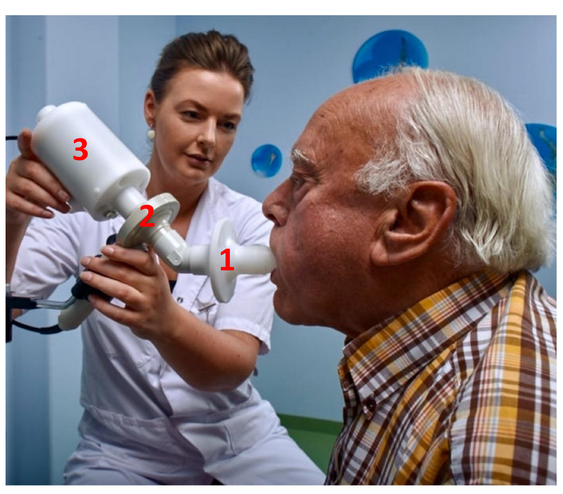
Multi-centre cross-sectional design using the diagnostic and monitoring visits of the day-to-day care in clinical practice.

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 (Matlab2014)
- Signal processing
- Environment correction based on alveolar gradients (De Vries J. Breath Res. 2015)
- 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.

Fig 1. SpiroNose measurement setup.
(1) Mouthpiece / nose clamp / bacteria filter
(2) Spirometer (3) SpiroNose.



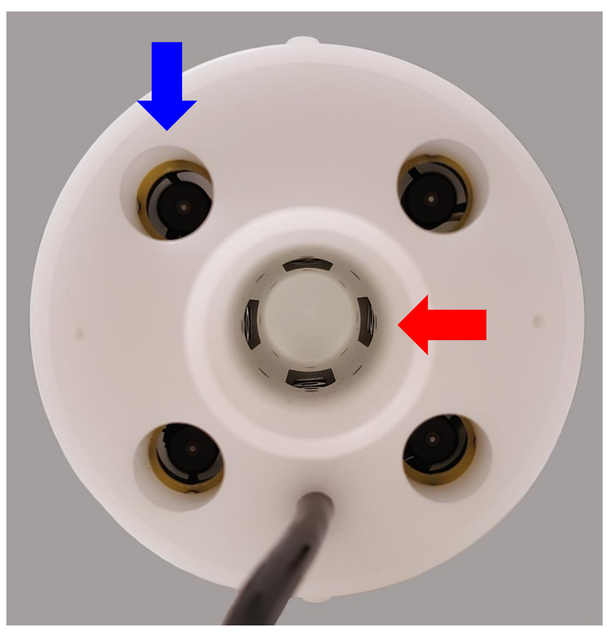


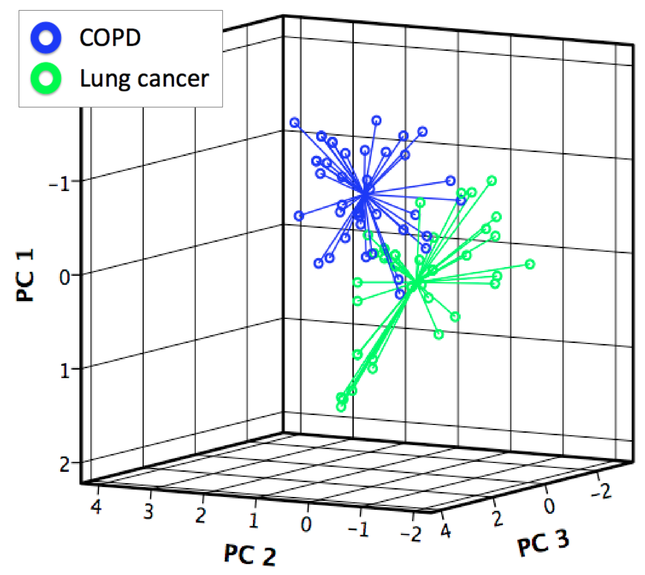
Fig 2. Frontview of the SpiroNose. (De Vries J. Breath Res. 2015)
4 identical sensor arrays monitoring exhaled breath.
4 reference sensor arrays monitoring ambient VOCs.

Results

Table 1. Patient characteristics

	COPD	Lung cancer
No	55	43
Age, years	63(8)	64(11)
FEV1 %pred	52(21)*	73(19)*
Pack years	34(13)*	29(15)*
GOLD (II/III/IV)	16/29/10	0/4/8
Lung cancer stage I/II/III/IV	NA	0/3/15/25
Lung cancer (SCLC/NSCLC)	NA	13/31
ICS-use	53*	14*

*Significant difference (p<0.05)

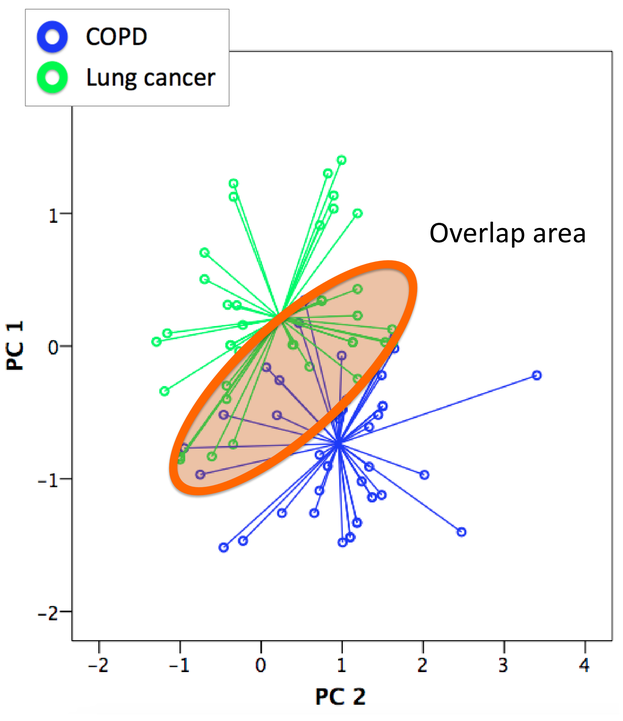


- Principal component 1 (p<0.01) and 2 (p=0.021) showed a significant difference between COPD and lung cancer patients with **a cross-validation value of 84%** and a **ROC-AUC of 0.89 ± 0.10**.
- Positive predictive value (PPV) = 94%
- Negative predictive value (NPV) = 81%

Table 2. Patients allocated in the overlap area

	COPD	Lung cancer
No. allocated in overlap area	10	13
Age, years	64(7)	65(8)
FEV1 %pred	50(8)*	59(19)*
Pack years	36(11)*	31(12)*
GOLD (II/III/IV)	2/4/4	0/3/7
Lung cancer stage I/II/III/IV	NA	0/0/2/11
Lung cancer (SCLC/NSCLC)	NA	1/12
ICS-use	10	10

*Significant difference (p<0.05)



Overlap area:
- 13 lung cancer patients were classified as COPD.
- Patient characteristics revealed that 10 of these 13 lung cancer patients (77%) were also diagnosed with co-morbid COPD.

Co-morbidity:
- 12 lung cancer patient with co-morbid COPD were included in this study.
- 10 of these 12 patients (83%) were correctly allocated in the overlap area.

The effect size obtained when discriminating the patient groups was 5.2 till 7.4-fold higher than the normal sensor variability, indicating a good signal-to-noise ratio.

Conclusion

Exhaled breath analysis by SpiroNose is able to discriminate between COPD and lung cancer patients. Patients with a double diagnosis are correctly allocated in the overlap area.

Implication

The overlap between COPD and lung cancer as obtained by eNose driven classification is real and mostly based on co-morbidity. This shows the value of eNose assessment in patients with COPD and/or lung cancer.

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