LEMP
Laboratory Experimental Medicine & Pediatrics
University of Antwerp

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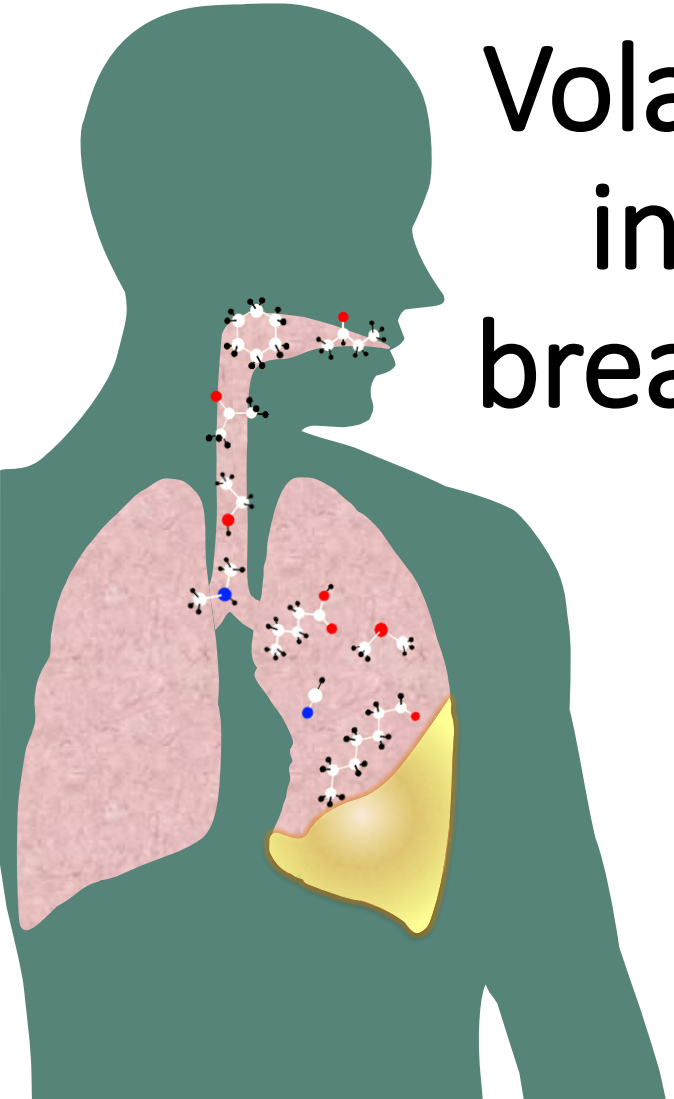

Volatile organic compounds in health and disease: a breathtaking breakthrough?

Kevin Lamote, PhD
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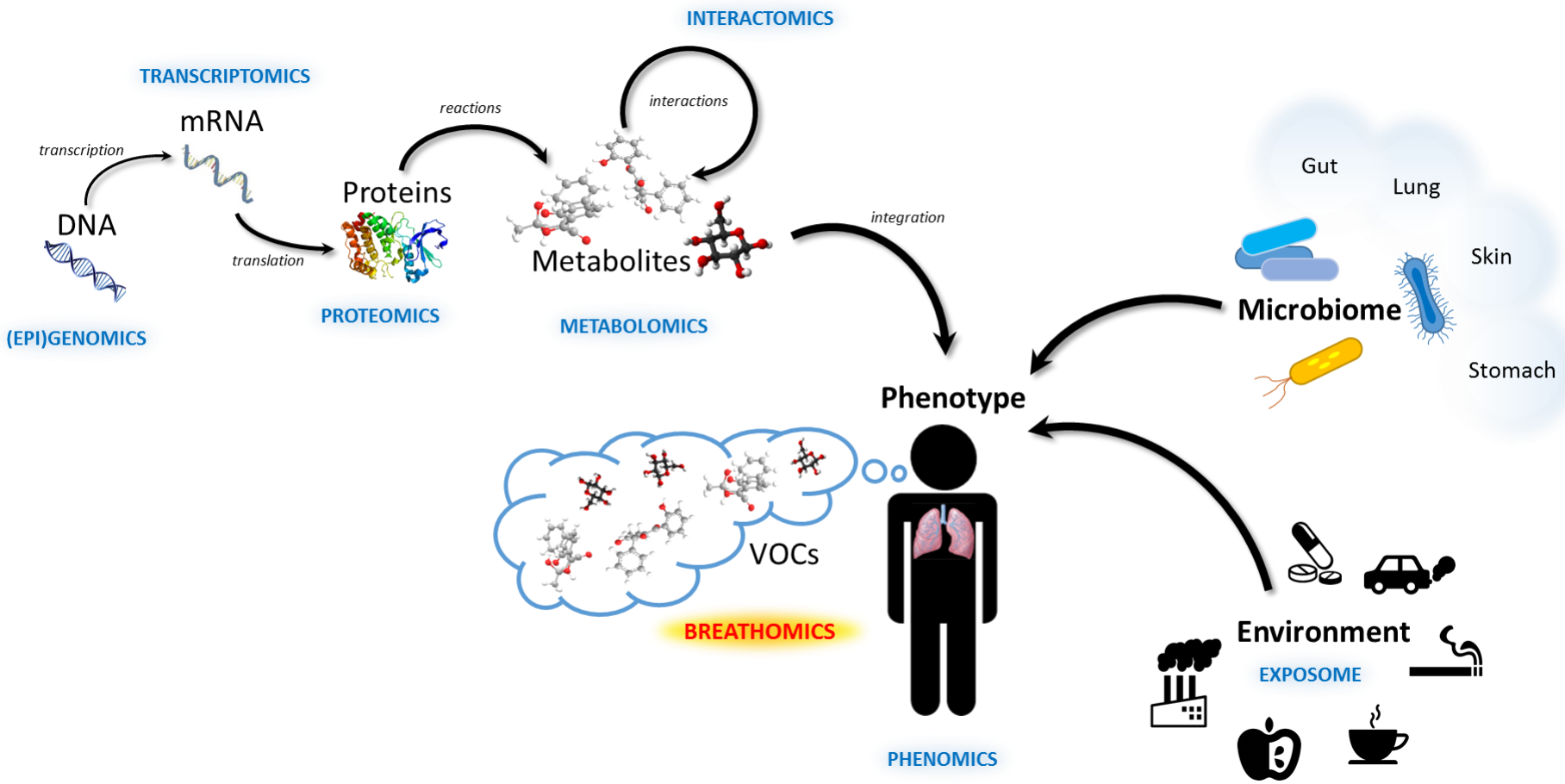
Research Club
October 4, 2017

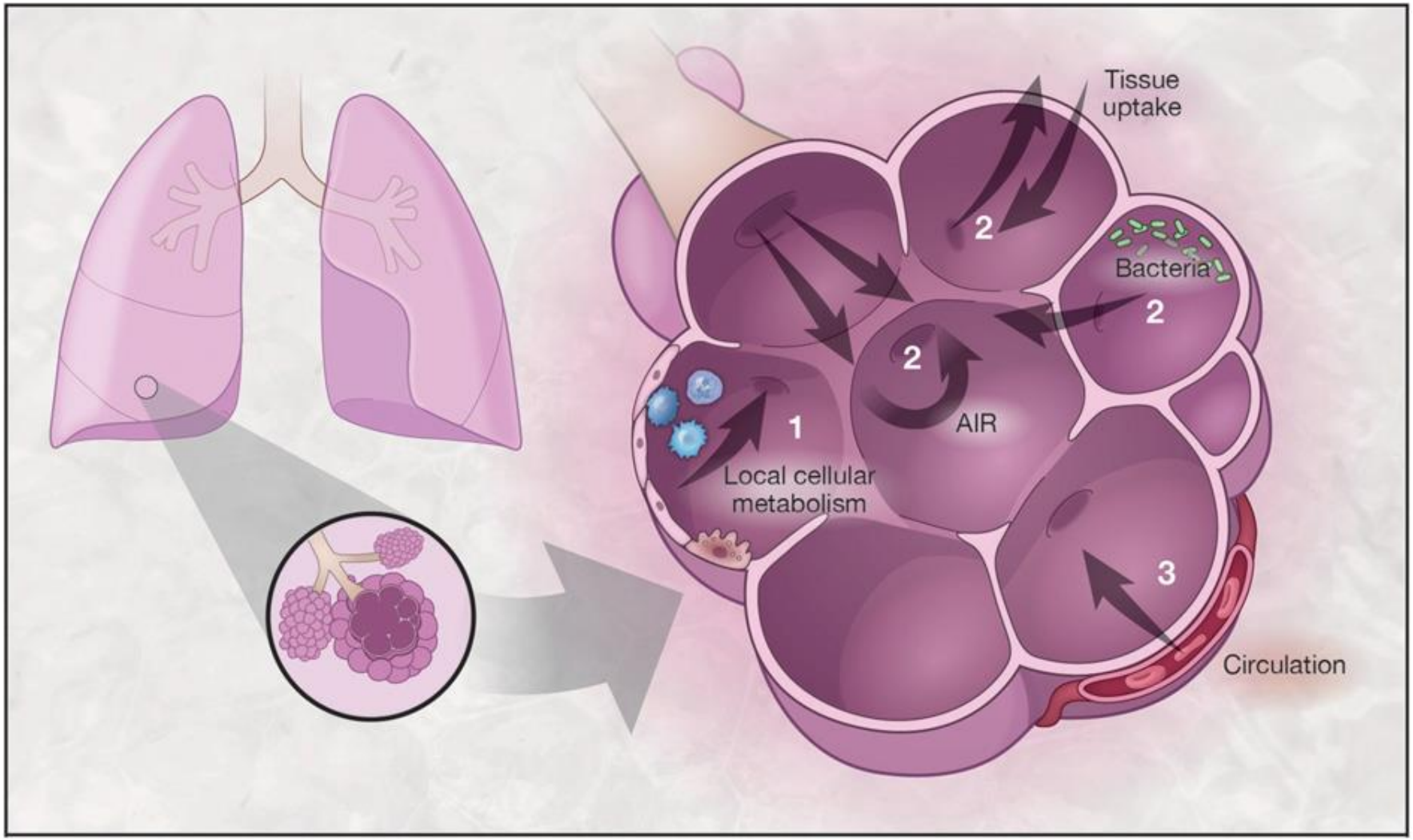
Overview

- The world of *"-omics"*
- Volatile Organic Compounds (VOCs)
  - Origin
  - Breath biopsy
  - Stool, blood, tissue
- Technology
- Applications
  - Biomarker
  - Precision medicine
  - Patient selection
  - Monitoring
  - Early detection/screening
- Future perspectives

The world of *"–omics"*

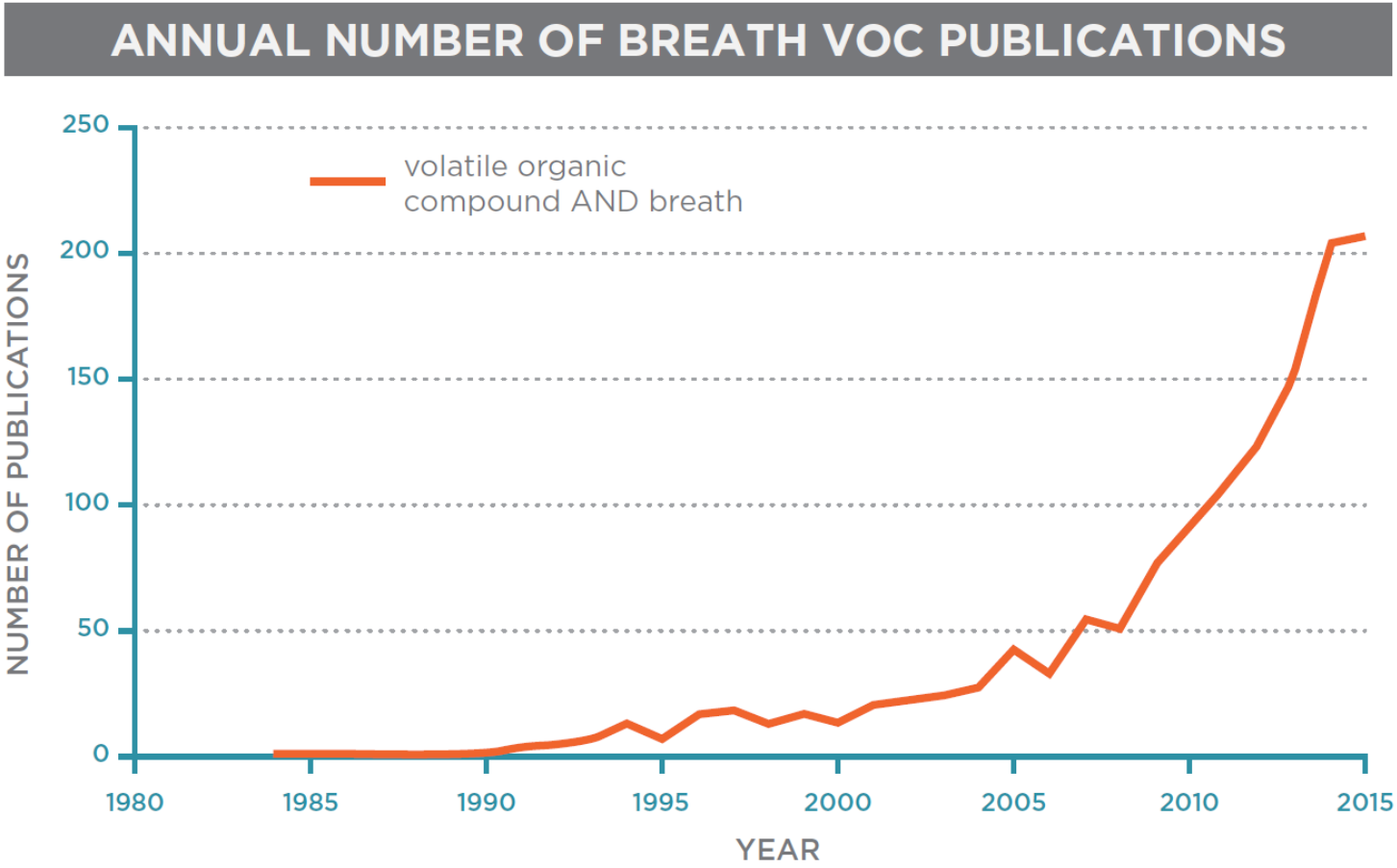


Breath analysis
Volatile Organic Compounds (VOCs)



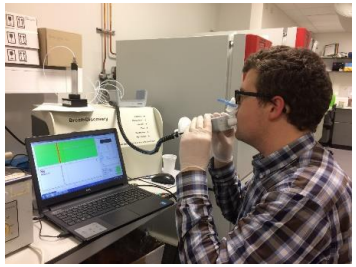
Van der Schee *et al.* Chest. 2015

Historical breath analysis

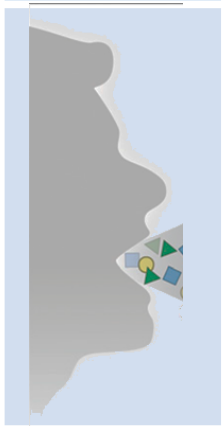
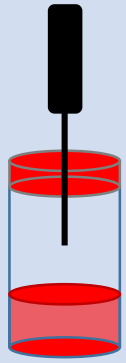
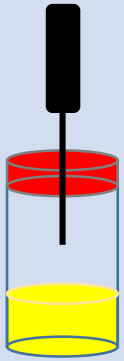
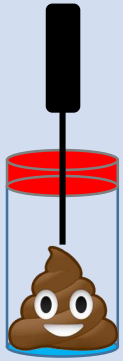
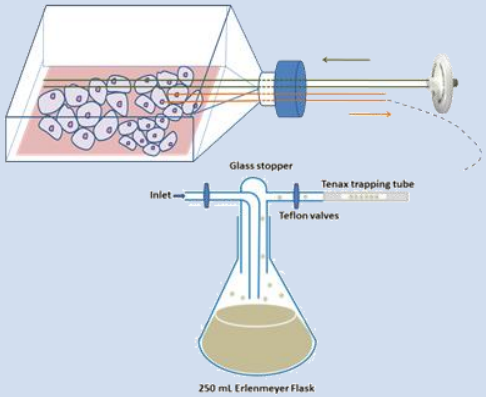


VOC analysis

Key factors – What to consider

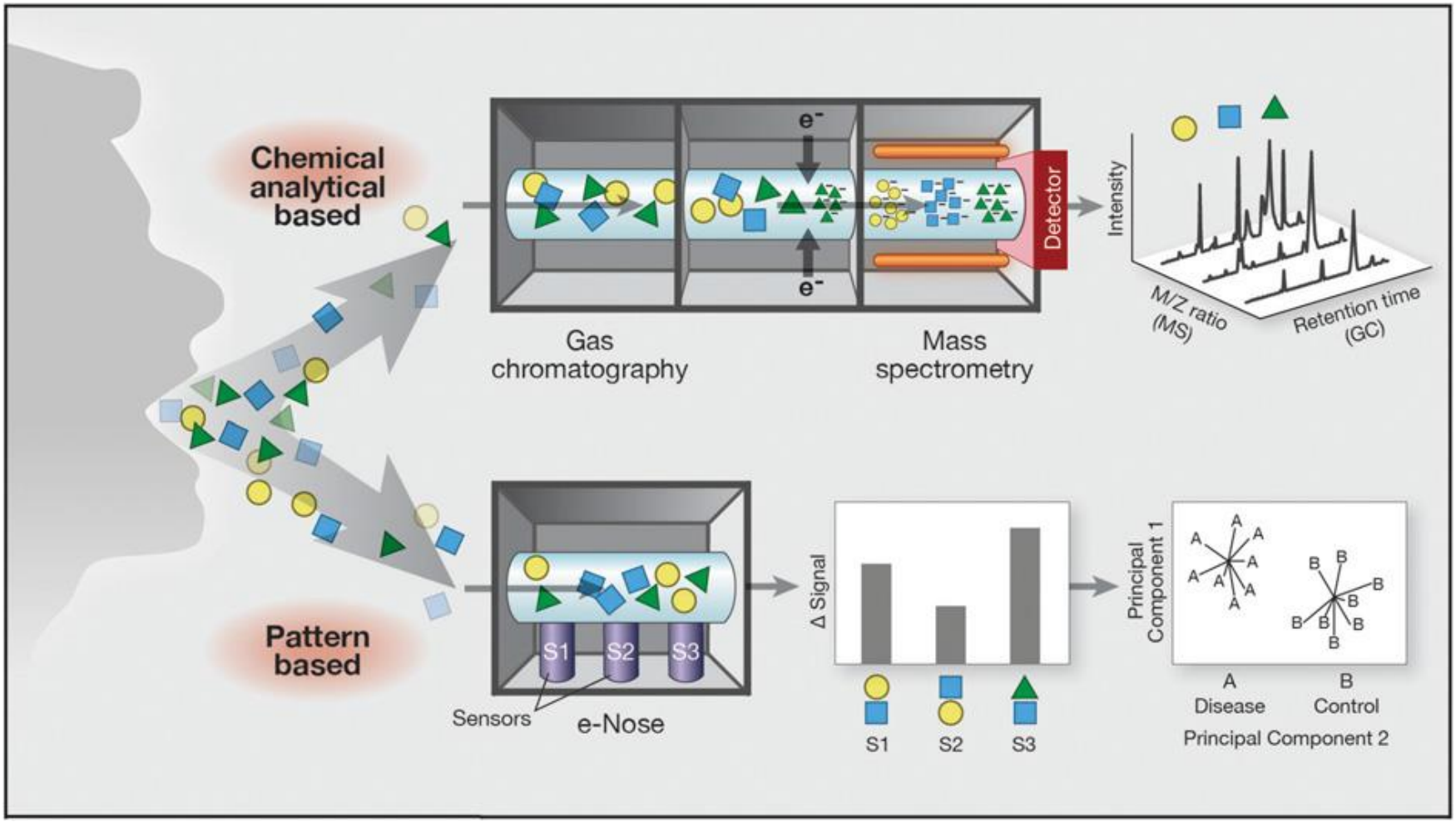


- Sampling
  - Online
  - Offline
    - Bags (Tedlar, Mylar)
    - Canisters (Stainless steel)
    - Adsorbent tubes (Tenax^{GR})
    - Solid phase microextraction (SPME) fibers
- Sources

Breath	Blood	Urine	Stool	Skin	cell lines/bacteria
					

Breath Analysis

Techniques



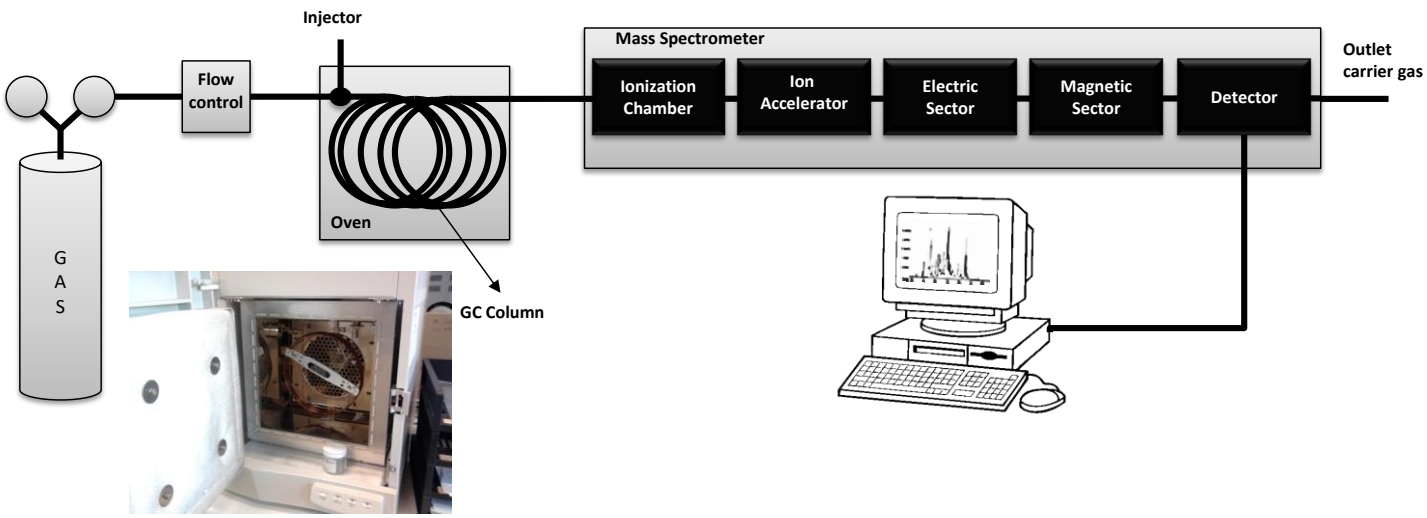
Van der Schee *et al.* Chest. 2015

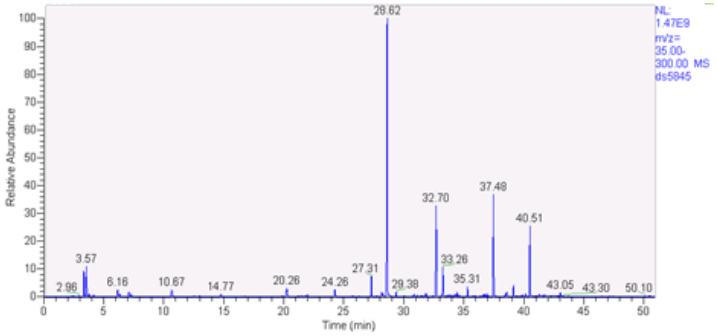
Breath Analysis
Techniques

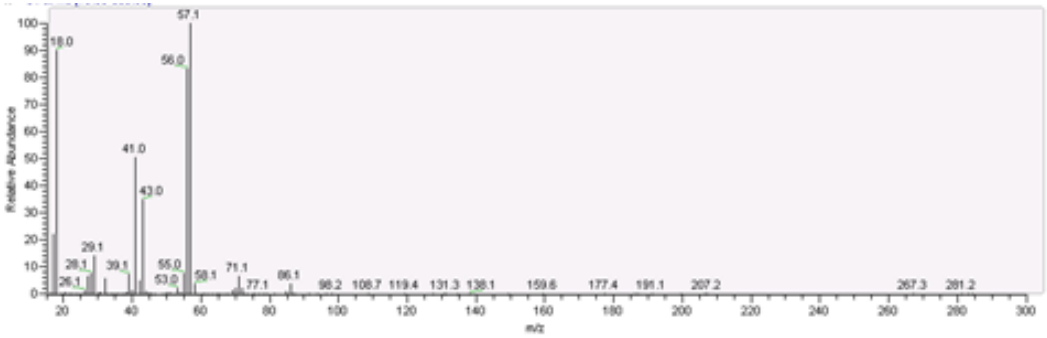
- Gas chromatography – mass spectrometry (GC-MS)

Breath Analysis
Techniques

- Gas chromatography – mass spectrometry (GC-MS)



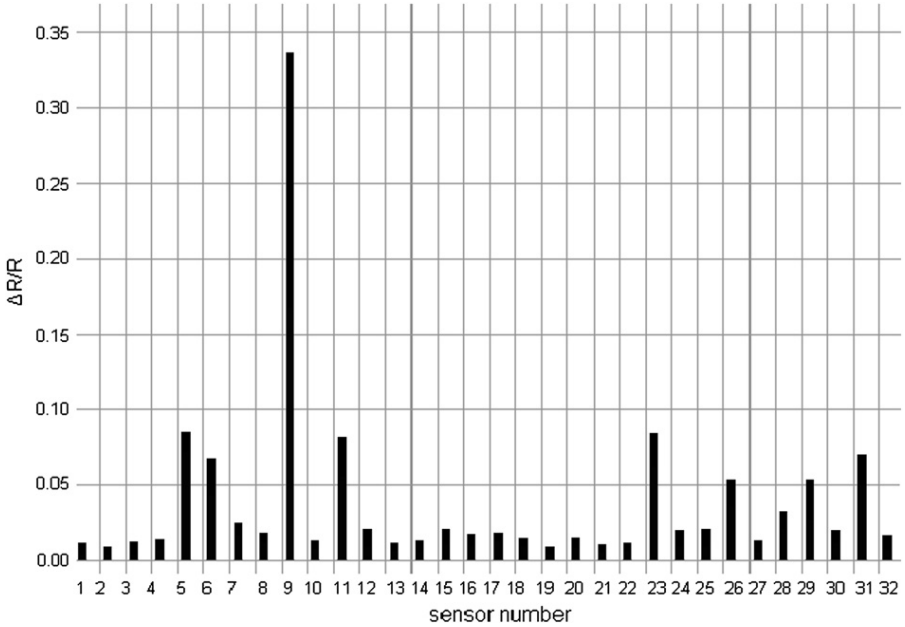


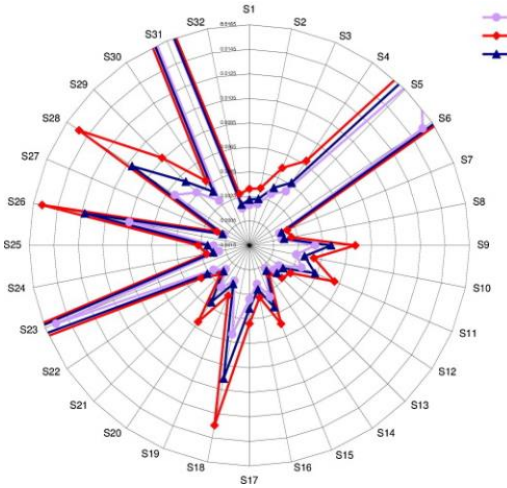


Lamote K *et al.* Cancer Epidemiol Biomark Prev, 2014

Breath Analysis
Techniques

- Electronic nose (eNose)



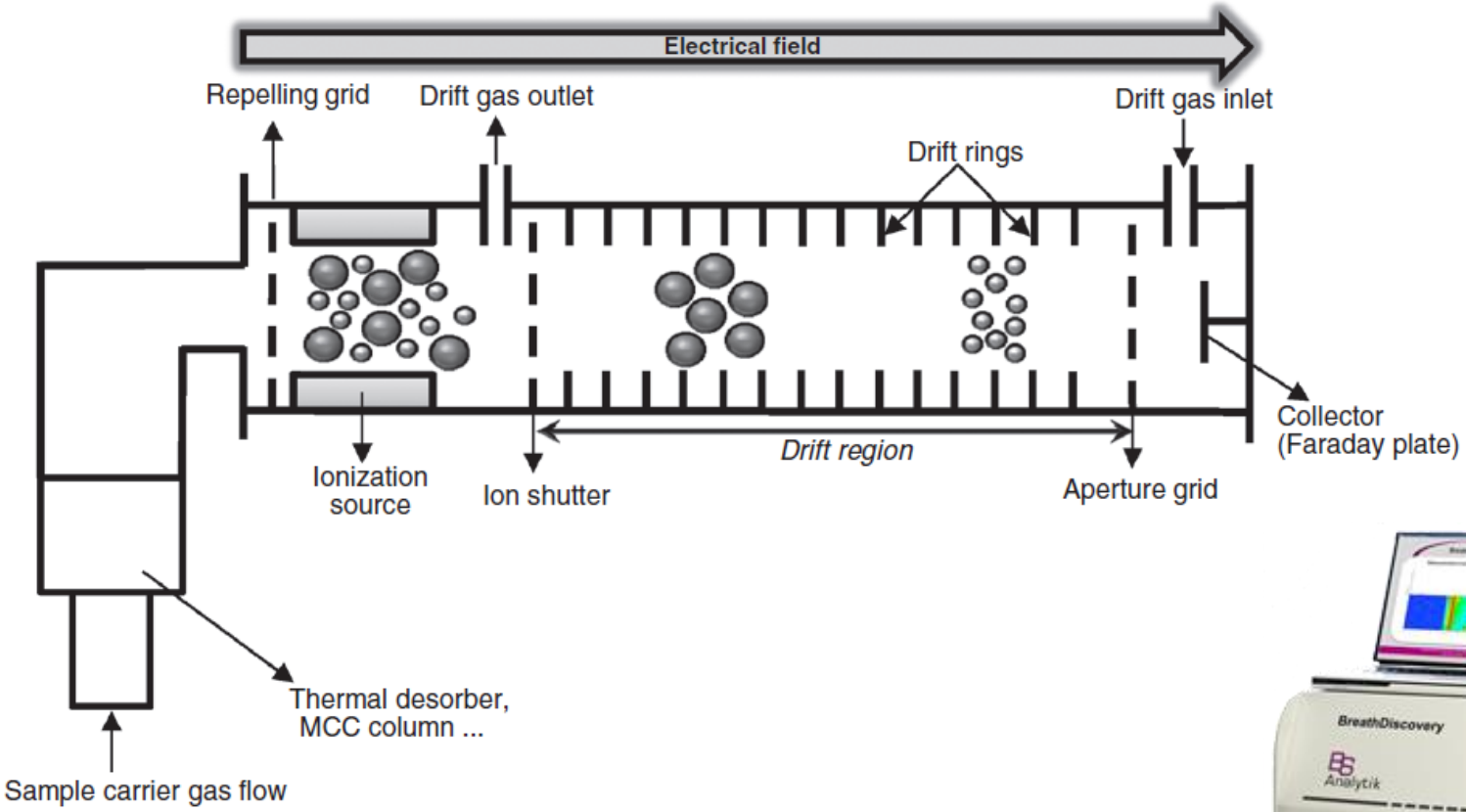


Healthy *Disease*

Lamote K *et al.* Cancer Epidemiol Biomark Prev, 2014

Breath Analysis
Techniques

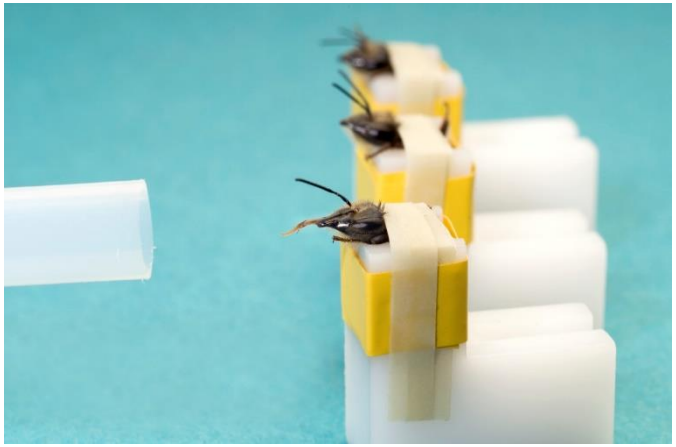
- Multicapillary column - ion mobility spectrometry (MCC/IMS)

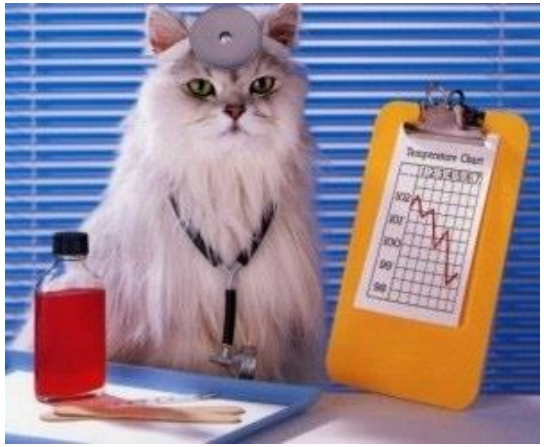


Lamote K *et al.* Cancer Epidemiol Biomark Prev, 2014

Breath Analysis
Techniques

- Animals





Lamote K *et al.* Cancer Epidemiol Biomark Prev, 2014

Breath Analysis
Methods

GC-MS	eNose	IMS	Canine scent
▪ Sensitive (pp_m-pp_t)	▪ No Specific VOC identification	▪ Sensitive (pp_b-pp_t)	▪ Time consuming (dog training)
▪ Identification, detection, quantification of VOCs	▪ Black box	▪ VOC identification possible with MCC column	▪ No quantification/identification of VOCs
▪ Vacuum conditions	▪ Ambient conditions	▪ Ambient conditions	▪ Ambient conditions
▪ Slow	▪ Fast, easy	▪ Fast, easy	▪ Fast, easy
▪ *Offline* sampling	▪ *Offline* sampling	▪ *Online* sampling	▪ *Online* sampling
▪ Large, immovable set-up	▪ Transportable	▪ Transportable	▪ Transportable
▪ Very expensive	▪ Cheap	▪ Cheap	▪ Expensive
▪ Specific technician training	▪ No specific operator training	▪ No specific operator training	▪ No specific operator training
▪ Gold standard			

Abbreviations: pp_b, parts per billion by volume; pp_m, parts per million by volume; pp_t, parts per trillion by volume.

Lamote K *et al.* Cancer Epidemiol Biomark Prev, 2014

Breath Analysis
Applications

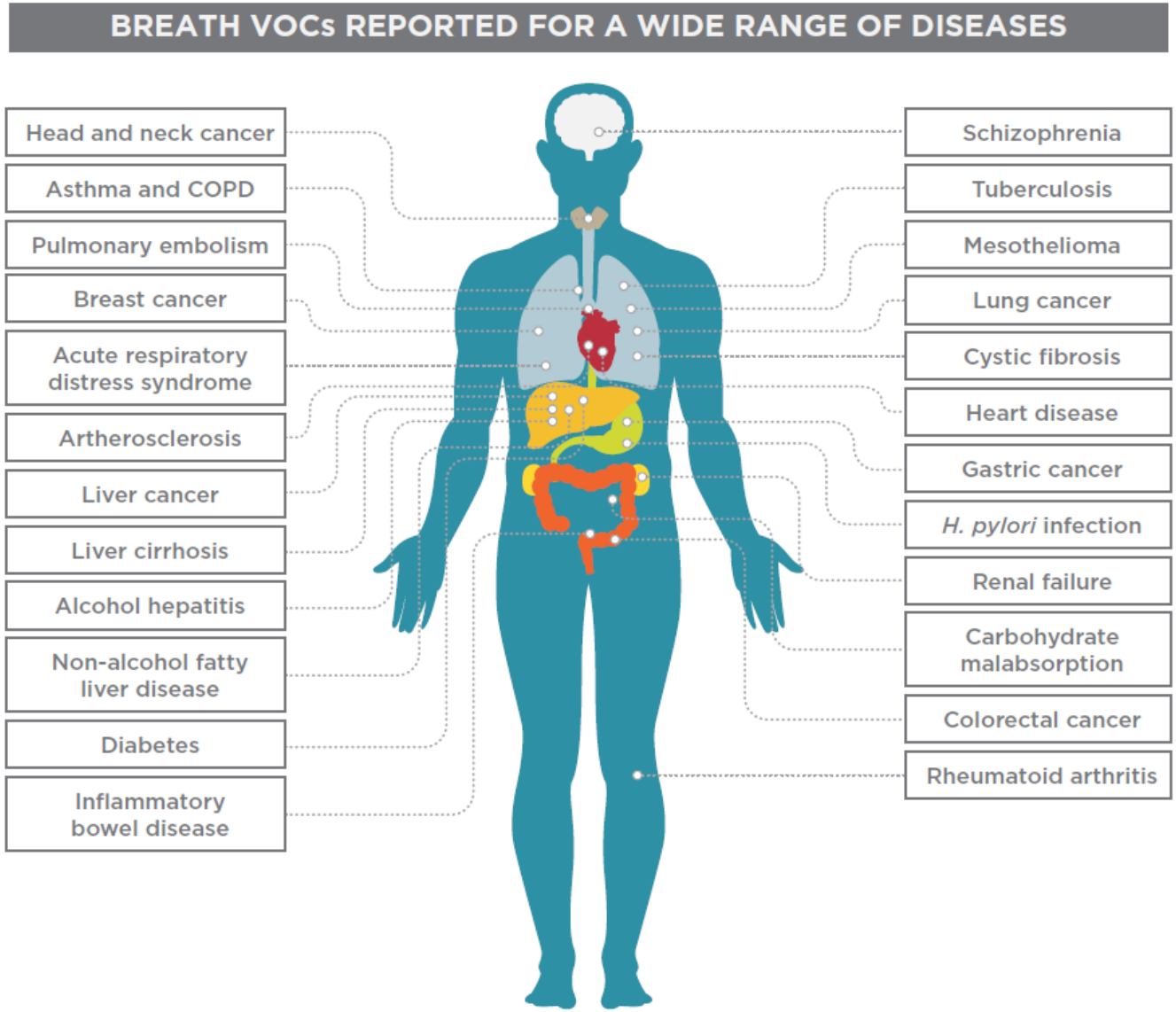
- Clinical diagnostics and prognosis (*infections*)
- Early detection and screening (*cancer*)
- Disease monitoring *(COPD exacerbations)*
- Precision medicine
  - Companion diagnostics
  - Patient stratification *(eos-neutro asthma, cancer mutations ...)*
  - Treatment response *(corticosteroid response)*
  - Toxicity *(radiation, pollution)*

Breath Analysis
Approved applications

Test	VOC
Capnography	CO_2
^{13}C-urea breath test for *H. pylori* infection	$^{13}CO_2$
Neonatal jaundice	CO
Disaccharaide adsorption deficiency	H_2, CH_4
Monitoring asthma therapy	FeNO
Heart transplant rejection	Alkanes
^{13}C-octanoic acid Gastric Emptying Breath test	$^{13}CO_2$
CO testing smokers	CO
Roadside intoxication	CH_3CH_2OH

Amann *et al.* J Breath Res, 2014

Breath Analysis
Applications



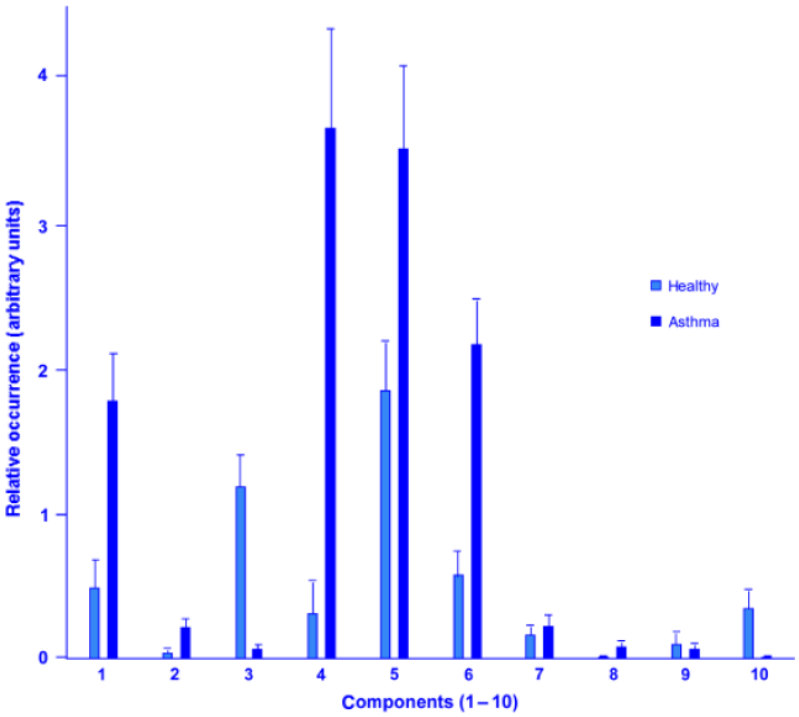
Breath Analysis
Asthma

- 63 asthmatic children
- 57 healthy control children
- 95% specificity, 89% sensitivity, 92% accuracy

Table 2. Overview of the most important components used to discriminate asthma patients from healthy controls

Number*	Component
1	(Branched) hydrocarbon ($C_{13}H_{28}$)
2	Carbon disulphide (CS_2)
3	1-penten-2-on
4	butanoic acid
5	3-(1-methylethyl)-benzene
6	(Branched) hydrocarbon ($C_{13}H_{28}$)
7	Unsaturated hydrocarbon ($C_{15}H_{26}$)
8	Benzoic acid
9	p-xylene
10	(Branched) hydrocarbon ($C_{11}H_{24}$)

*Numbers represent the order in which the components were included in the discriminant analysis.

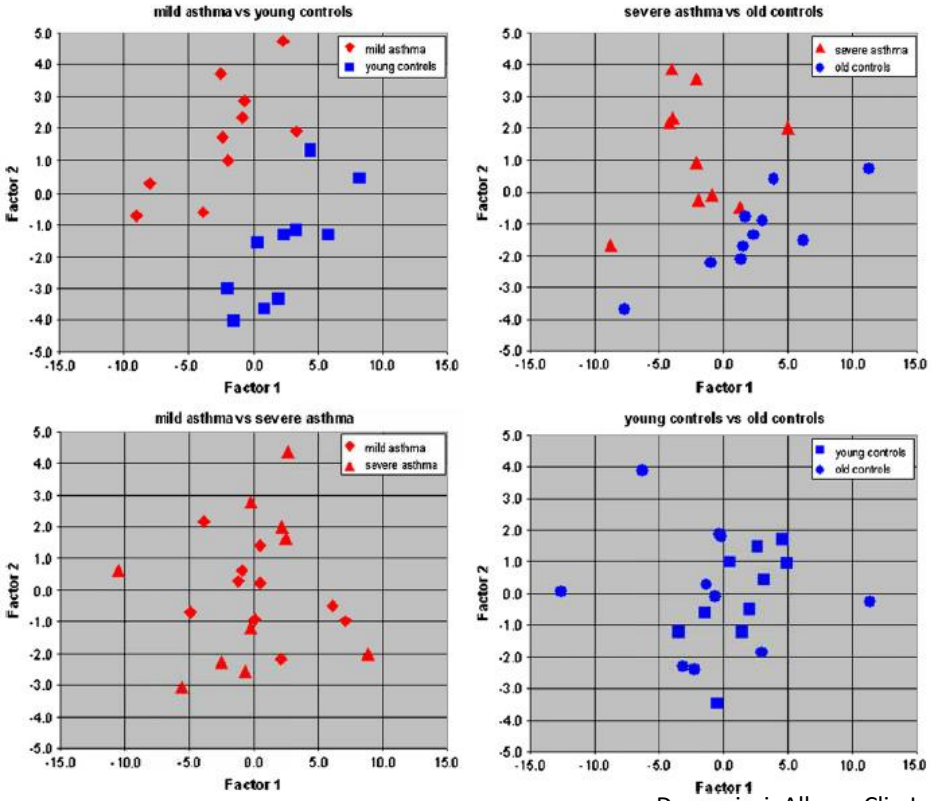


Dallinga et al. Clinical & Experimental Allergy, 2009

Breath Analysis
Asthma

- 10 young patients with mild asthma
- 10 older patients with severe asthma
- 10 young / 10 older healthy controls

- Mild vs healthy: 100%
- Severe vs Healthy: 90%
- Mild vs severe: 65%



Dragonieri. Allergy Clin Immunol 2007

Breath Analysis
Asthma

- Phenotyping:
  - 35 asthmatic patients
  - 23 matched healthy controls

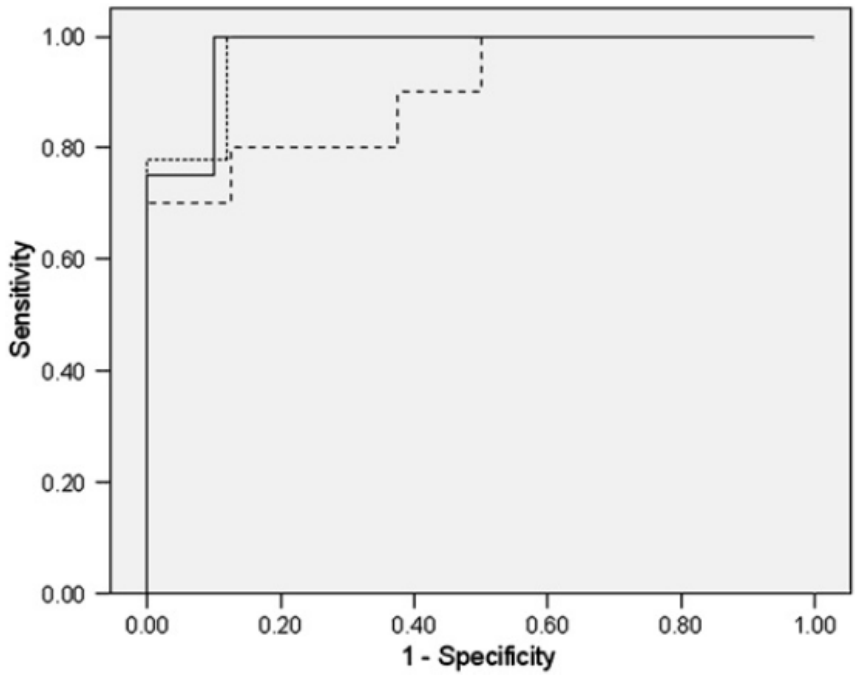


Figure 2 Receiver operating characteristic curves for the models predicting eosinophilic versus non-eosinophilic asthma (solid line); neutrophilic versus non-neutrophilic asthma (dashed line) and controlled versus uncontrolled asthma (dotted line).

Table 3 Receiver operating characteristics of the multivariate models for the asthma phenotypes of interest

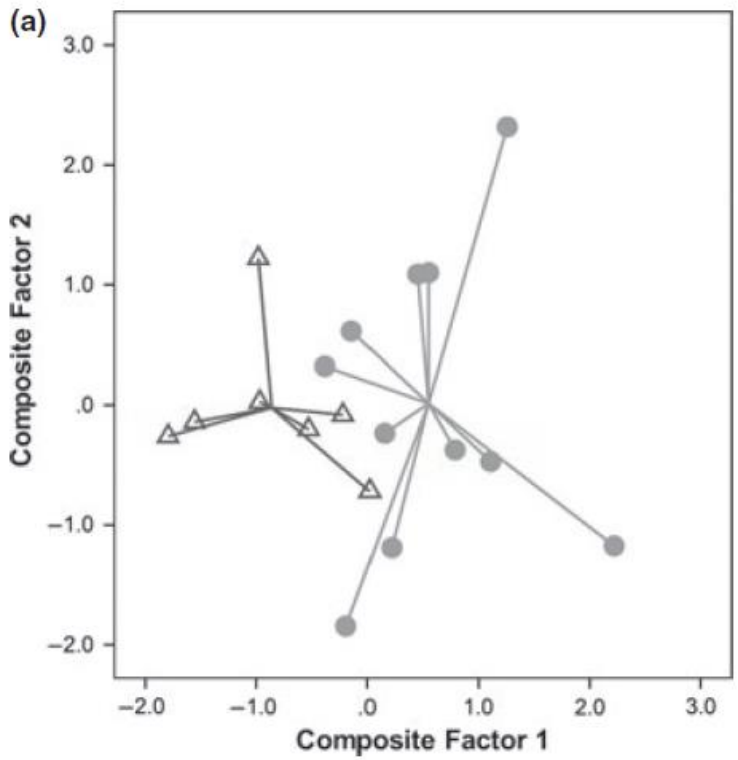
	Eosinophilic versus non-eosinophilic	Neutrophilic versus non-neutrophilic	Controlled versus not controlled
Sensitivity	0.75	0.80	0.89
Specificity	0.90	0.75	0.88
Positive predictive value	0.86	0.80	0.89
Negative predictive value	0.82	0.75	0.88
AUROC (95% CI)	0.98 (0.91 to 1.00)	0.90 (0.76 to 1.00)	0.97 (0.93 to 1.00)
Cross-validation accuracy	83%	72%	80%

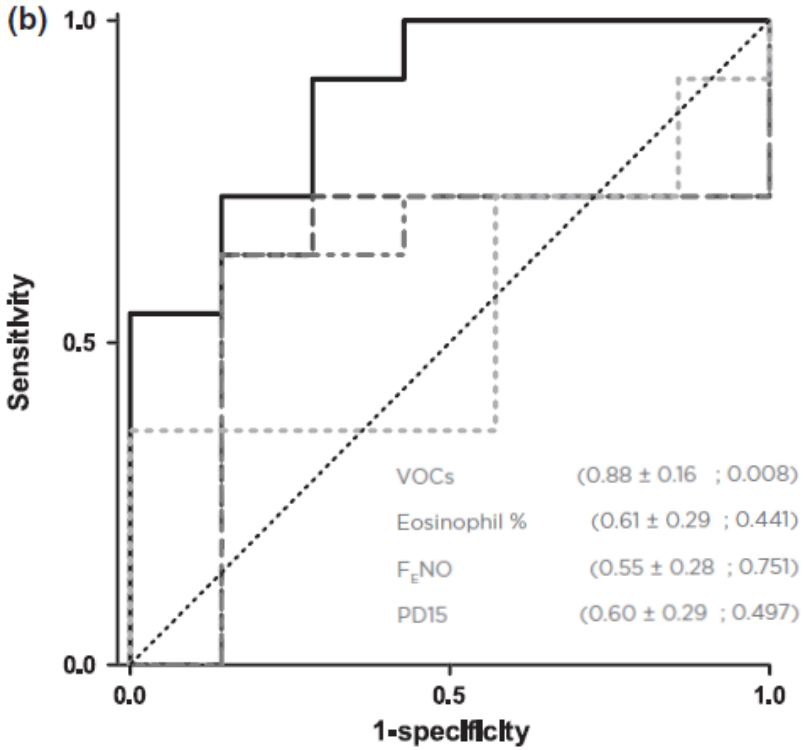
Leave-one-out cross-validation accuracy from discriminant function analysis also shown.
AUROC, area under the receiver operating characteristic.

Ibrahim et al. Thorax, 2011

Breath Analysis
Asthma

- Steroid responsiveness:
  - asthmatic patients (11 steroid responsive, 7 unresponsive)

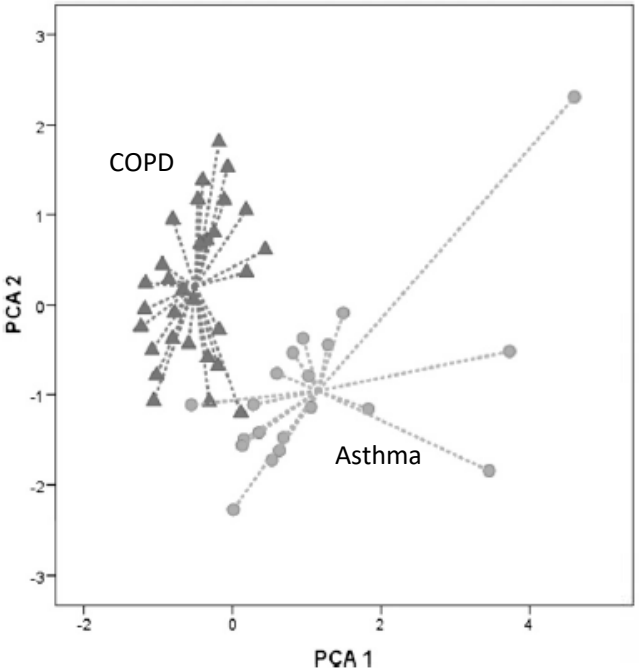


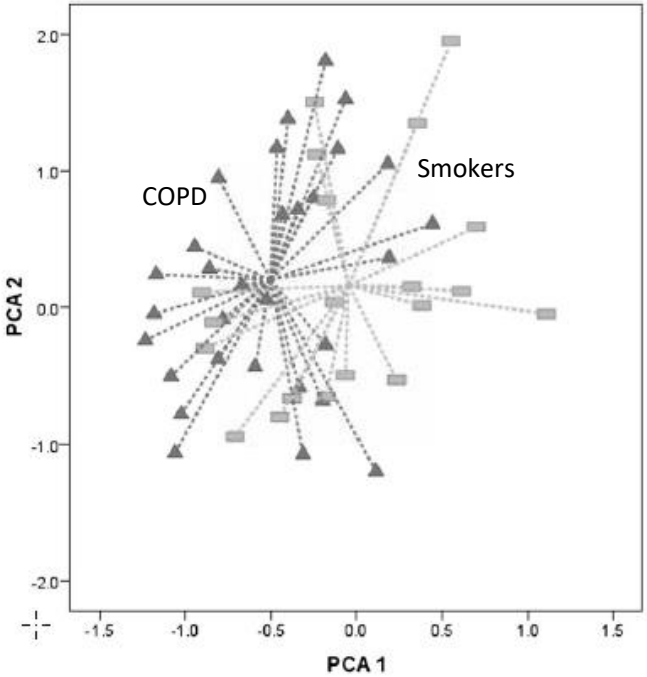


Van der Schee et al. Clin Exp Allergy, 2013

Breath Analysis
COPD

- 30 COPD patients
- 20 asthmatic patients
- 40 controls (20 non-smoking and 20 smoking)



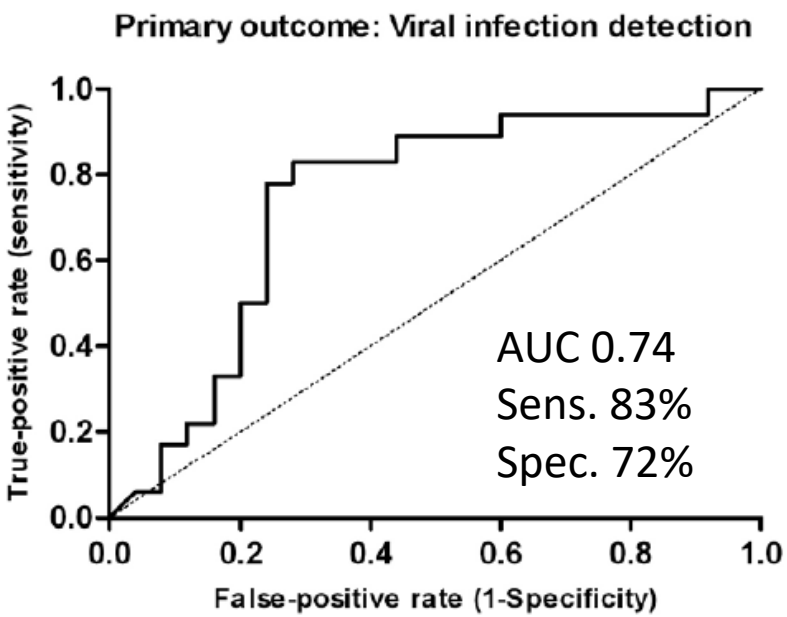


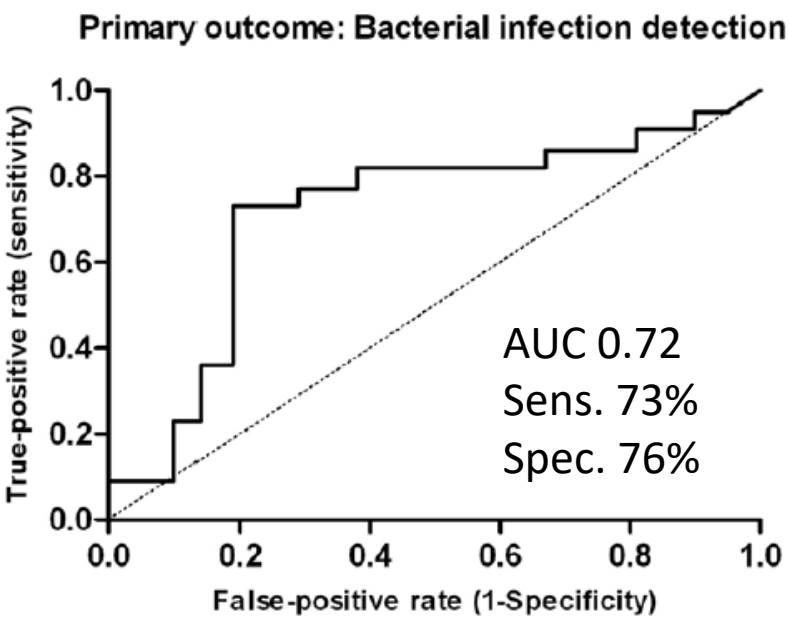
Analysis	Cross-validated Accuracy (%)	*P* Value
Asthma–COPD	96	<0.0001
Asthma–COPD smoking	97	<0.0001
Asthma–COPD ex-smoking	95	<0.0001
Asthma–COPD ICS	97	<0.0001
Asthma–COPD no ICS	95	<0.0001
Asthma–nonsmoking control subjects	95	<0.0001
COPD–smoking control subjects	66	0.006
COPD smoking–smoking control subjects	72	0.018
COPD ex-smoking–smoking control subjects	61	0.026
COPD ICS–smoking control subjects	70	0.024
COPD no ICS–smoking control subjects	65	0.047
Control subjects–smoking control subjects	63	0.016

Fens et al. Am J Respir Crit Care Med, 2009

Breath Analysis
COPD

- Infections in acute exacerbations:
  - 43 COPD patients
    - 22 bacterial infections, 18 viral infections (9 both viral and bacterial infections)
    - 12 no infections

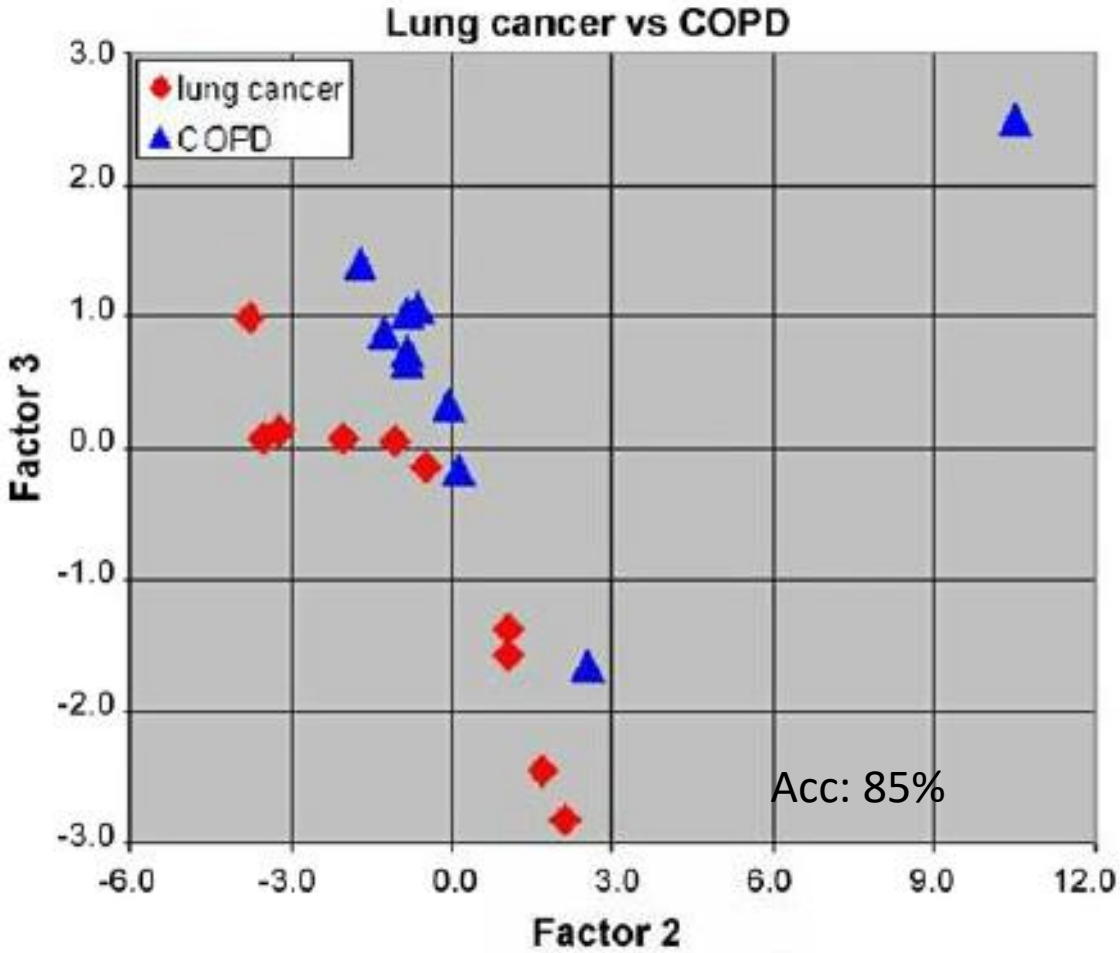




Van Geffen et al. J Breath Res, 2016

Breath Analysis
COPD

- COPD vs Lung Cancer:
  - 10 Lung cancer, 10 COPD



Dragonieri et al. Lung Cancer, 2009

Breath Analysis
Oncology – Lung cancer

- Poor prognosis
- Early detection proven to increase patients outcome
  - Low dose CT screening reduced mortality by 20%

- Breath analysis for screening for cancer?

Breath Analysis
Oncology – Lung cancer

Group	Method	Patients	Controls	Model Characteristics	VOCs	Remarks
Gordon et al. (1985)	TD-GC-MS	12 LC	17 HC	Acc:93%	Acetone, methylethylketone, n-propanol	
Phillips et al. (1999)	TD-GC-MS	60 LC	48 HC	Se: 71.7% Sp: 66.7%	Styrene, 2,2,4,6,6-pentamethylheptane, 2-methylheptane, Decane, propylbenzene, Undecane, methylcyclopentane, 1-methyl-2-pentylcyclopropane, trichlorofluoro-methane, benzene, 1,2,4-trimethyl-benzene, isoprene, 3-methyloctane, 1-hexene, 3-methylnonane, 1-heptene, 1,4-dimethylbenzene, 2,4-dimethyl-heptane, Hexanal, Cyclohexane, 1-methylethenyl-benzene, Hepatanal	
Phillips et al. (2003)	TD-GC-MS	82 LC	91 non-cancer 41 HC	Se: 85.1% Sp: 80.5%	C_4-C_{20} monomethylated alkanes	No effect stage, smoking, histology
Poli et al. (2005)	SPME-GC-MS	36 NSCLC 25 COPD	35 smokers 50 non-smokers	Se: 80%	2-methylpentane, isoprene, pentane, ethylbenzene, xylene, trimethylbenzene, toluene, benzene, heptane, decane, styrene, octane, pentamethylheptane	
Ligor et al. (2009)	SPME-GC-MS	65 LC	31 Controls	-	2-methylpentane, 1-propanol, 3-butyn-2-ol, benzaldehyde, 3-methylpentane, n-pentane, n-hexane, 2-butanone	Acetonitrile, 2,5-dimethylfuran, benzene ~smoking
Chen et al. (2007)	SPME-GC-MS	29 LC	13 HC	Se: 86.2% Sp: 69.2%	Styrene, decane, isoprene, benzene, undecane, 1-hexene, hexanal, propylbenzene, 1,2,4-trimethylbenzene, heptanal, methylcyclopentane	
Phillips et al. (2007) Abstract		193 LC	211 Controls	Se: 84.6% Sp: 80%		Independent of smoking, stage
Phillips et al. (2008)		193 LC	211 Controls	Se: 84.5% Sp: 81%		WDA, No influence of smoking
Gaspar et al. (2009)	TD-GC-MS	18 LC	10 Controls	Se: 100% Sp: 100%	C_{14}-C_{24} hydrocarbons	
Peng et al. (2010)	SPME-GC-MS	30 LC 26 Colon Ca 20 Breast Ca 18 Prostate Ca	22 HC	-	1-methyl-4-(1-methylethyl)benzene, toluene, dodecane, 3,3-dimethyl pentane, 2,3,4-trimethyl hexane, 1,1'-(1-butenylidene)bis benzene	
Poli et al. (2010)	SPME-GC-MS	40 NSCLC	38 non-smokers	Acc: 90%	C_3-C_9 aldehydes	No influence smoking, age
Song et al. (2010)	SPME-GC-MS	43 NSCLC	41 HC	Se: 95.3-93% Sp:85.4-92.7%	1-butanol, 3-hydroxy-2-butanone	Stage independent
Fuchs et al. (2010)	SPME-GC-MS	12 LC	12 Smokers 12 non-smokers	Se: 75% (pentanal) Sp: 95.8%	C_1-C_{10} aldehydes	No difference between SCLC and NSCLC
Rudnicka et al. (2011)	SPME-GC-MS	23 LC	30 HC	-	Propane, isopropyl alcohol, carbon disulphide, ethyl benzene	LC pts were older, ethylbenzene=exogenous
Peled et al (2012)	SPME-GC-MS	53 LC	19 benign lung diseases	Acc: 88%	1-octene	
Wang et al. (2012)	SPME-GC-MS	88 LC	70 benign lung disease 85 HC	Se: 96.5% Sp: 97.5%	23 VOCs (abstract)	Stage independent
Poli et al. (2008)	SPME-GC-MS	36 NSCLC			After resection: ↓ Isoprene, benzene ↑ Pentane, toluene, ethyl benzene	

Breath Analysis
Oncology – Lung cancer

Lung Cancer → Ox stress ↑

Inflammation

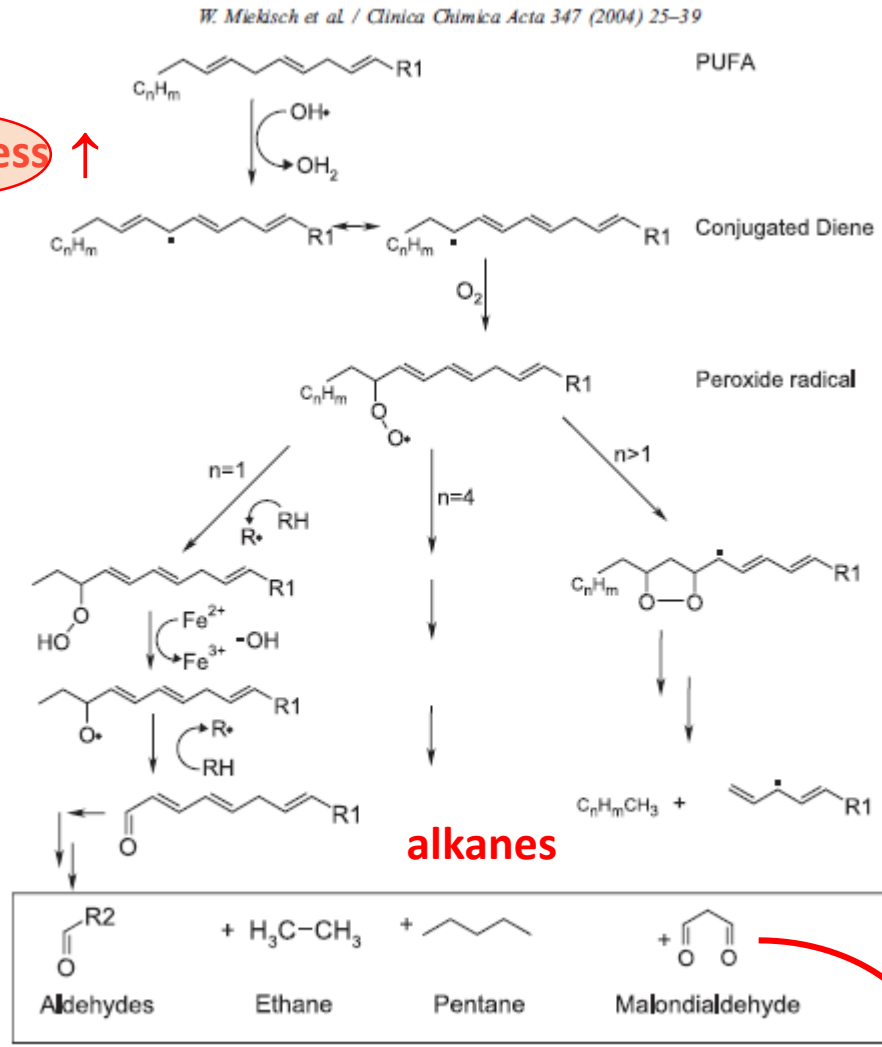


Fig. 1. Free radical-mediated lipid peroxidation: possible reactions and reaction products.

alcohol ← Alcohol dehydrogenase

CYP-enzymes

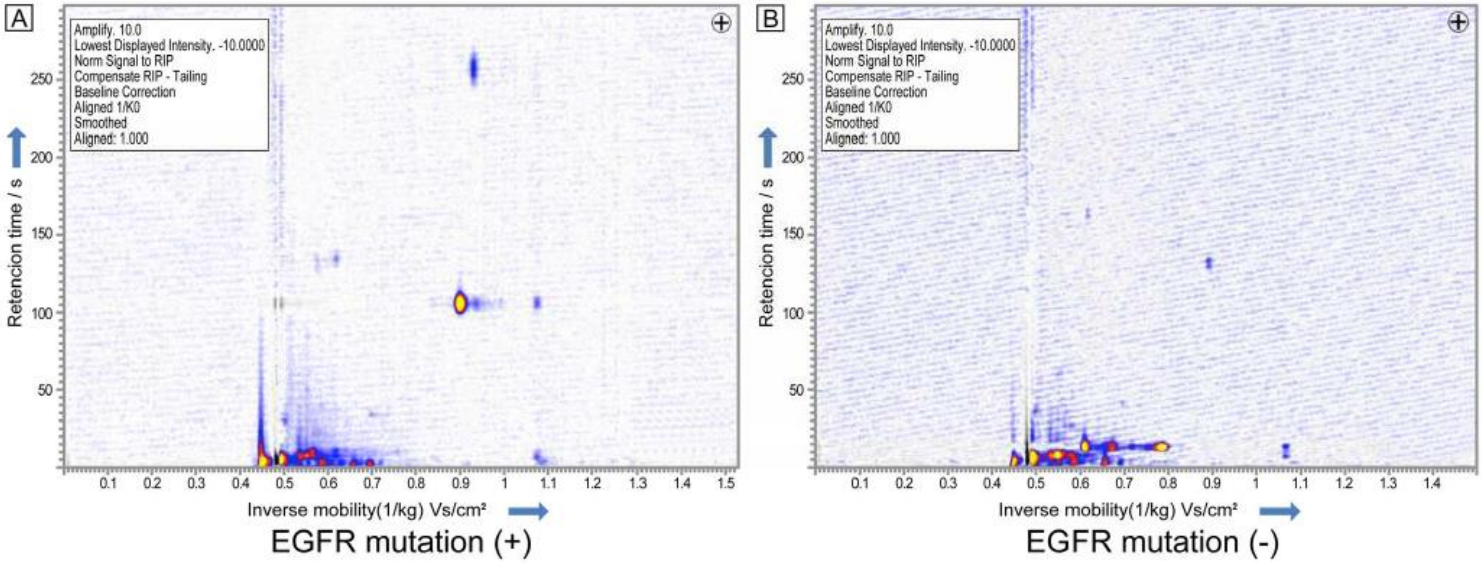
Degradation

Breath Analysis
Oncology – Lung cancer

- Mutations

- 32 Adenocarcinoma, 10 squamous cell, 8 small cell
- 39 healthy controls

- n-dodecane

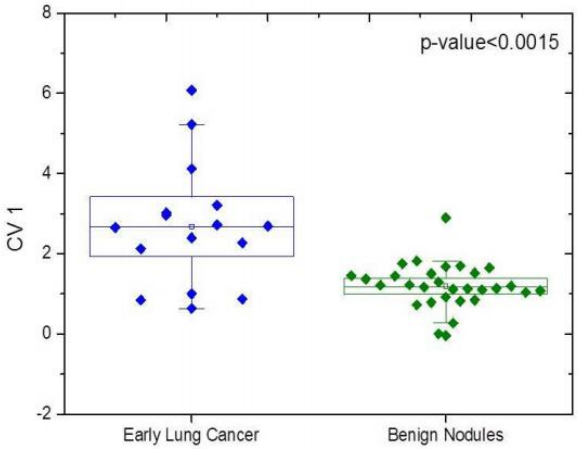


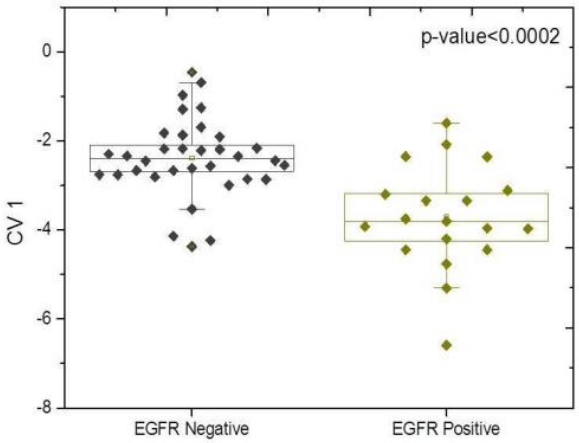
Handa et al. Plos One, 2014

Breath Analysis
Oncology – Lung cancer

- Mutations
  - 30 benign nodules
  - 89 lung cancer patients
    - 16 early stage, 73 advanced stage
    - 19 EGFR(+), 34 wild-type

Group	Acc	Sens	Spec	PPV	NPV
Early Lung Cancer vs. Benign Nodules	87%	75%	93%	88%	88%
EGFR mutation vs. wild type	83%	79%	85%	75%	88%



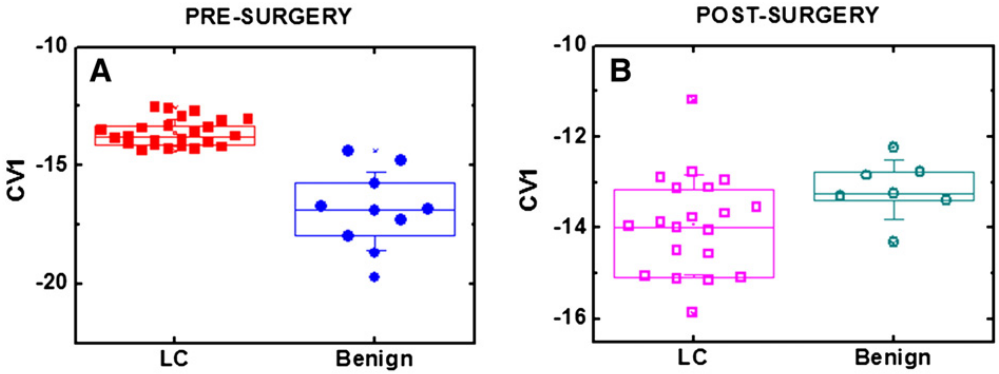


Shlomi et al. J Thorac Oncol, 2017

Breath Analysis
Oncology – Lung cancer

- Treatment
  - Surgery
    - 15 patients with suspicion for lung cancer were resected
    - 11 had early-stage lung cancer, 4 were benign
    - Breath sample at baseline and 3 weeks after resection

    - 5 VOCs reduced after surgery
    - Sens 100%
    - Spec: 80%

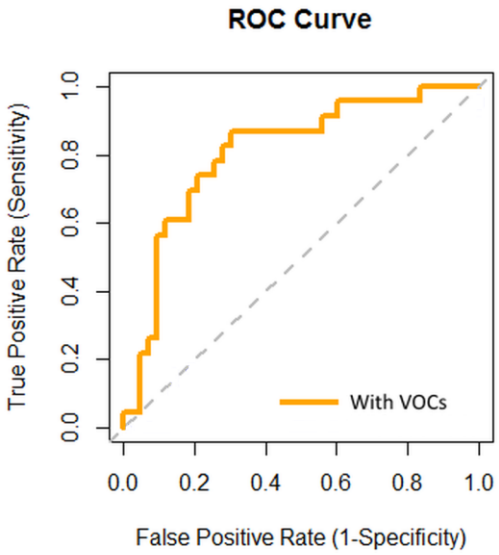


Broza et al. Nanomedicine, 2013.

Breath Analysis
Oncology – pleural mesothelioma

- Participants:
  - **21** healthy non asbestos-exposed individuals (HC)
  - **22** healthy occupational asbestos-exposed individuals (AEx)
  - **23** MPM patients (treatment-naive)

	MPM vs HC+AEx With VOCs
Characteristic	**Outcome (95% CI)**
Sensitivity	0.87 (0.69 – 0.97)
Specificity	0.70 (0.55 – 0.82)
PPV	0.61 (0.43 – 0.76)
NPV	0.91 (0.77 – 0.98)
Accuracy	0.76 (0.64 – 0.98)
AUC_{ROC}	0.81 (0.69 – 0.91)



VOCs: P1, P3, P5, P30, P50, P54 , 7P1

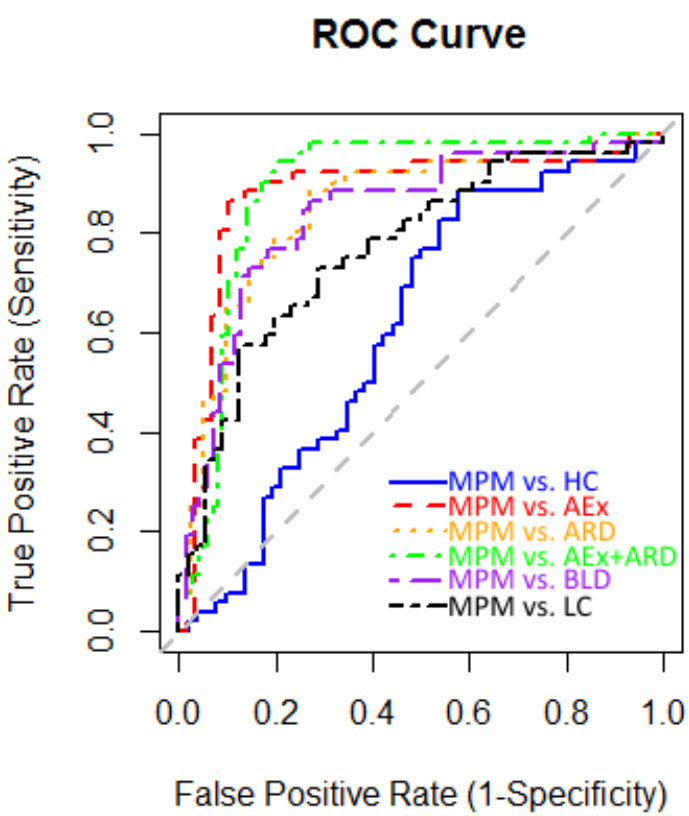
Lamote K *et al.* J Breath Res, 2016.

Breath Analysis
Oncology – pleural mesothelioma

- Participants:
  - **52** healthy non asbestos-exposed individuals (HC)
  - **59** healthy occupational asbestos-exposed individuals (AEx)
  - **41** patients with benign asbestos-related diseases (ARD)
  - **70** patients with benign non-asbestos-related diseases (BLD)
  - **56** primary lung cancer patients (LC)
  - **52** MPM patients (treatment-naive)

Lamote K *et al.* Eur Respir J, 2017.

Breath Analysis
Oncology – pleural mesothelioma

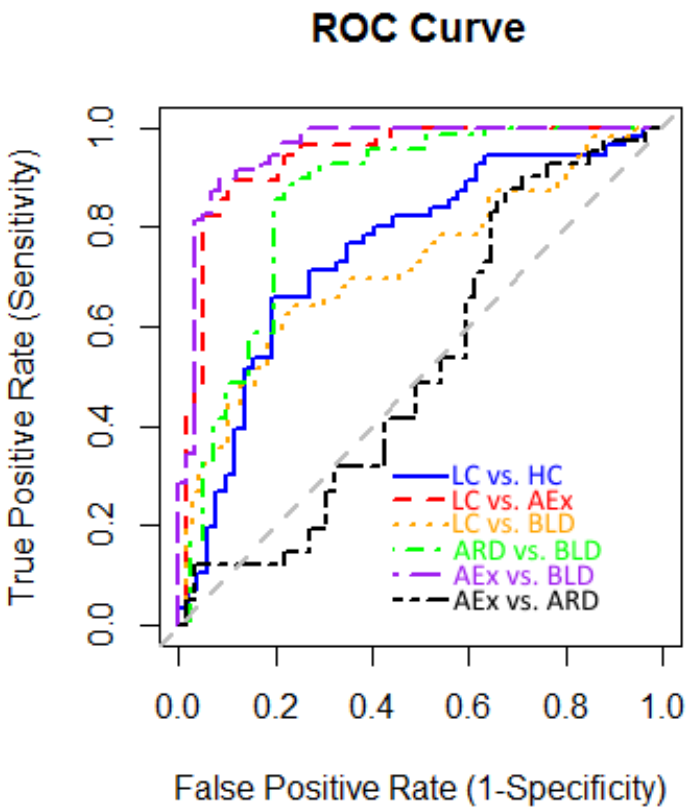


	MPM vs AEx+ARD	MPM vs LC
Sensitivity	94.2% (85.1%-98.5%)	73.1% (59.9%-83.8%)
Specificity	80.0% (71.3%-87.0%)	71.4% (58.7%-82.1%)
PPV	71.0% (59.6%-80.8%)	70.4% (57.3%-81.4%)
NPV	96.4% (90.5%-99.1%)	74.1% (61.2%-84.4%)
Accuracy	84.9% (78.5%-89.9%)	72.2% (63.3%-80.0%)
VOCs (>50% of times selected)	**P1**, **P3**, **P7**, **P9**, **P15**, **P21**, **P26**, P70, P83, **P84**, **P88**, **P101**, P110, P118, **P122**, P123, P142, **P151**, **P153**, **P159**, **P161**, **P167**, **P173**, **P178**, P222, P235, **P236**, **P240**	**P0**, **P7**, **P8**, P9, P15, **P21**, **P28**, **P37**, **P42**, **P43**, **P48**, P64, **P73**, **P78**, **P107**, **P108**, **P115**, **P116**, **P117**, P123, **P129**, **P136**, **P145**, **P150**, **P151**, **P156**, P172, **P181**, **P186**, **P215**, **P216**, **P223**, **P224**, **P225**, P231, **P237**, **P244**

AEx: asymptomatic former asbestos-exposed controls. ARD: patients with benign asbestos related diseases. AUC_{ROC}: area under the receiver operator characteristic curve. MPM: malignant pleural mesothelioma. NPV: negative predictive value. PPV: positive predictive value. VOC: volatile organic compound.

Lamote K *et al.* Eur Respir J, 2017.

Breath Analysis
Oncology – pleural mesothelioma



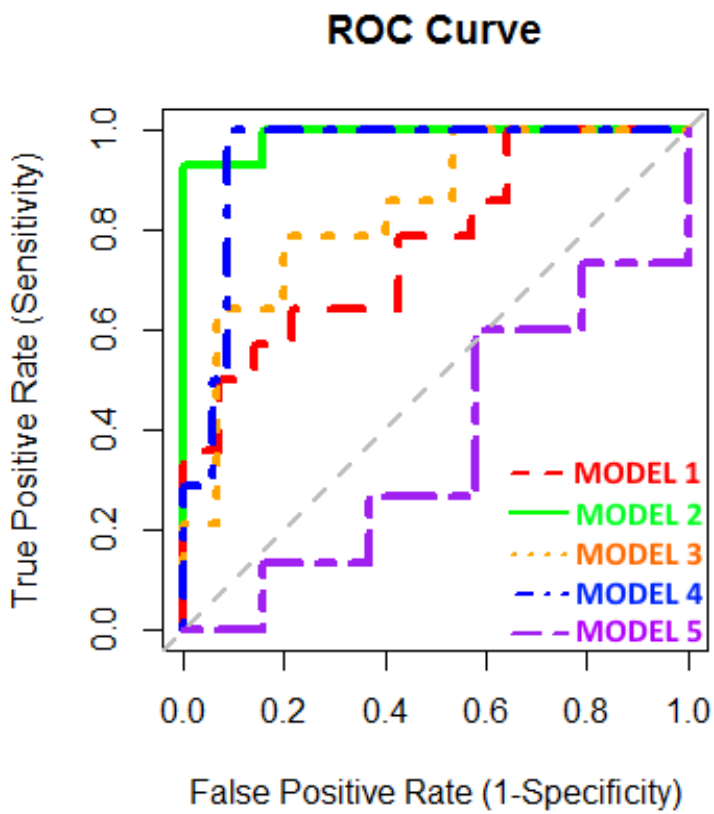
	LC vs AEx	AEx vs ARD
Sensitivity	89.3% (79.1%-95.5%)	82.9% (69.2%-92.2%)
Specificity	89.8% (80.1%-95.8%)	35.6% (24.2%-48.4%)
PPV	89.3% (79.1%-95.5%)	47.2% (36.0%-58.7%)
NPV	89.8% (80.1%-95.8%)	75.0% (56.7%-88.3%)
Accuracy	89.6% (83.0%-94.2%)	55.0% (45.2%-64.5%)
VOCs (>50% of times selected)	P0, **P1**, **P3**, P14, **P21**, **P26**, P43, **P61**, **P65**, **P66**, P72, P84, **P88**, P90, **P101**, P112, **P114**, P115, **P116**, **P118**, P129, **P136**, **P141**, P158, **P176**, **P180**, **P181**, P187, P199, **P203**, P205, **P216**, P227, **P229**, P230, **P231**, **P233**, P244	P1, **P3**, P20, P23, P26, P34, P37, P44, P66, P69, P70, P80, P83, P84, **P90**, P92, **P99**, P101, **P103**, P120, P123, P126, P134, P137, P144, P166, P169, P170, P180, P183, P184, **P190**, P192, **P199**, P201, **P203**, P223, P226, P234, P237, P244

AEx: asymptomatic former asbestos-exposed controls. ARD: patients with benign asbestos related diseases. AUC_{ROC}: area under the receiver operator characteristic curve. NPV: negative predictive value. PPV: positive predictive value. VOC: volatile organic compound.

Lamote K *et al.* Eur Respir J, 2017.

Breath Analysis
Oncology – pleural mesothelioma

- Participants



t-naïve)

	MPM vs AEx+ARD	AEx vs ARD
Sensitivity	100% (80·7%-100%)	60·0% (34·6%-81·9%)
Specificity	91·2% (77·9%-97·7%)	42·1% (21·9%-64·6%)
PPV	82·4% (59·2%-95·3%)	45·0% (24·7%-66·7%)
NPV	100% (90·8%-100%)	57·1% (31·2%-80·4%)
Accuracy	93·8% (84·0%-98·4%)	50·0% (33·6%-66·4%)
AUC_{ROC}	0·943 (0·866-1·000)	0·365 (0·435-0·818)

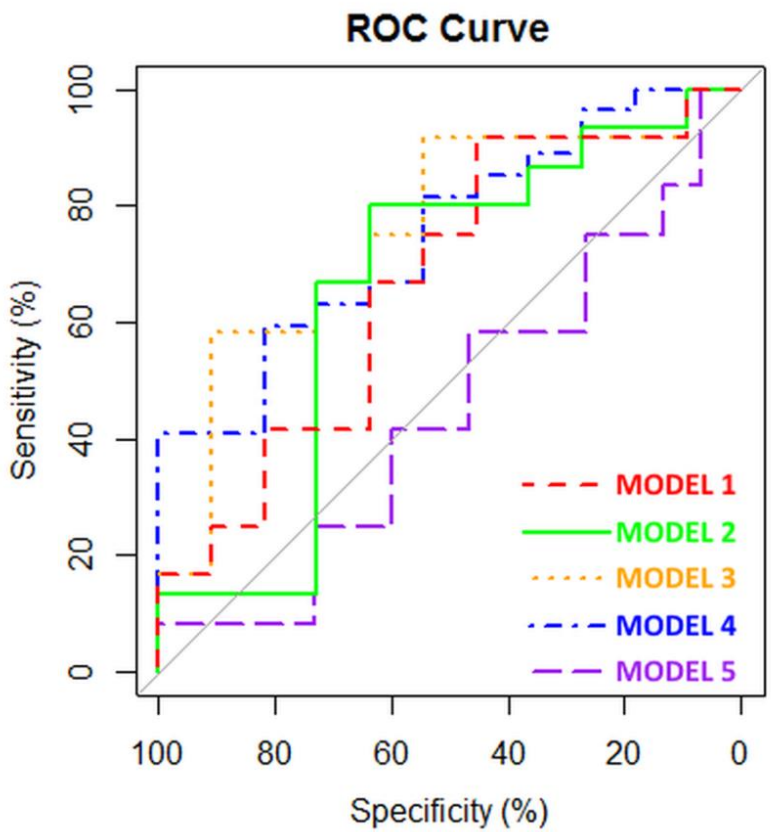
AEx: asymptomatic former asbestos-exposed controls. ARD: patients with benign asbestos related diseases. AUC_{ROC}: area under the receiver operator characteristic curve. HC: healthy controls. I_K: Kováts retention index. MPM: malignant pleural mesothelioma. NPV: negative predictive value. PPV: positive predictive value. VOC: volatile organic compound.

VOCs:

Diethyl ether
Limonene
Nonanal
Cyclohexane
VOC I_K 1287
Isothiocyanatocyclohexane
Hexane

Lamote K *et al.* Oncotarget, 2017.

Breath Analysis
Oncology – pleural mesothelioma



	MPM vs AEx+ARD	AEx vs ARD
Sensitivity	81.5% (63.7%-92.9%)	58.3% (30.3%-82.8%)
Specificity	54.5% (26.0%-81.0%)	46.7% (23.2%-71.3%)
PPV	81.5% (63.7%-92.9%)	46.7% (23.2%-71.3%)
NPV	54.5% (26.0%-81.0%)	58.3% (30.3%-82.8%)
Accuracy	73.7% (58.1%-85.8%)	51.9% (33.4%-70.0%)
AUC_{ROC}	0.747 (0.582-0.913)	0.550 (0.322-0.778)

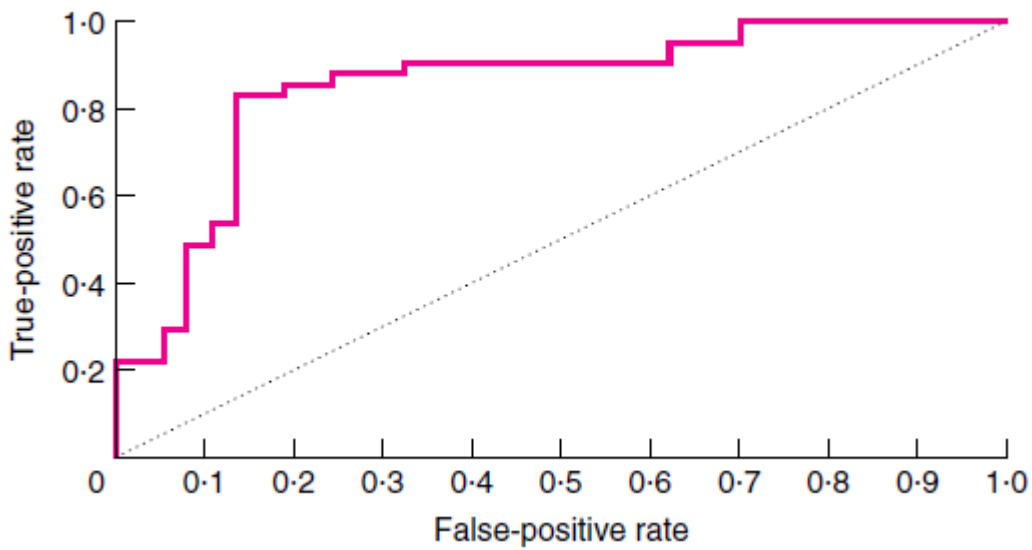
AEx: asymptomatic former asbestos-exposed controls. ARD: patients with benign asbestos related diseases. AUC_{ROC}: area under the receiver operator characteristic curve. HC: healthy controls. MPM: malignant pleural mesothelioma. NA: not applicable. NPV: negative predictive value. PPV: positive predictive value.

Lamote K *et al.* Oncotarget, 2017.

Urine Analysis
Oncology – colorectal cancer

- Fecal Immunochemical Testing (se: 66%-88%; sp: 87%-96%)
- Breath VOCs (37 CRC patients, 41 controls)

Nonanal
4-Methyl-2-pentanone
Decanal
2-Methylbutane
1,2-Pentadiene
2-Methylpentane
3-Methylpentane
Methylcyclopentane
Cyclohexane
Methylcyclohexane
1,3-Dimethylbenzene
4-Methyloctane
1,4-Dimethylbenzene
A (4-methylundecane, RT = 11·3)
B (trimethyldecane, RT = 13·2)

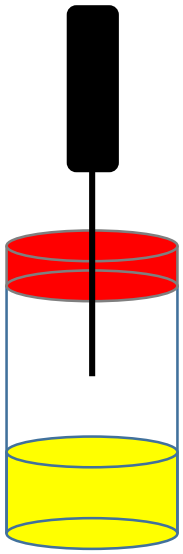


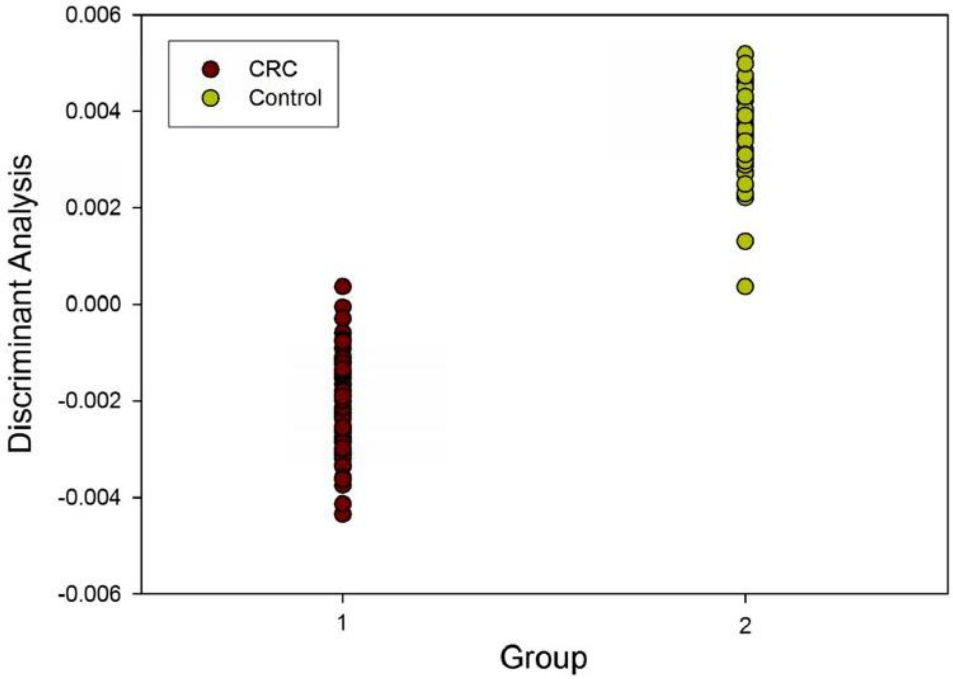
Acc: 85%, se: 86%, sp: 83%

Altomare et al, Brit J Surg, 2013

VOC Analysis
Oncology – colorectal cancer

- Urine VOCs (83 CRC patients, 50 controls)





Acc: 74%, sens: 88%, spec: 60%

Arasaradnam et al, Plos One, 2014

Breath Analysis
Inflammatory bowel disease

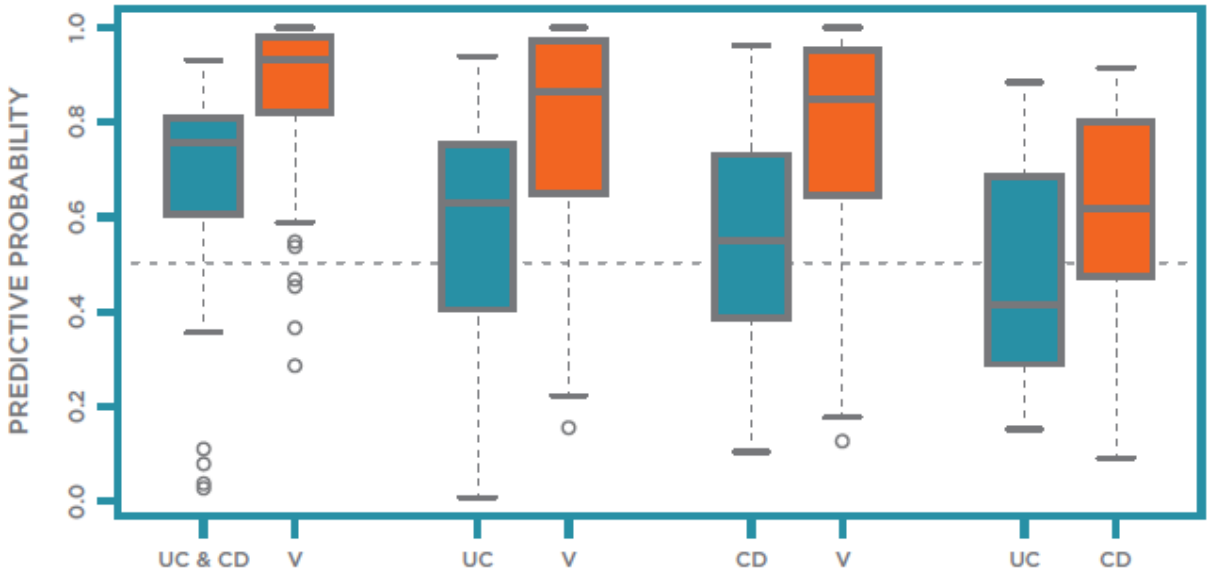
- Crohn's disease (CD)
- Ulcerative colitis (UC)

- Interaction between genes, environment and microbiome

- Accurate phenotyping:
  - Treatment selection
  - Endoscopy

Breath Analysis
Inflammatory bowel disease

- 25 CD patients
- 29 UC patients
- 22 Healthy Controls



Sens: 74%
Spec: 75%
AUC: 0.82

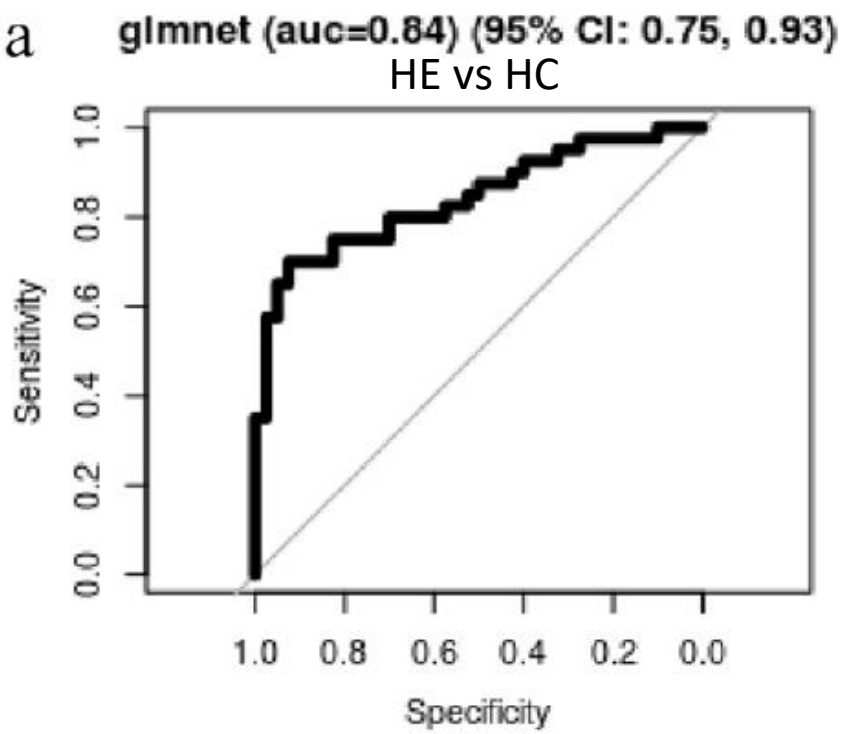
Sens: 67%
Spec: 67%
AUC: 0.70

Arasaradman et al. Dig Liver Dis, 2016

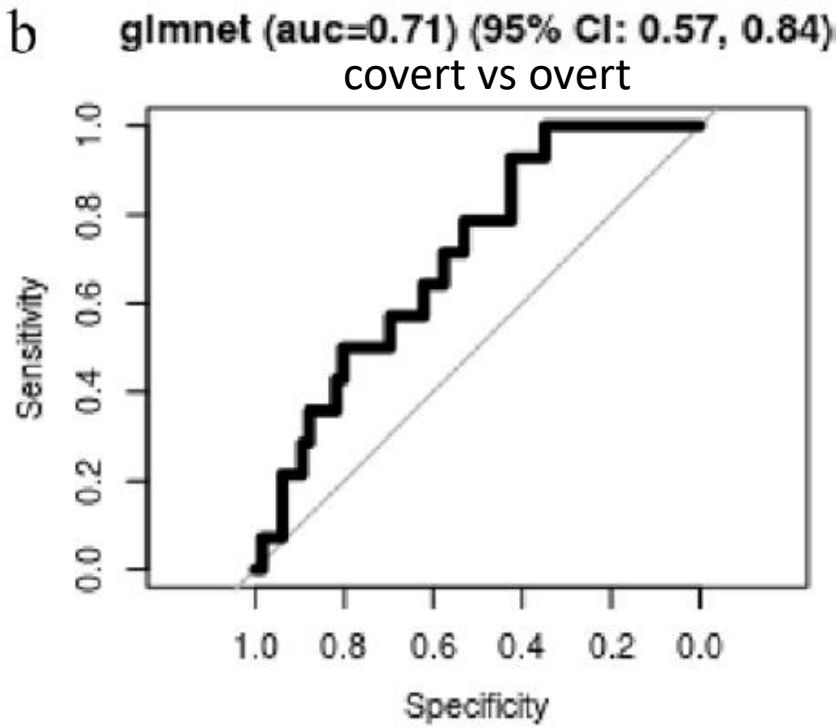
Breath Analysis
Liver disease

Arasaradnam et al. J Breath Res, 2016

- 22 patients with hepatic encephalopathy (HE; 13 covert, 9 overt)
- 20 healthy controls



Sens: 88% (73%-95%)
Spec: 68% (51%-81%)

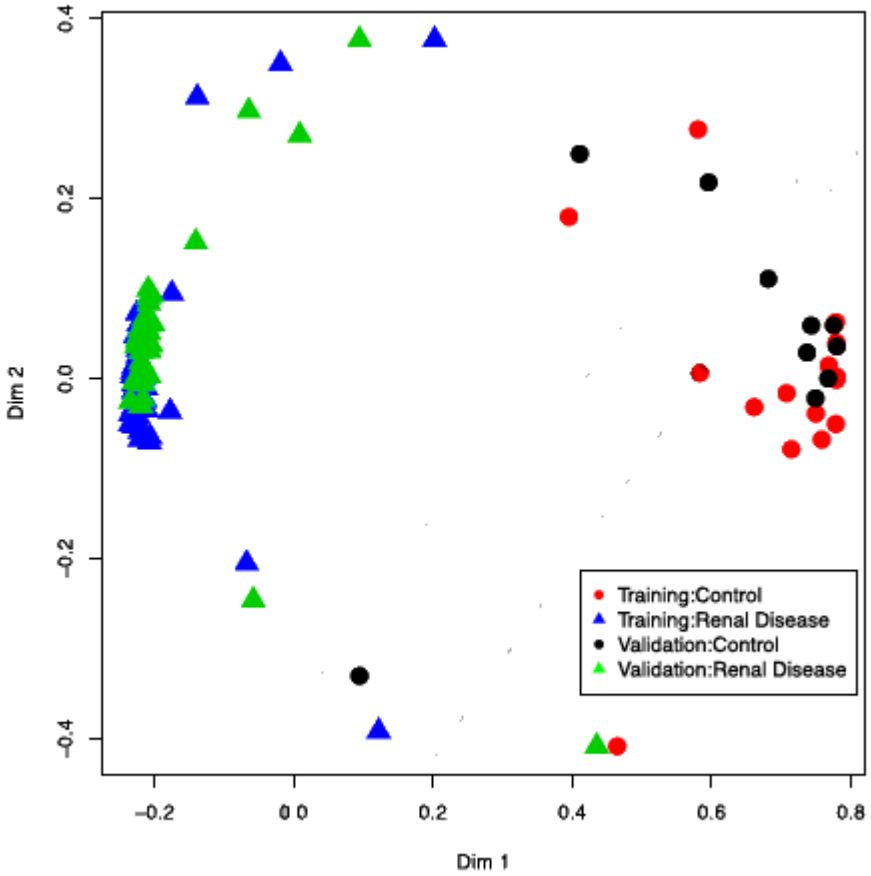


Sens: 88% (73%-95%)
Spec: 68% (51%-81%)

Breath Analysis
Renal failure

- 86 patients with end stage renal failure
- 26 healthy controls

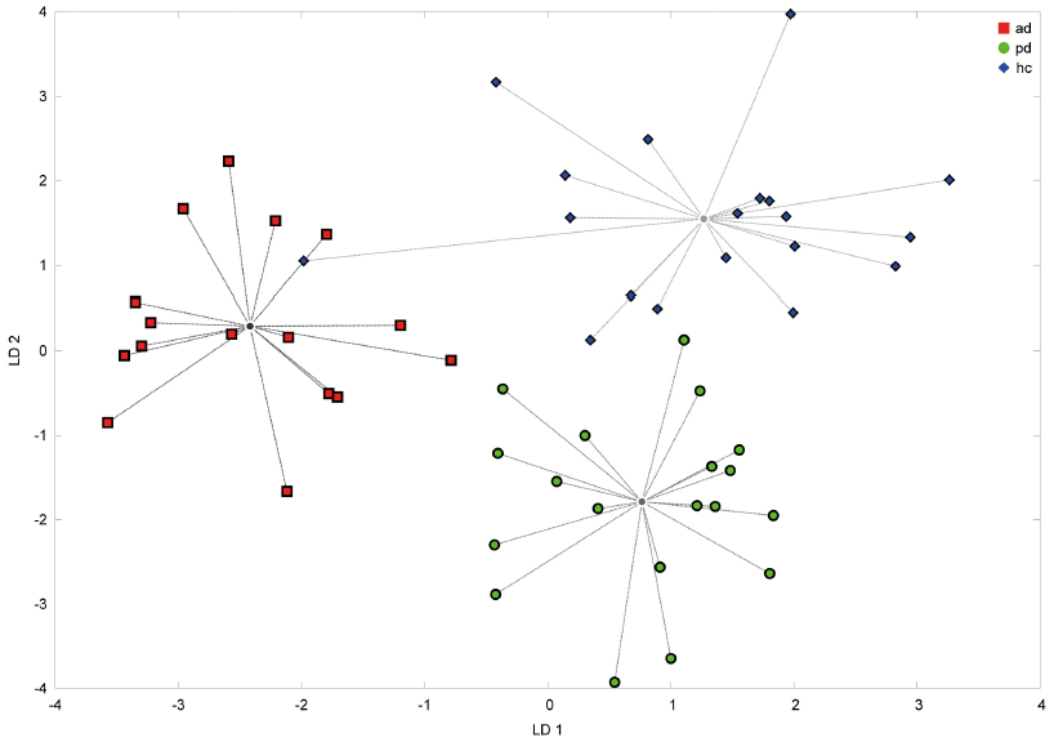
- Five VOCs:
  - Ammonia
  - Acetaldehyde
  - 2-propanol
  - $NO^{+}76$
  - $O_2^{+}50$



Demirjian et al. J Breath Res, 2017

Breath Analysis
Neurological disease

- 39 patients with Alzheimer's disease
- 16 patients with Parkinson's disease
- 35 healthy controls



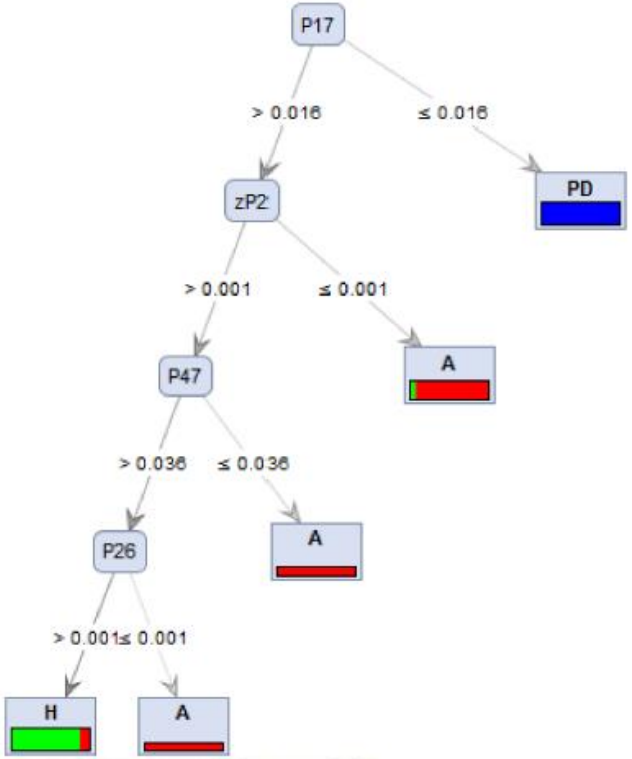
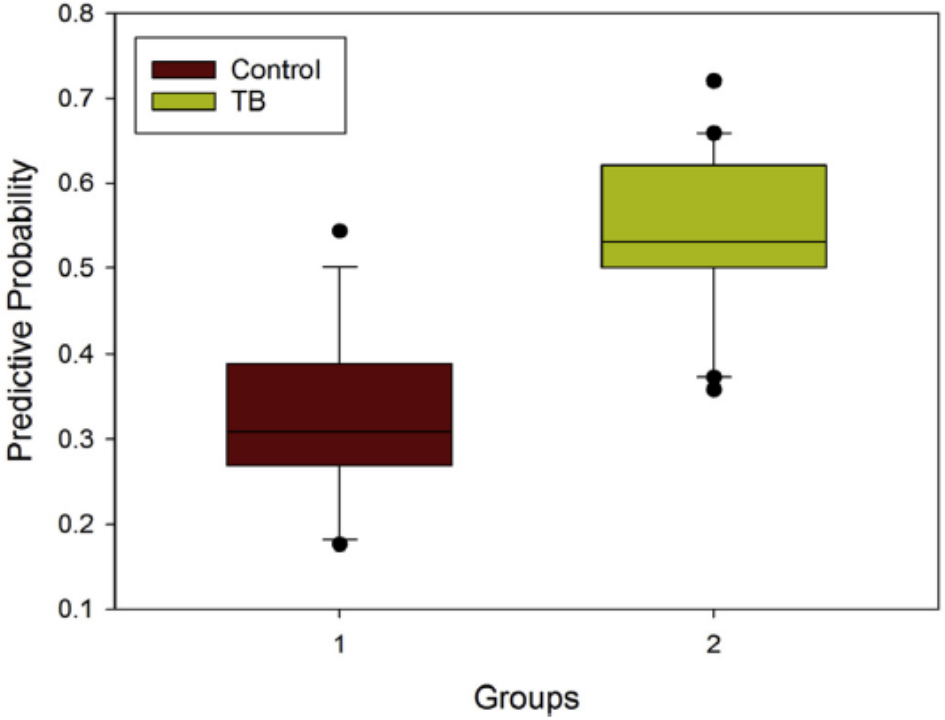


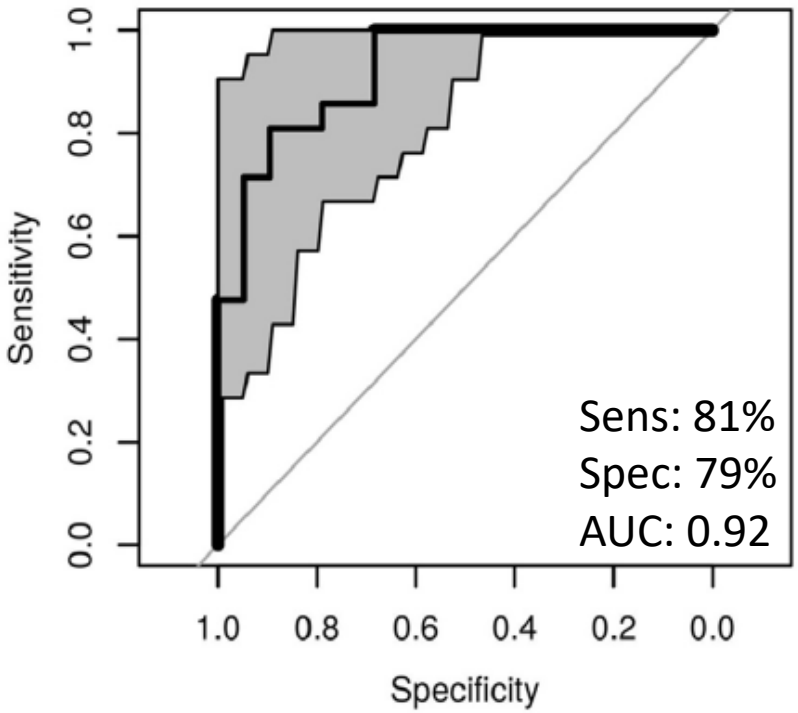
Fig 2. Decision tree of four variables measured using IMS. Exhaled breath from 21 AD, 16 PD patients and 16 HC was analysed using IMS. A decision tree based on four compounds is shown in Fig 2. Samples are grouped according to the means of the peak intensity of each compound, at which point, the maximum number of samples are classified correctly. Relative numbers of classified HC are green, and numbers of classified patients with AD are red. PD is marked in blue. Total numbers of classified samples are given for each compound. P denotes the concentration of a compound. Using a decision tree with four characteristics, the method shows a accuracy of 94% when differentiating patients with AD from HC. Considering PD/AD vs. HC, sensitivity of 95% and specificity of 94%, positive predictive value of 97%, negative predictive value of 88% were calculated.

Bach et al. Plos One, 2015

Breath Analysis
Infectious disease - tuberculosis

- *Mycobacterium tuberculosis*
- Sputum test: 62% sensitivity
- Breath:

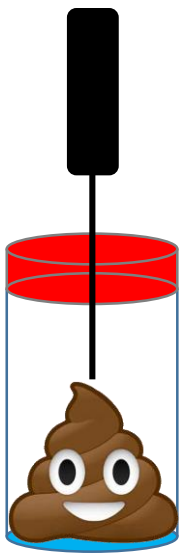


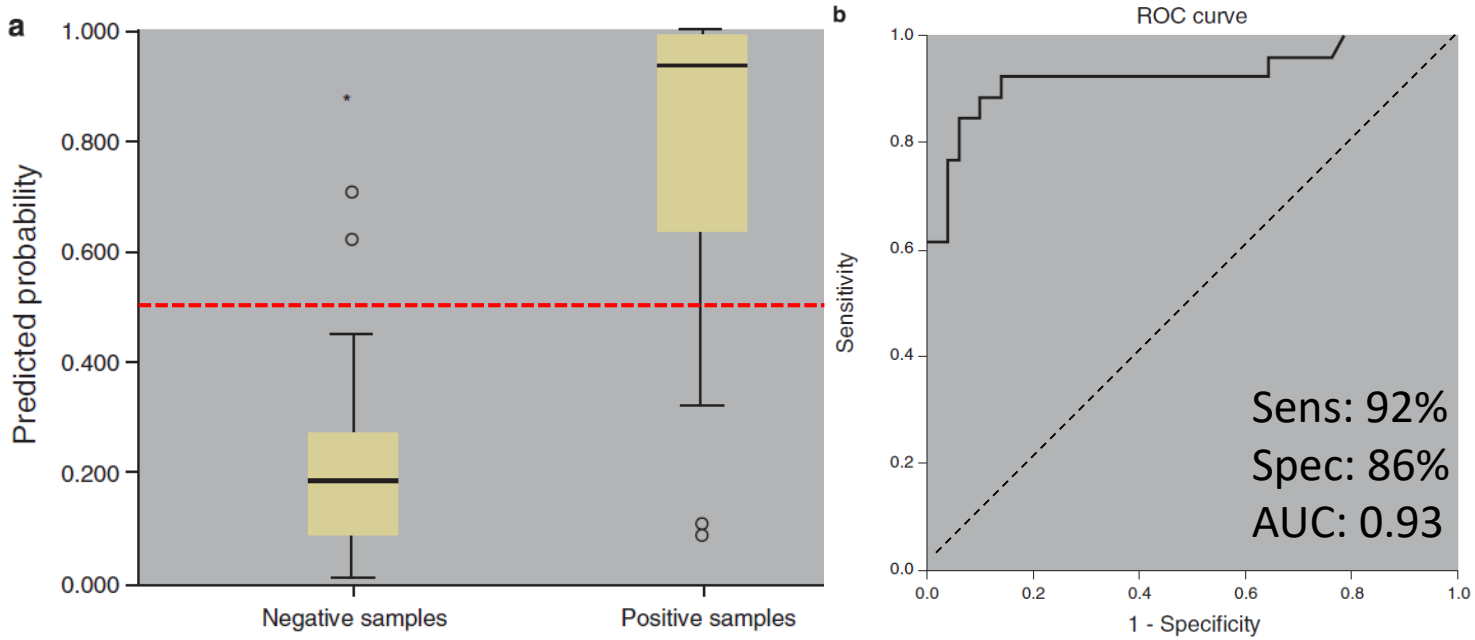


Sahota et al. Tuberculosis, 2016

VOC Analysis
Infectious disease – *C. difficile*

- 213 samples analysed
- 71 confirmed *C. difficile* positive microbiological evaluation



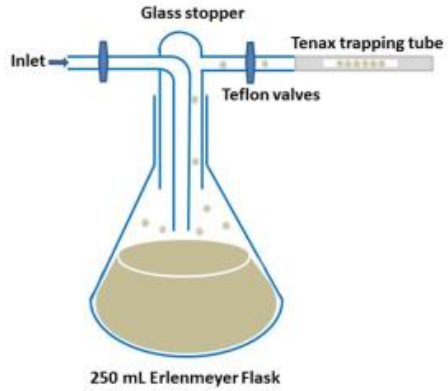


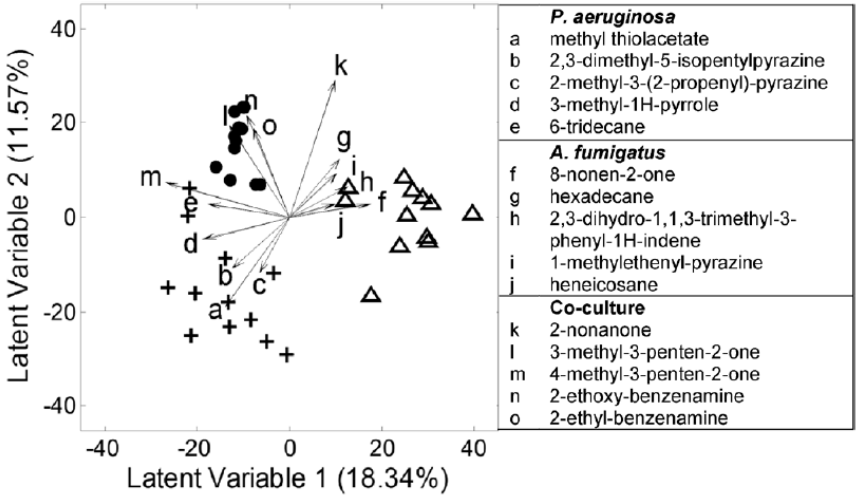
Bomers et al. Am J Gastrointesterol, 2015

Breath Analysis
Infectious disease – *Cystic fibrosis*

- 13 CF patients *S. aureus* +
- 5 CF patients *S. aureus* -
- Sens: 100%, spec: 80%

- Headspace mono- and coculture of *P aeruginosa* and *A fumigatus*





Neerincx et al. J Breath Res, 2016

Future Perspectives

- Challenges: technical

TABLE 2] Key Factors in Breath Collection and Handling

Category	Key Factors
Air sampling	Direct sampling
	Reusable collection bag with thorough cleaning
	Disposable collection bag
Air collection device	VOCs derived from collection device
	Disposable collection device
	Reusable collection device (cleaning agent VOCs)
Air collection method	Nasal/oral sampling
	Tidal breathing vs forced exhalation
	Exhalation after breath hold
	Forced exhalation
	Flow
Environmental influences	Baseline samples of environmental air
	Wash-out period by inspiratory VOC filter
Storage	Direct analysis
	Storage on sorbent tubes for prolonged stabilization of VOCs
	Storage conditions

VOC = volatile organic compound.

TASK FORCE REPORT
TECHNICAL STANDARD

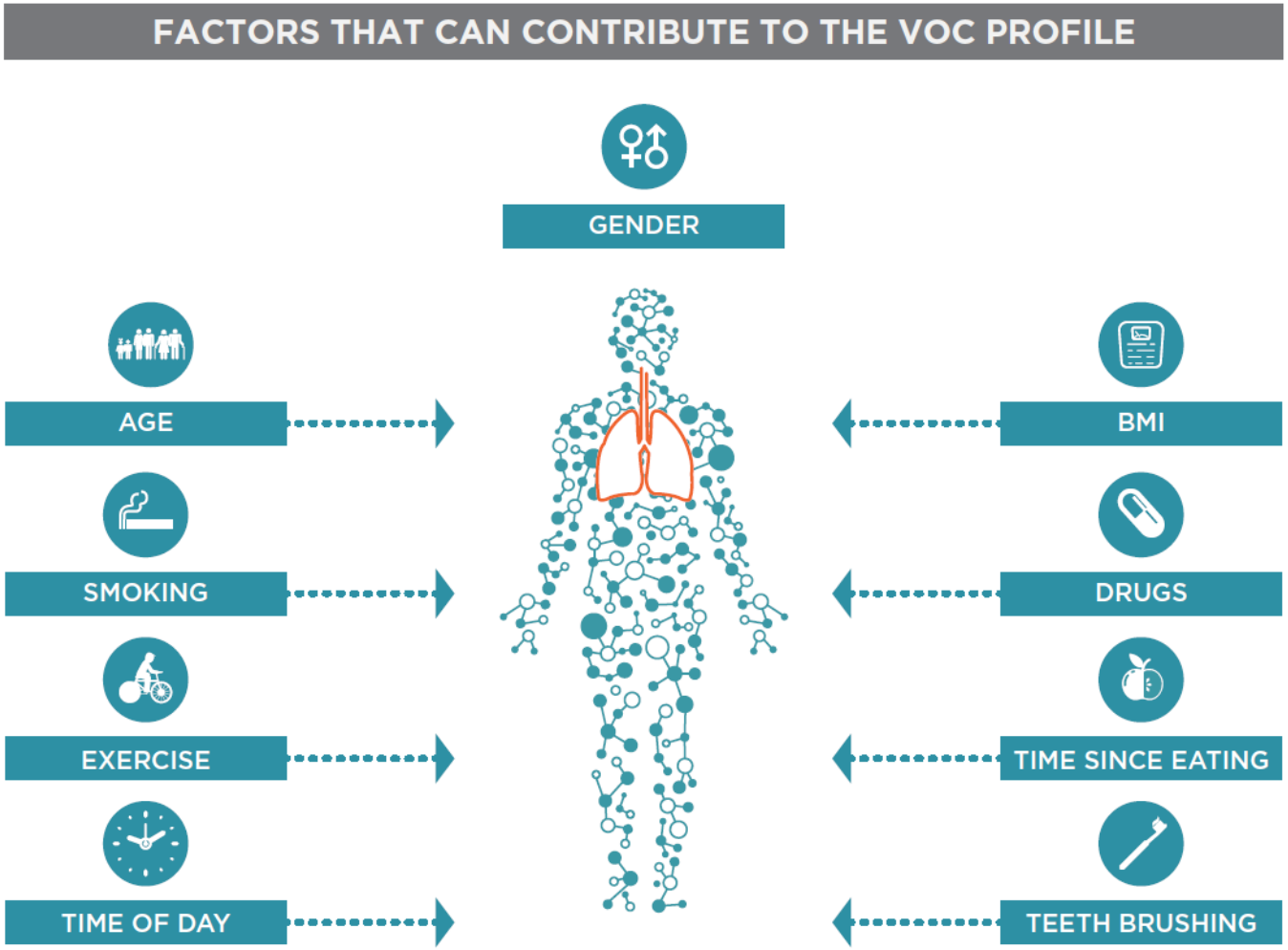
A European Respiratory Society technical standard: exhaled biomarkers in lung disease

Ildiko Horváth (task force co-chair)[1], Peter J. Barnes (task force co-chair)[2], Stelios Loukides (group chair)[3], Peter J. Sterk (group chair)[4], Marieann Högman (group chair)[5], Anna-Carin Olin (group chair)[6], Anton Amann[7], Balazs Antus[8], Eugenio Baraldi[9], Andras Bikov[10], Agnes W. Boots[11], Lieuwe D. Bos[12], Paul Brinkman[4], Caterina Bucca[13], Giovanna E. Carpagnano[14], Massimo Corradi[15], Simona Cristescu[16], Johan C. de Jongste[17], Anh-Tuan Dinh-Xuan[18], Edward Dompeling[19], Niki Fens[4], Stephen Fowler[20], Jens M. Hohlfeld[21,22], Olaf Holz[21], Quirijn Jöbsis[23], Kim Van De Kant[19], Hugo H. Knobel[24], Konstantinos Kostikas[25], Lauri Lehtimäki[26], Jon Lundberg[27], Paolo Montuschi[28], Alain Van Muylem[29], Giorgio Pennazza[30], Petra Reinhold[31], Fabio L.M. Ricciardolo[32], Philippe Rosias[19,33], Marco Santonico[30], Marc P. van der Schee[4], Frederik-Jan van Schooten[11], Antonio Spanevello[34], Thomy Tonia[35] and Teunis J. Vink[24]

Van der Schee *et al.* Chest. 2015

Future Perspectives

- Challenges: environment



Take Home messages

- VOC analyisis is promising for a plethora of applications
  - Breath
  - Headspace (skin, urine, stool, cell lines, tissue)
- No single biomarker fits all
  - Focus on combinations
  - Increase number of patients
- Standardisation needed
  - Sampling
  - Underpowered clinical trials
  - Current ERS technical standards on exhaled biomarkers
- Focus on combining techniques
  - Optimal information gathering
- Statistically challenging
  - High throughput
  - ‘omics’ approach

VOC analysis in health and disease