Maastricht University

The Detection of Primary Sclerosing Cholangitis by Fecal Headspace & Exhaled Breath Analyses

NUTRIM

KWF KANKER BESTRIJDING

TRANSCAN-2

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Background

In Primary Sclerosing Cholangitis (PSC) inflammation of the bile ducts results in accumulation of waste products in the liver, causing liver damage and cirrhosis. PSC is closely related to Inflammatory Bowel Disease (IBD). Approximately 8% of IBD patients develop PSC, and 75% of PSC patients develop IBD. To provide proper care, PSC and IBD patients are frequently invasively screened (e.g. using colonoscopy, liver function tests, liver biopsy, see Table 1), highlighting a need for non-invasive screening tests to screen and monitor both diseases. In this study we investigate the utility of Volatile Organic Compounds (VOCs) analysis in fecal headspace and exhaled breath to distinguish IBD from PSC.

Objective

Distinguishing Primary Sclerosing Cholangitis from Inflammatory Bowel Disease using Volatile Organic Compounds in fecal headspace and exhaled breath.

Table 1: Imaging modalities to detect PSC.

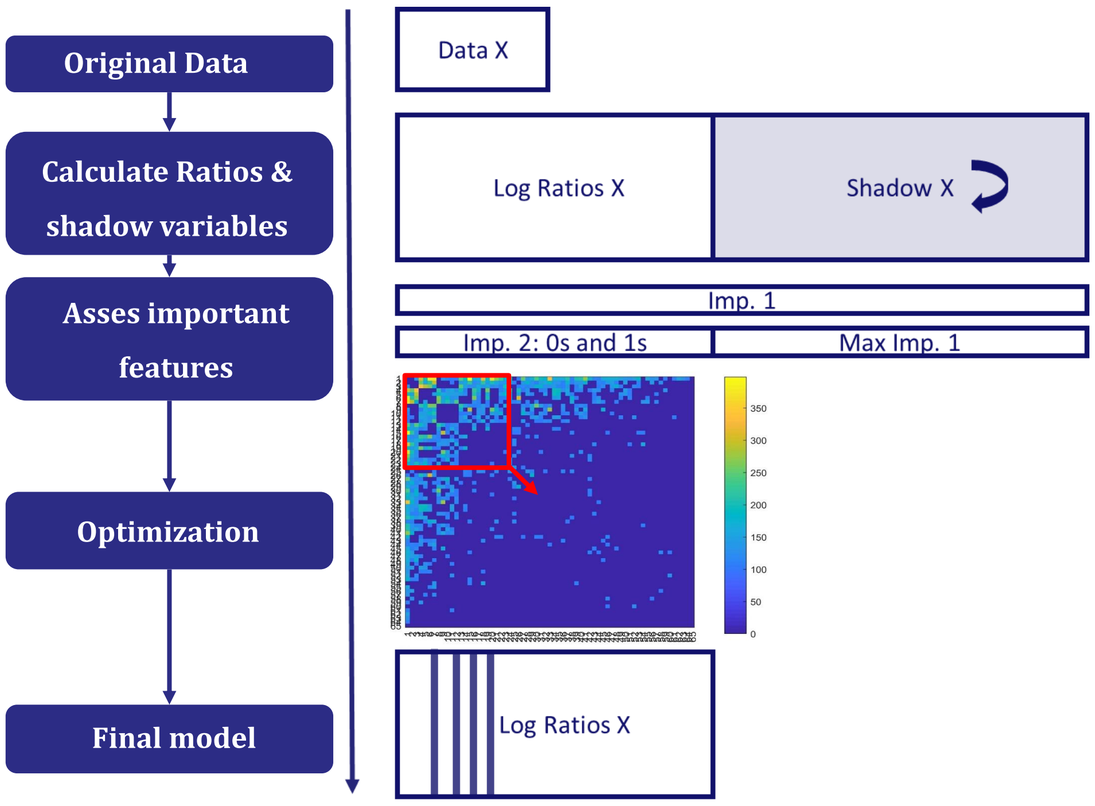
modality	Accuracy	Disadvantage
MRCP	90%	Not early stage
ERCP	97%	Not early stage
Fibroscan	-	Only pregression, not onset of disease
Biopsy	“Gold Standard”	Non-specific & heterogeneously distributed features.

Methods

Sampling: Fecal (0.25 grams) headspace was trapped on Thermal desorption Tubes using Microchamber Thermal Extractor, using 5 min equilibration (defrost) time, 5 min sampling time, and 15 min dry purging. Exhaled breath analysis using ReCIVA breath sampler.

Data-Analysis: High variation in fecal VOC profiles prohibits data normalization. To overcome this, we applied Log Ratios & Advanced Interpretation.

Predictive modelling of PSC versus IBD: Population: PSC+IBD (n=16 / 31); PSC (n=8 / 16); IBD (n=49 / 94). Targeted (62 VOCs) & untargeted. Breath: targeted (based on literature search). Modelling by Random Forest (RF) and Data Fusion by Proximity Stacking for increased accuracy.

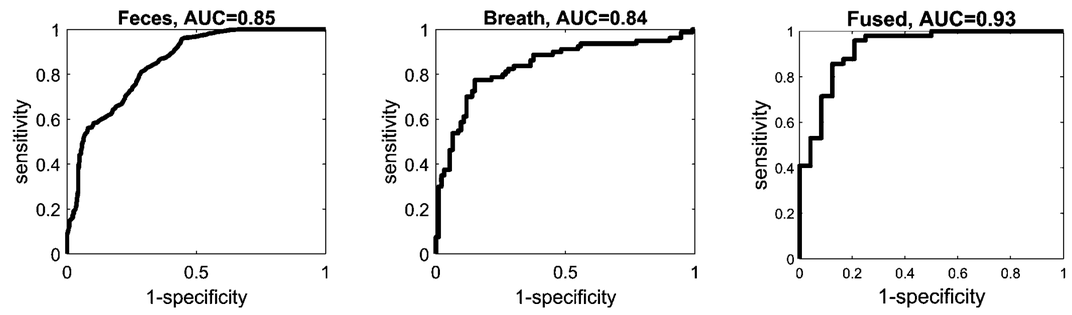


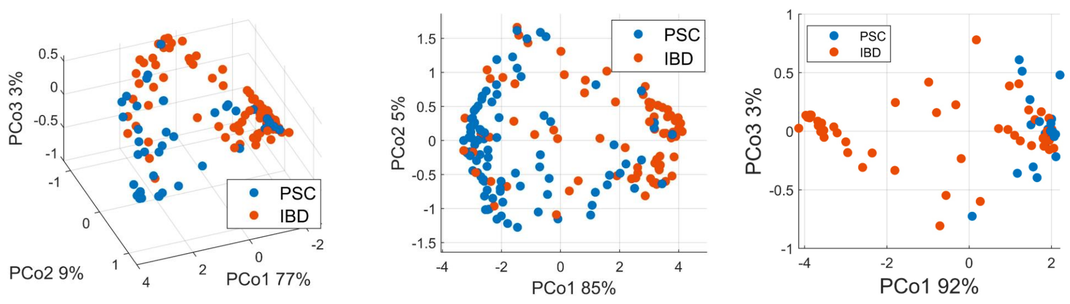
Figures Data-Analysis (2): The application of Log Ratios for predictive modelling.

Table 2: Selected fecal VOCs of targeted set.

VOCs	Origin
Phenol	**Not beneficial** fermentation of proteins
Styrene	Not beneficial: microbiome, **exposure**, diet, disease activity (IBD).
Indole	Beneficial: **tight junctions, anti-inflammatory.**
2-Hexanone	**IBD**, Microbiome, **signaling for inflammation**
Isobutyric Acid	Not beneficial: **Cause leakage (i.e. pathogens, metabolites)** into blood stream and lowgrade systemic inflammation.
Nonanal	Signaling VOC for **inflammation**

Results





Figures predictive modelling (3): Feces: Sensitivity=78%, Specificity=75%;

Breath: Sensitivity=78%, Specificity=80% Fused: Sensitivity=86%, Specificity=88%

Conclusion

- ***The Microchamber is a High-Throughput method for fecal VOC profiling, but data characteristics show it’s suboptimal.***
- ***PSC can be differentiated from IBD using fecal VOCs. When fused with breath provides very high accuracy. Larger multi-centre populations are needed to prospectively investigate early stage diagnostics. Results do point towards involvement of microbiome.***
- ***Future: Investigate relationship of Volatiles in fecal headspace and in exhaled breath.***

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