Plasma metabolites as first-line responders in lung cancer

Plasma metabolite biomarkers for improved lung cancer diagnosis in patients with solitary pulmonary nodules

Jill Meynen[1] ; Peter Adriaensens[2] ; Maarten Criel[1,3] ; Karolien Vanhove[1,4,5] ; Wouter Marchal[6] ; Liesbet Mesotten[1,7] ; Elien Derveaux[2]

1 Faculty of Medicine and Life Sciences, Hasselt University, Hasselt
2 Applied and Analytical Chemistry, NMR Group, Institute for Materials Research (imo-imomec), Hasselt University, Hasselt
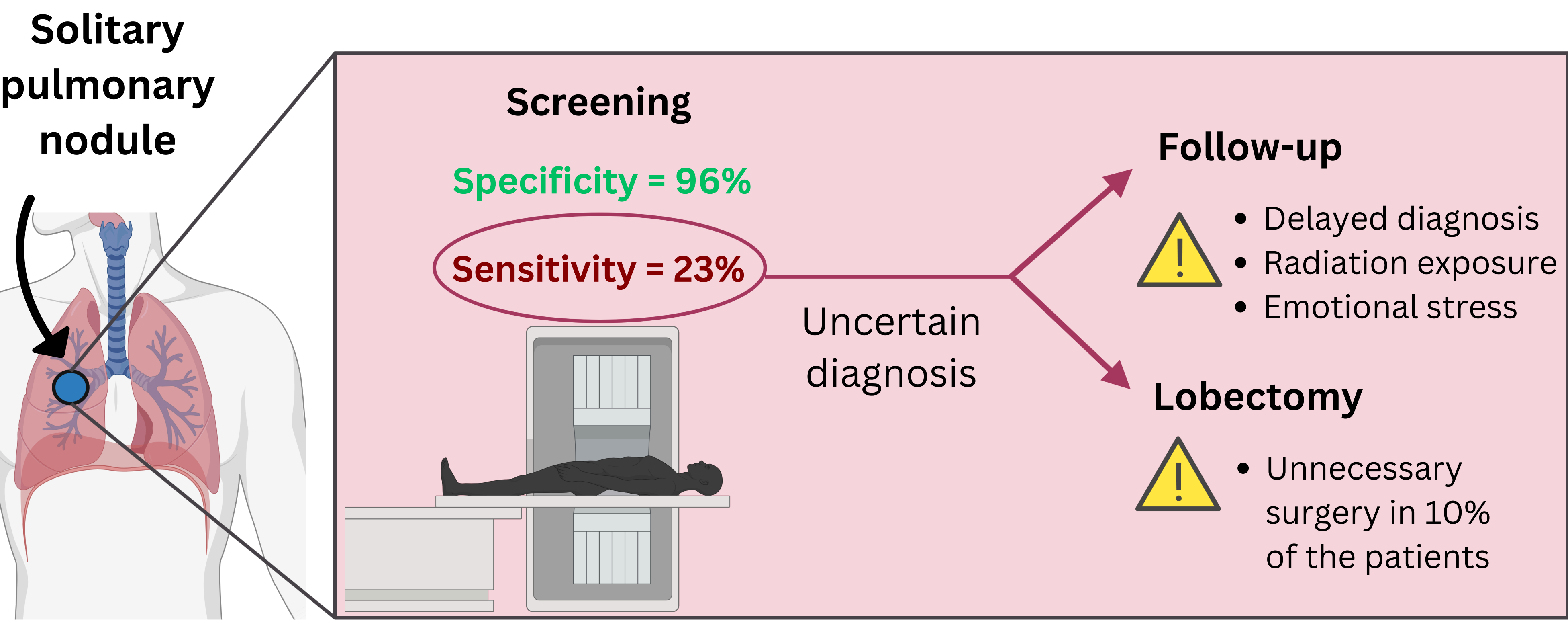3 Department of Respiratory Medicine, Ziekenhuis Oost-Limburg, Genk
4 Department of Respiratory Medicine, University Hospital Leuven, Leuven
5 Department of Respiratory Medicine, Algemeen Ziekenhuis Vesalius, Tongeren
6 Applied and Analytical Chemistry, Institute for Materials Research (imo-imomec), Hasselt University, Hasselt
7 Department of Nuclear Medicine, Ziekenhuis Oost-Limburg, Genk

Problem

Solitary pulmonary nodule

Screening

Specificity = 96%

Sensitivity = 23%

Uncertain diagnosis

Follow-up
- Delayed diagnosis
- Radiation exposure
- Emotional stress

Lobectomy
- Unnecessary surgery in 10% of the patients

PET-CT is an important technique in lung cancer detection and staging. Besides the fact that almost every lesion is detected, this technique often **fails to discriminate benign from malignant PET-positive solitary pulmonary nodules (SPNs)**. This results in prolonged follow-up, delayed diagnosis, and even unnecessary surgery in at least 10% of the patients.
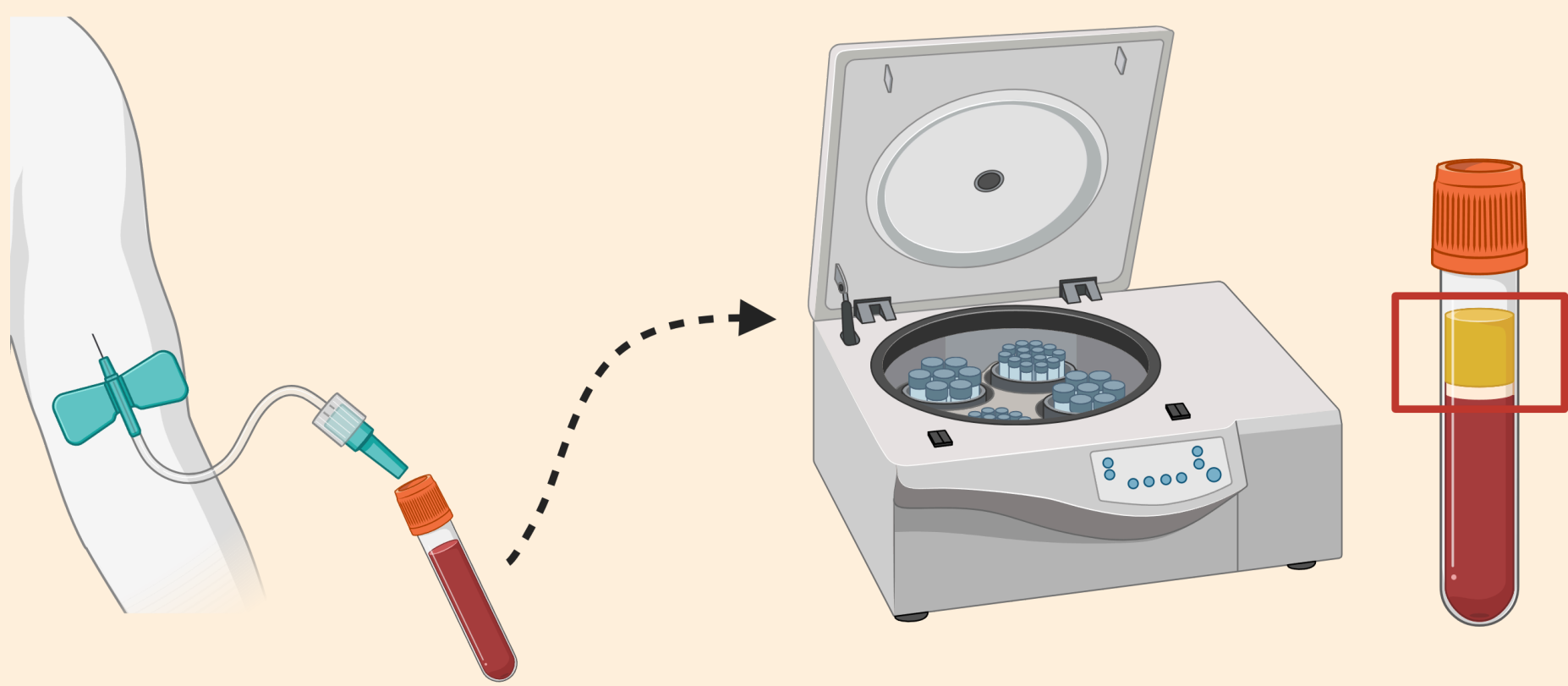
Solution

Potential plasma biomarkers

Plasma metabolites
- Amino acids
- Organic acids
- Sugars
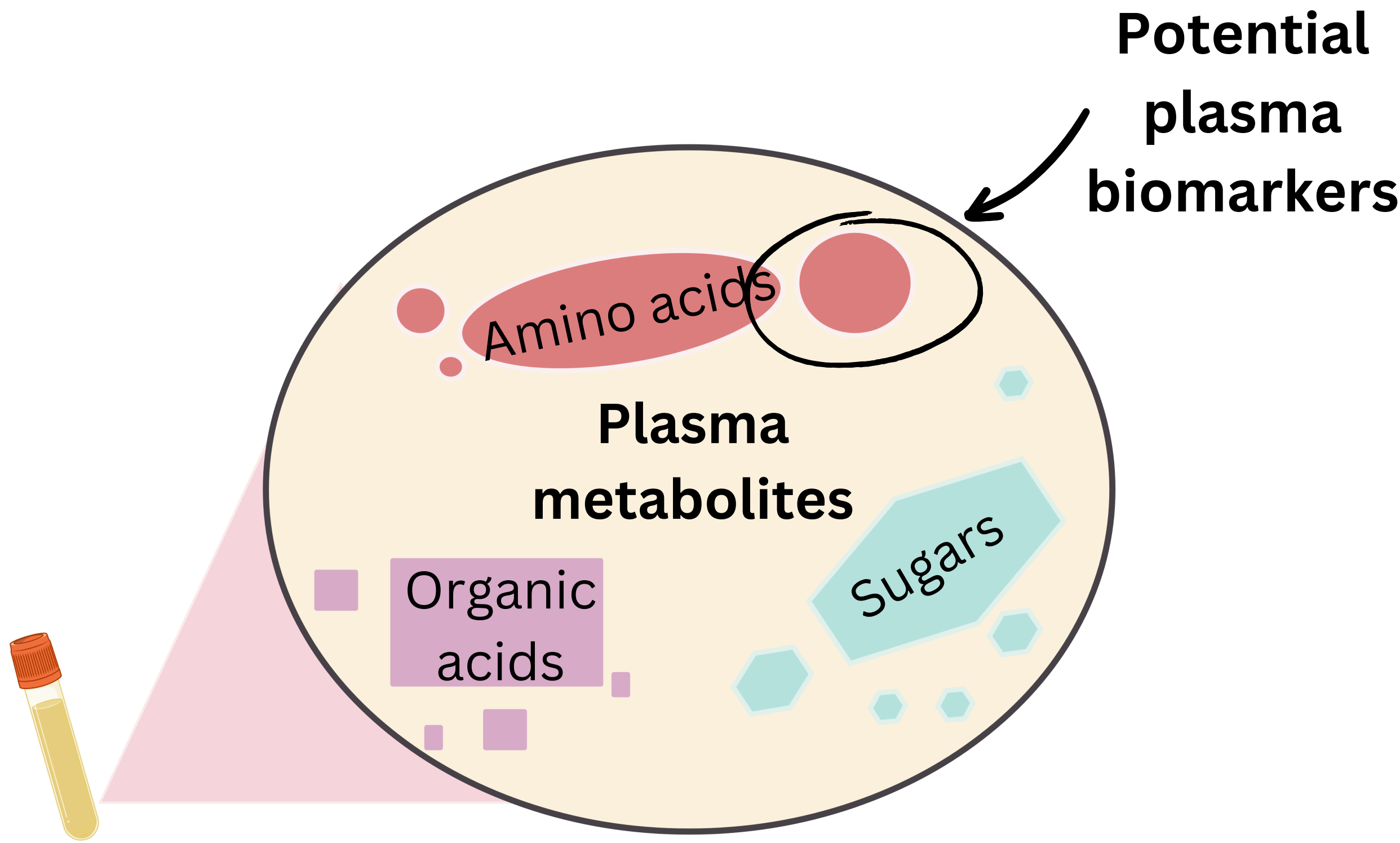
This research therefore aims to use **plasma metabolite biomarkers to discriminate between benign and malignant PET-positive SPNs.** The results on this poster will focus on the development of a **RP-HPLC method to detect plasma amino acids.**
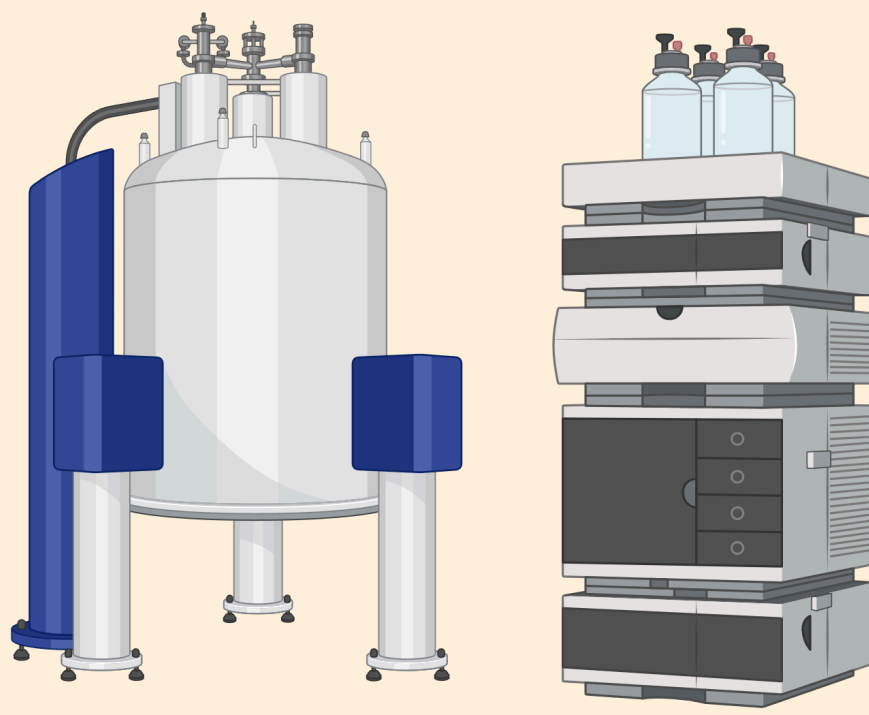
Methods
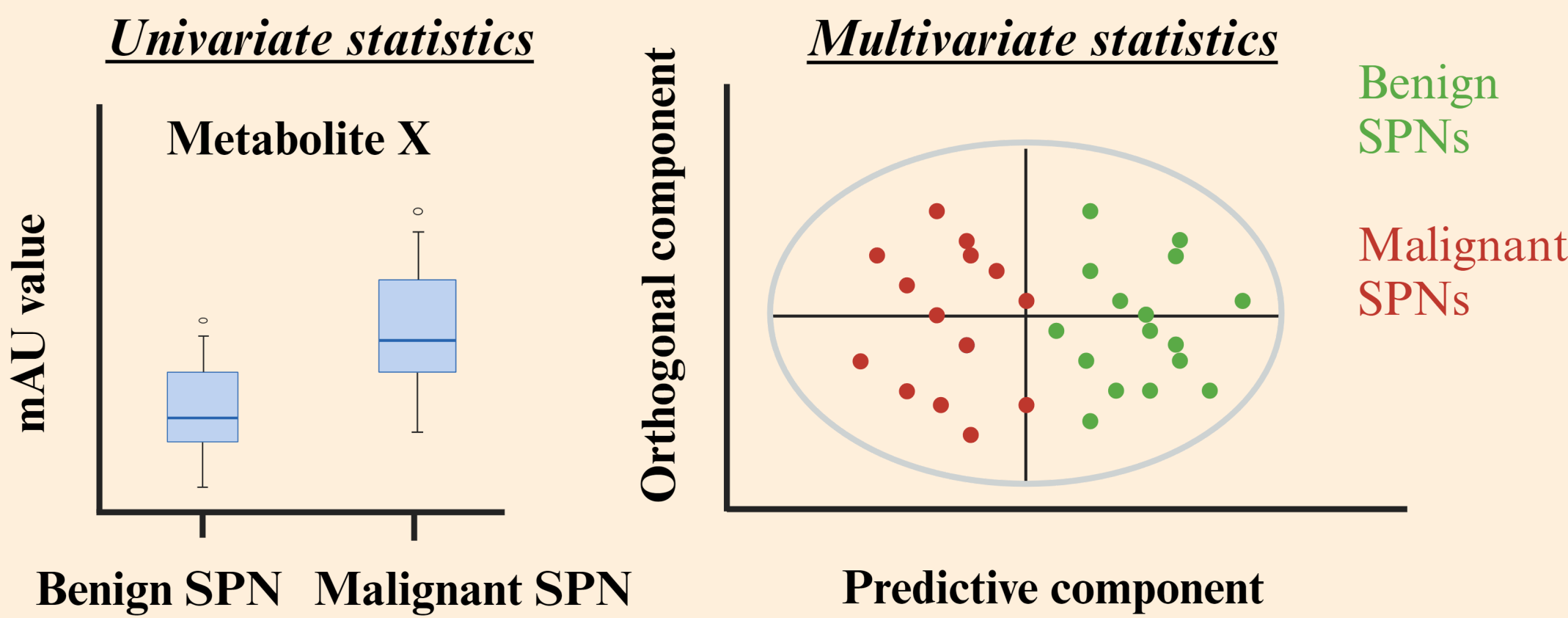
I. Plasma collection

Fasted blood samples are collected from all participants and plasma is isolated for further analyses. Samples are stored at -80 °C by UBiLim.

II. ^{1}H-NMR & HPLC analysis

Plasma samples are analysed with ^{1}H-NMR and HPLC. Two HPLC methods will be developed: one to detect the amino acids, one to detect the organic acids.

III. Statistics

Univariate statistics

Metabolite X

mAU value

Benign SPN   Malignant SPN

Multivariate statistics

Benign SPNs
Malignant SPNs

Orthogonal component

Predictive component

Univariate statistics (unpaired T-test or Mann-Whitney U test) will be performed for all metabolites in the HPLC chromatogram. Multivariate statistics (OPLS-DA) will be performed for all metabolites in the ^{1}H-NMR spectrum.

Results

HPLC method amino acid analysis
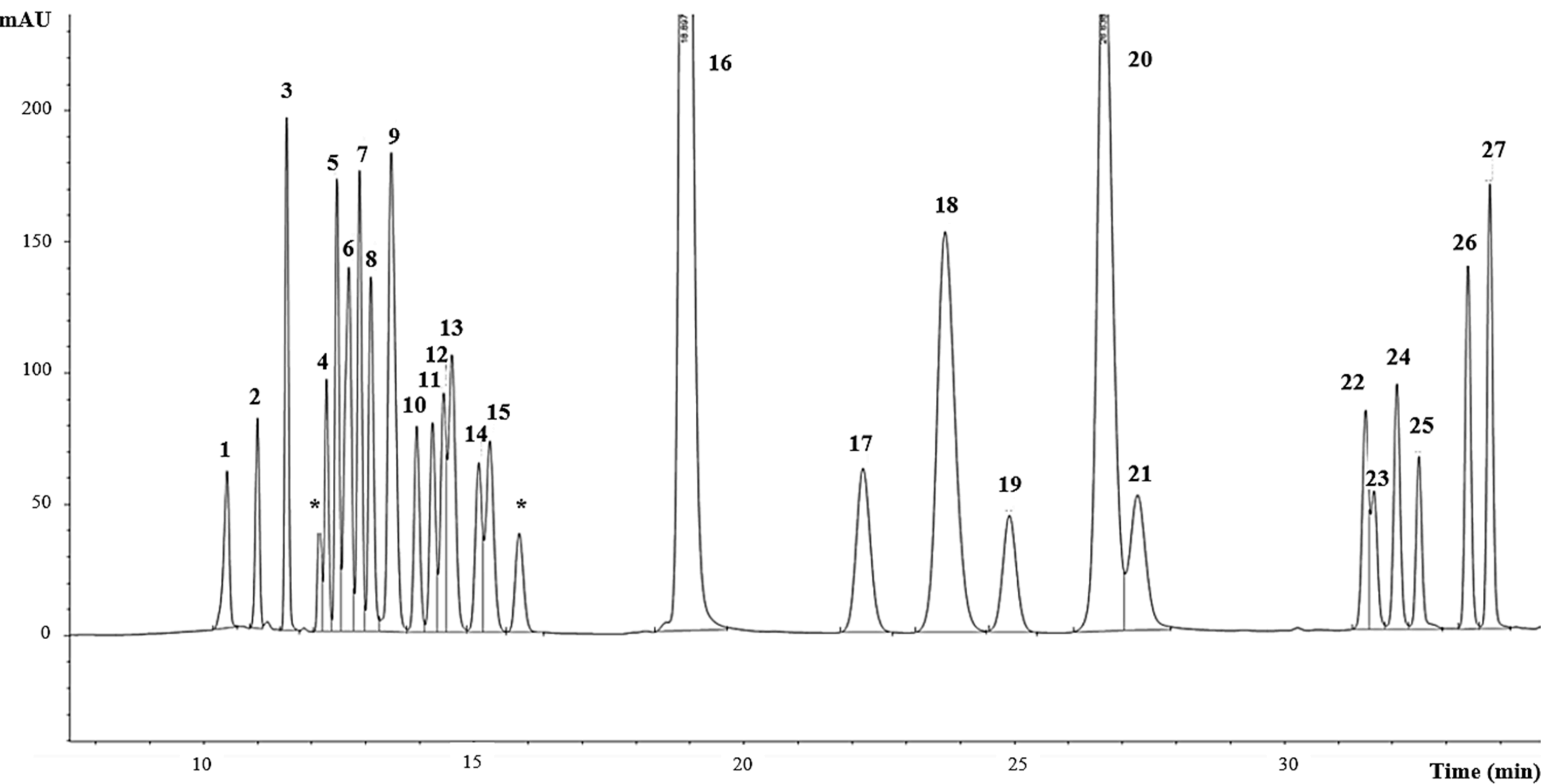
1: Aspartic acid; **2:** Glutamate; **3:** 3-OH-proline; **4:** Asparagine; **5:** Serine; **6:** Glutamine; **7:** Glycine; **8:** Histidine; **9:** Arginine; **10:** Threonine; **11:** Taurine; **12:** Alanine; **13:** 1-Methylhistidine; **14:** 3-Methylhistidine; **15:** Proline; **16:** AMQ; **17:** Tyrosine; **18:** Cysteine & Cystine; **19:** Valine; **20:** Norvaline (IS); **21:** Methionine; **22:** Leucine; **23:** Ornithine; **24:** Lysine; **25:** Isoleucine; **26:** Phenylalanine; **27:** Tryptophan. *Represent non-identified signals.

Conclusion

The HPLC method developed to analyse amino acids in plasma represents a crucial step towards identifying potential **plasma biomarkers**. While PET-CT remains invaluable in lung cancer detection, its inability to differentiate **between benign and malignant SPNs** creates a need for complementary diagnostic tools.

By combining plasma biomarker analysis with PET-CT, we aim to improve diagnostic accuracy, reduce unnecessary surgery, and improve patient outcomes. Future studies will focus on the validation and identification of specific biomarkers to further refine this approach.
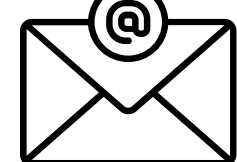
jill.meynen@uhasselt.be