



Metabolic phenotyping by ^1H -NMR spectroscopy to detect lung cancer via a simple blood sample

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Content

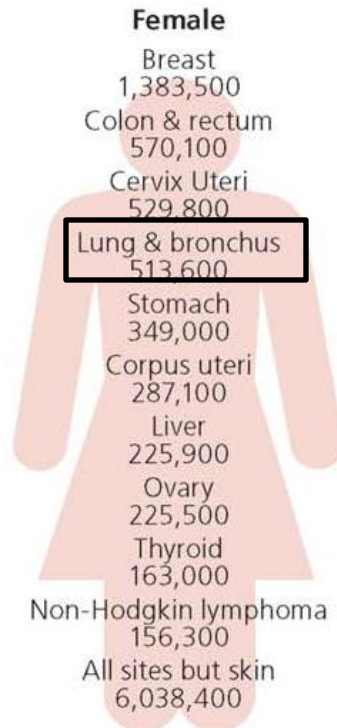
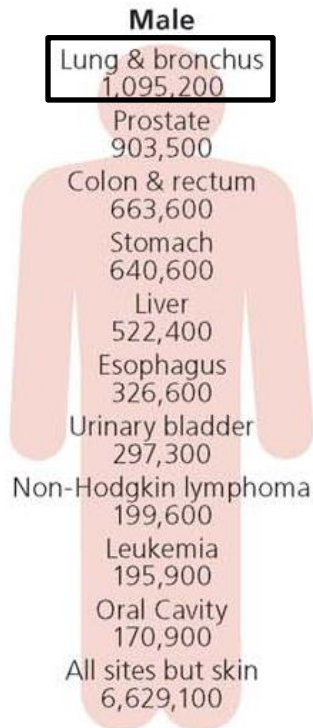
- Lung cancer
- Research question and methodology
- Results
- Future perspectives

Content

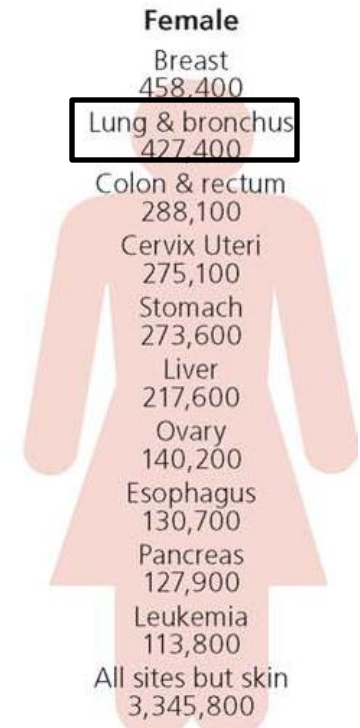
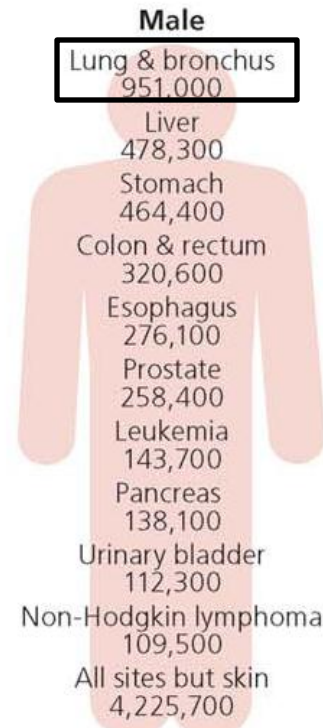
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Cancer – Worldwide

New cancer cases

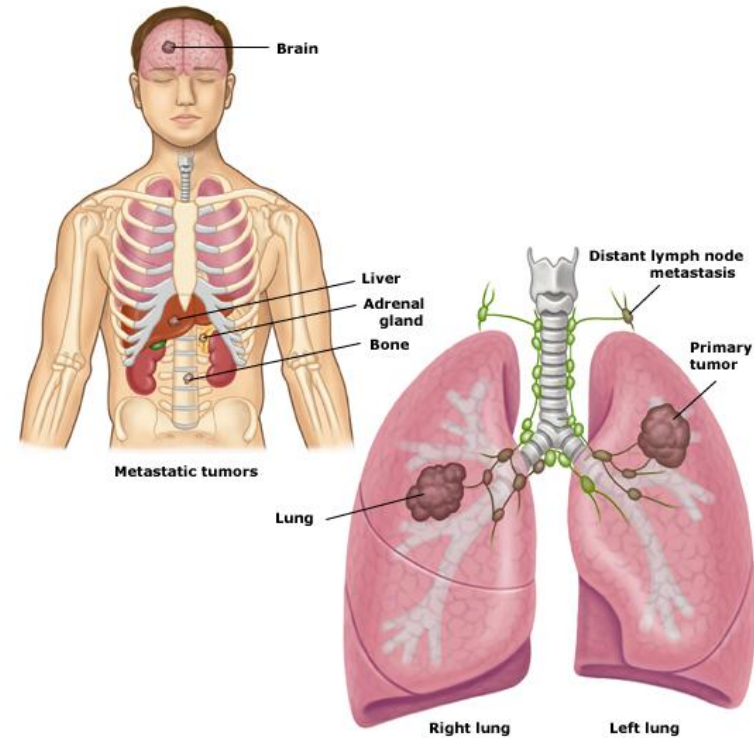


New cancer deaths



Lung cancer

- Average 5-year survival rate of $\pm 15\%$
- Often diagnosed in a metastatic stage
- Harmful and expensive chemotherapies



Link between tumor stage and prognosis

FIGURE 70 - LUNG CANCER: RELATIVE SURVIVAL BY STAGE IN MALES (BELGIUM, 2004-2008)

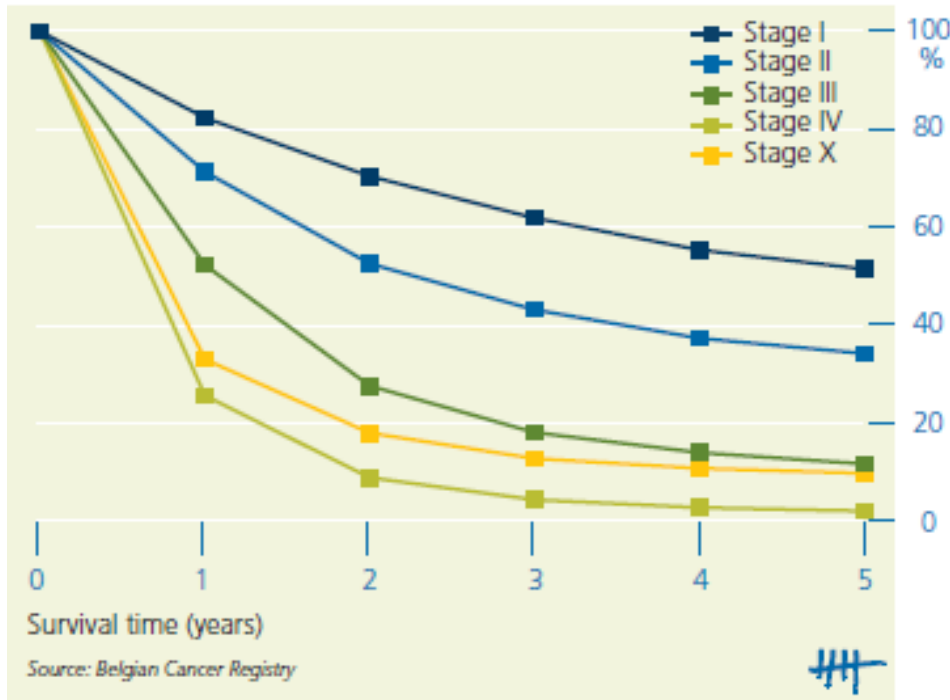
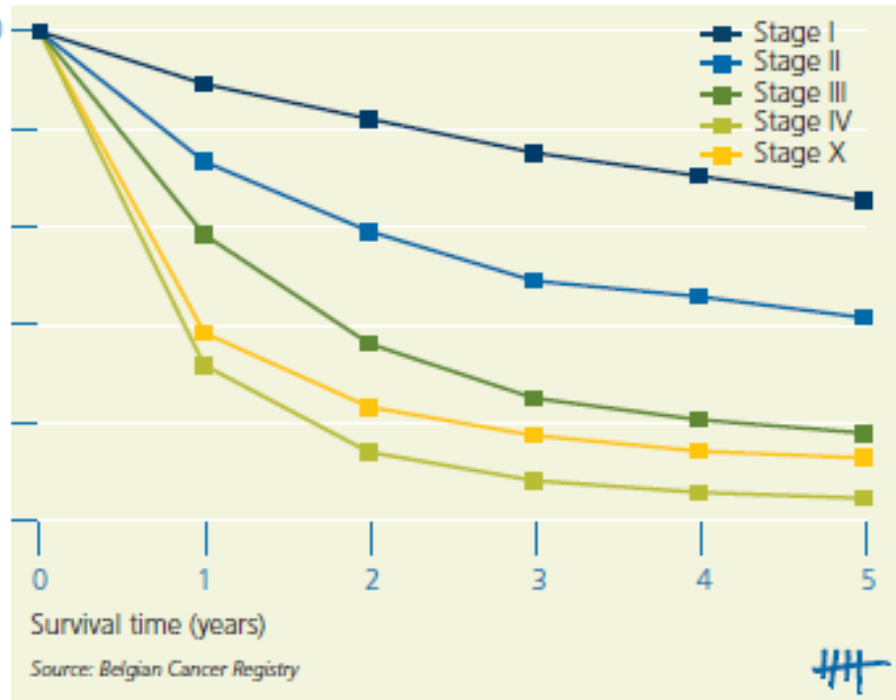


FIGURE 71 - LUNG CANCER: RELATIVE SURVIVAL BY STAGE IN FEMALES (BELGIUM, 2004-2008)



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Research question

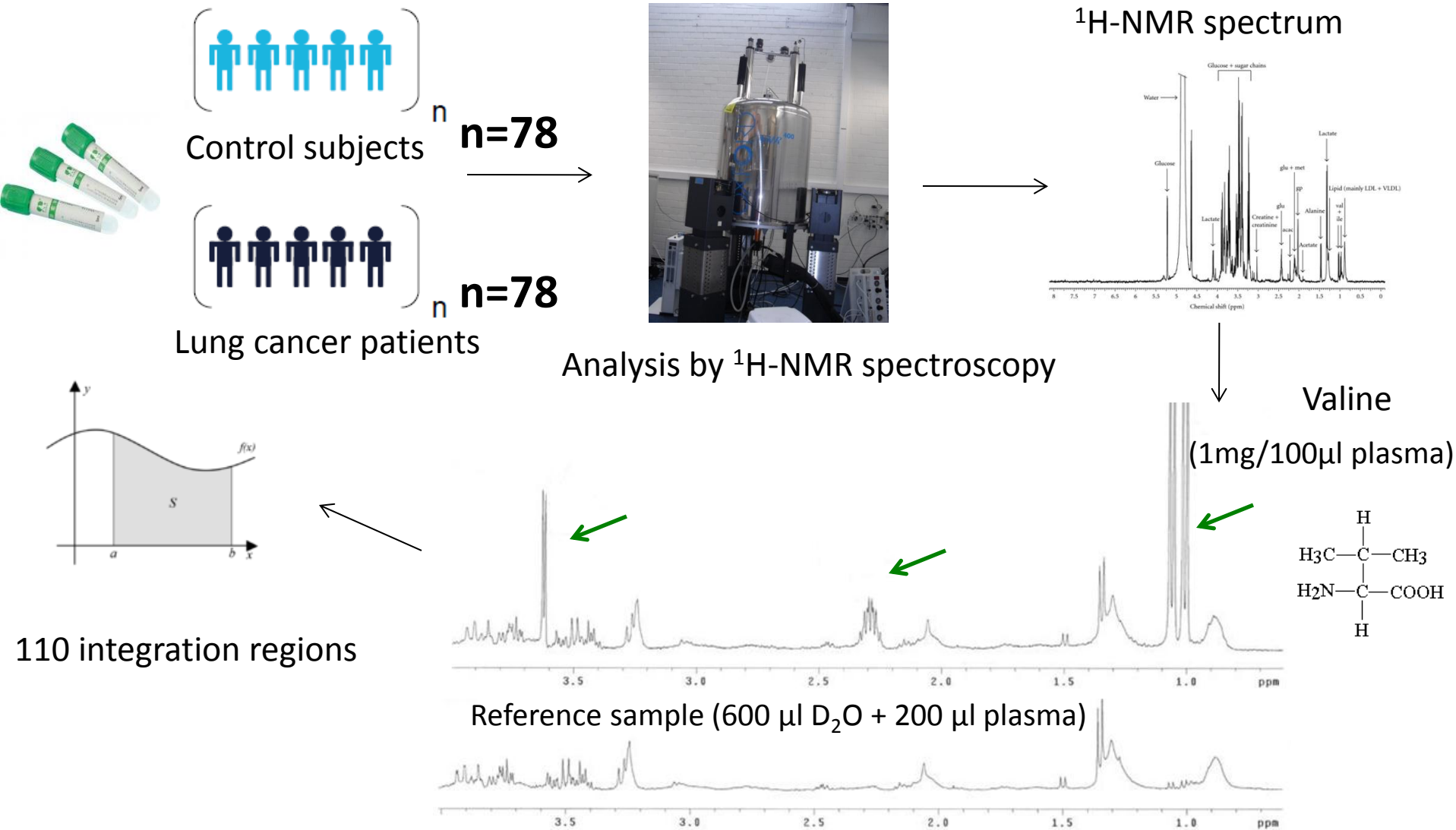
- Problem:

Urgent need for effective methods to detect lung cancer in an early stage

- Research question:


Does the analysis of the metabolite composition of blood plasma by ^1H -NMR spectroscopy allows to detect lung cancer?

Research methodology



Research methodology



 n **n=78**

Control subjects

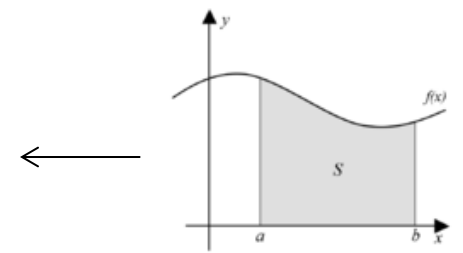
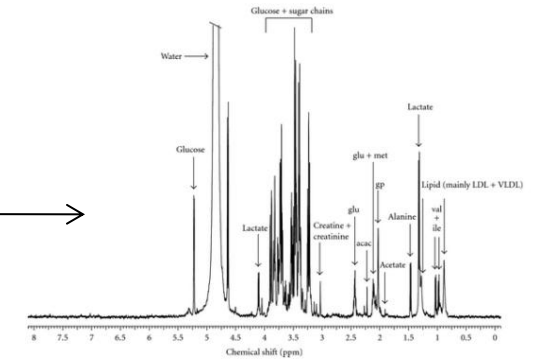
 n **n=78**

Lung cancer patients



Analysis by $^1\text{H-NMR}$ spectroscopy

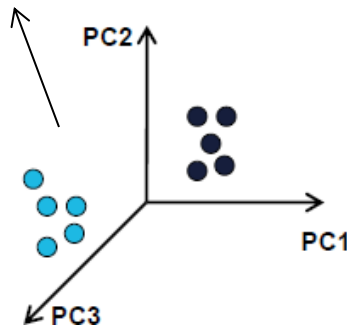
$^1\text{H-NMR}$ spectrum



110 integration regions (IR)

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
IR Value 1										
IR Value 2										
IR Value 3										
IR Value 4										
IR Value 5										
IR Value 6										
...										

Metabolic interpretation



Statistical analyses

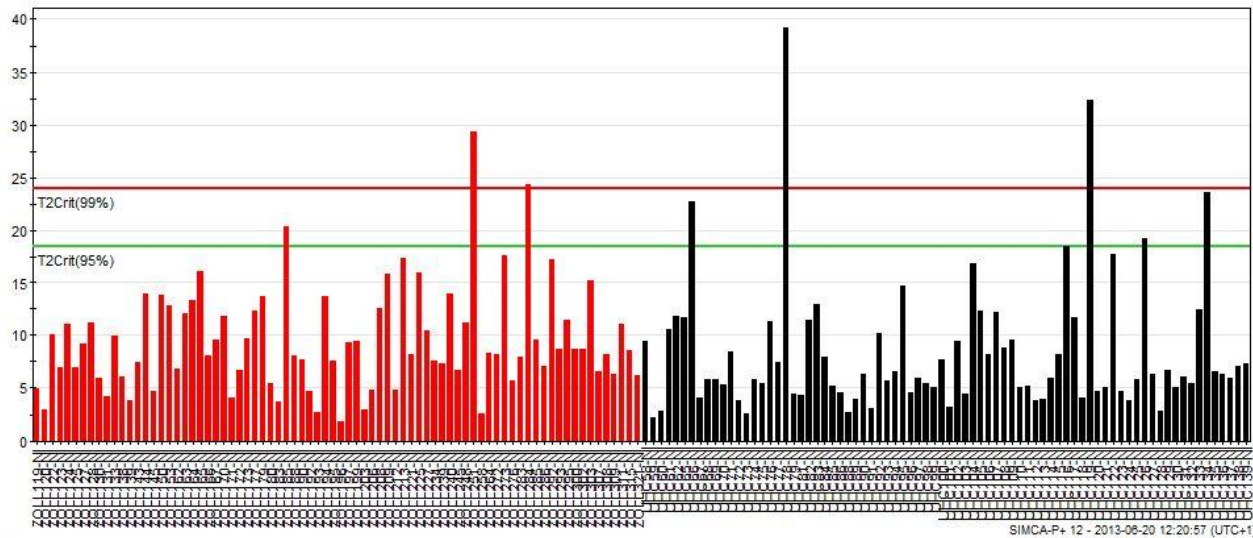
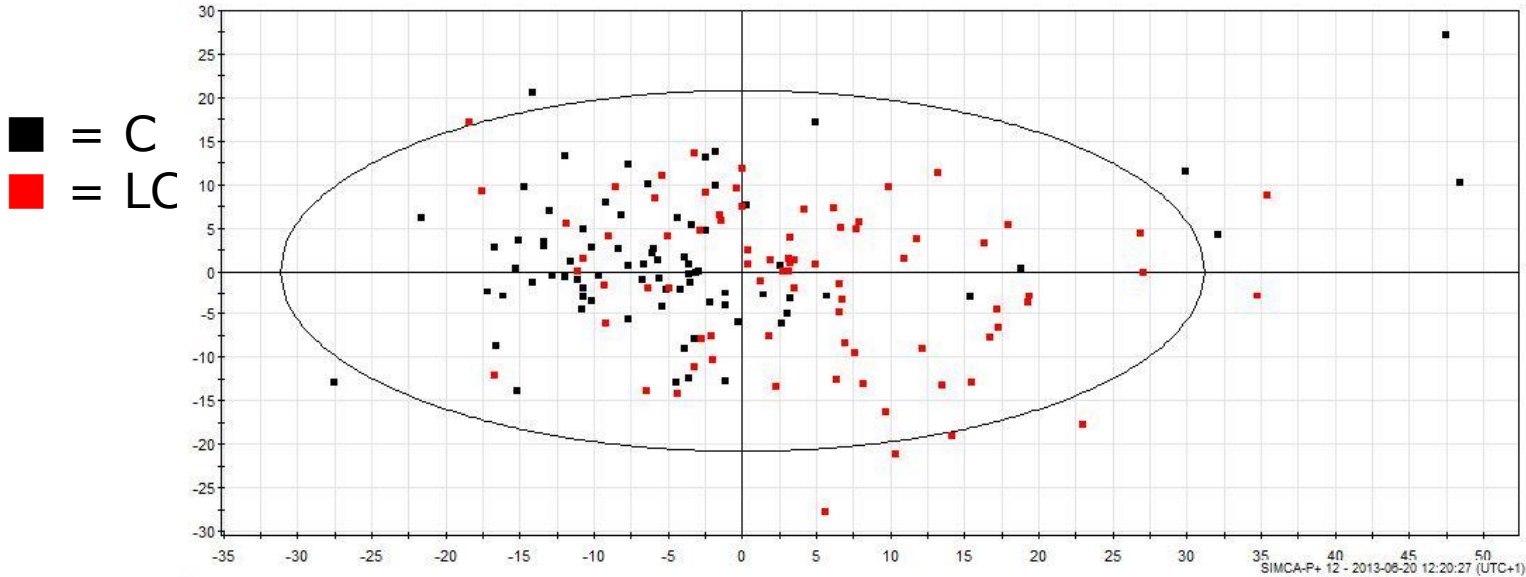
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Subject characteristics

	Lung cancer (LC) patients (■)	Control (C) subjects (■)
Number	78	78
Gender	Male: 53 (67%) Female: 26 (33%)	Male: 45 (58%) Female: 33 (42%)
Average age	68 ± 9	64 ± 13
Smoking habits	Active: 50 Stopped > 6m: 25 Never: 3	Active: 19 Stopped > 6m: 27 Never: 32

PCA and search for outliers

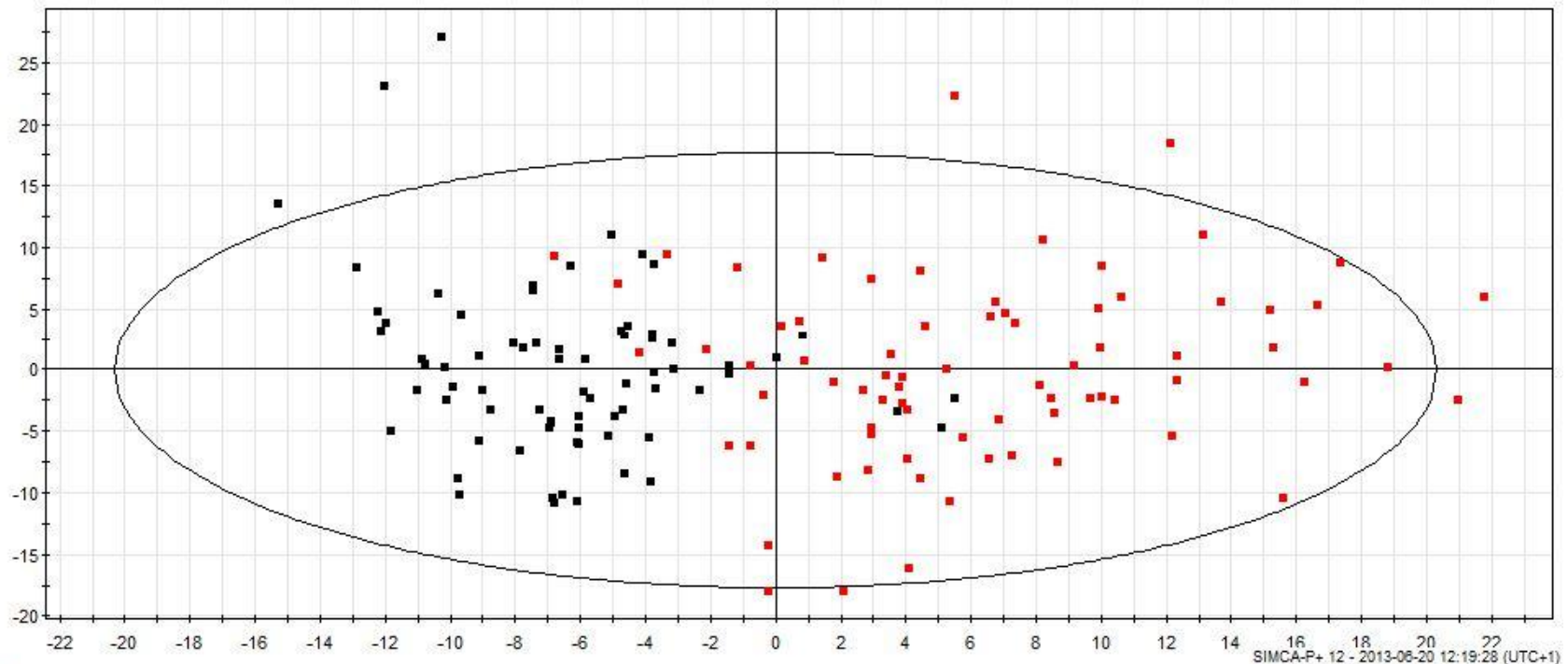


Hotelling's T_2 range plot shows 8 outliers: 3LC and 5C

OPLS-DA with all **110** integration regions

After

- Log transformation for not normally distributed variables
- Pareto scaling
- Removal of outliers



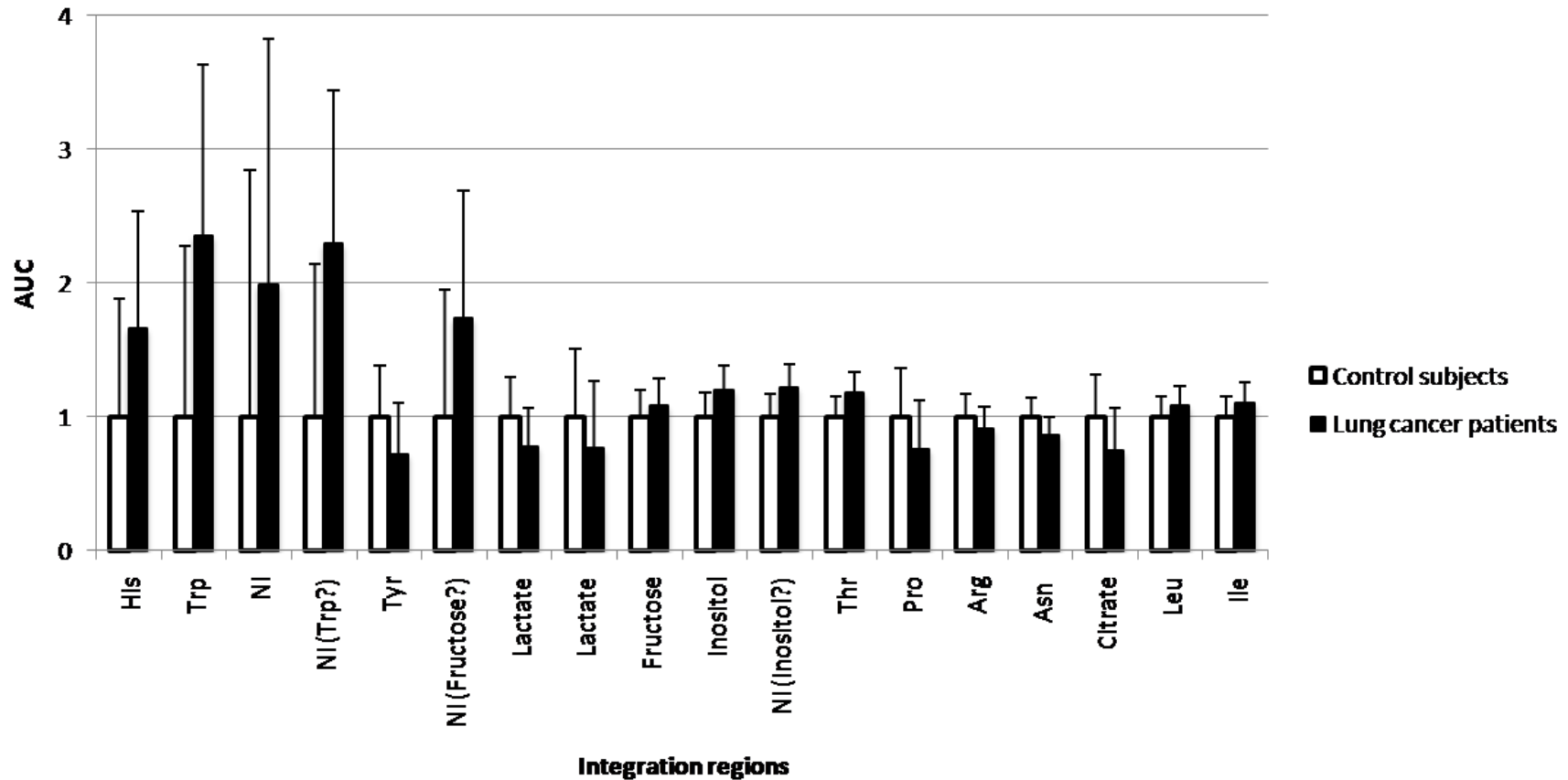
Specificity: 93% (68/73)

Sensitivity: 84% (63/75)

■ = C
■ = LC

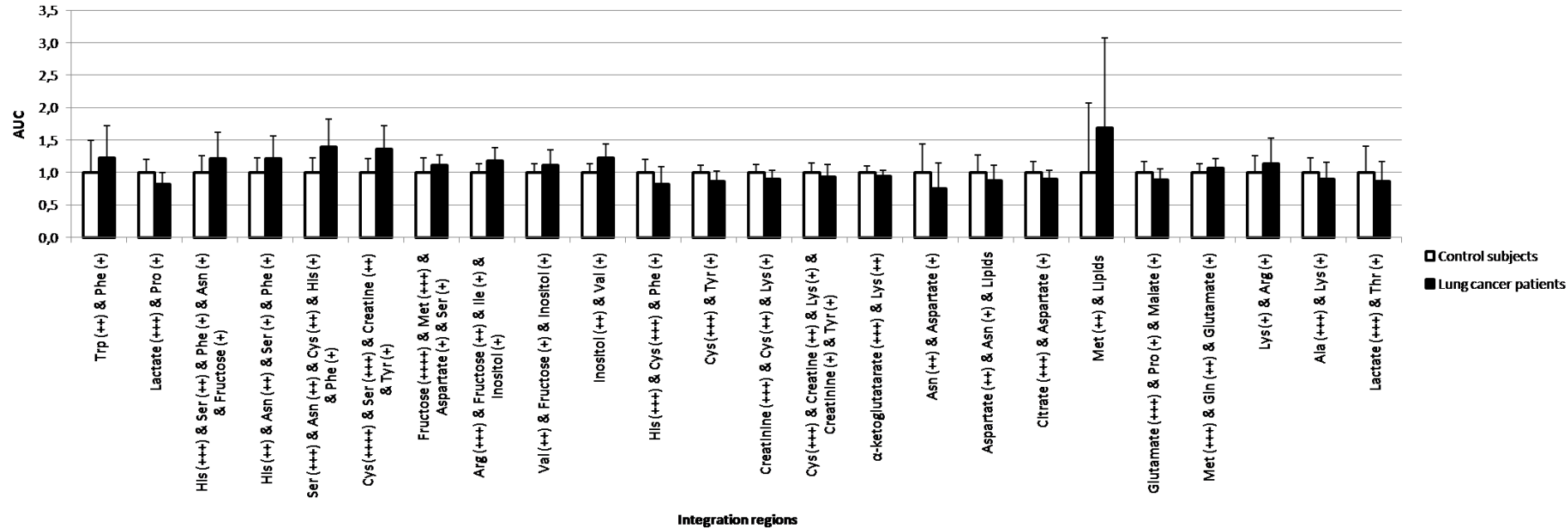
Significantly different integration regions

NI: non identified



18 integration regions specific for a single metabolite

Significantly different integration regions

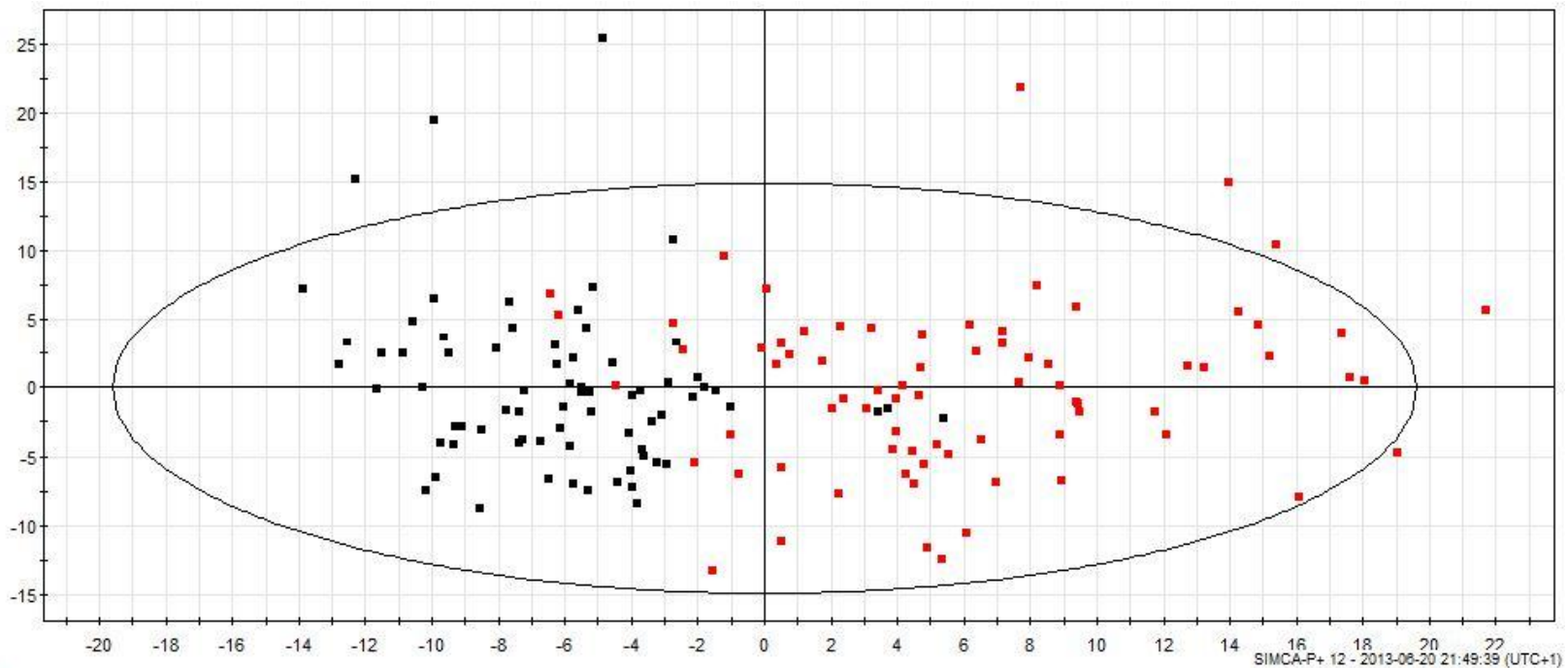


24 integration regions specific for 2 or more metabolites

OPLS-DA with 42 significantly different integration regions

After

- Log transformation for not normally distributed variables
- Pareto scaling
- Removal of outliers



Specificity: 96% (70/73)

Sensitivity: 87% (65/75)

■ = C
■ = LC

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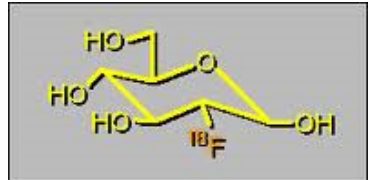
Future perspectives

- **Validation** of the constructed classifier in an independent study population
 - Aim: 250 LC - 250 C
- **Correlation** with biochemical pathways

Future perspectives

- Investigate whether the metabolic changes in the blood correlate with metabolic changes in the tumor, detected by a PET-CT scan after injection of radioactive ^{18}F -fluorodeoxyglucose

Prof.Boellaard, VUMC Amsterdam



Input		Output
<p><u>Patiënt characteristics</u></p> <p>Length (cm) Weight (kg) Gender Plasma glucose concentration (mmol/L)</p>	<p><u>PET-scan characteristics</u></p> <p>Injected dose of ^{18}F-FDG Time of injection Start time of PET-scan</p>	<p>Standardized Uptake Value Total Lesion Glycolysis</p>



Acknowledgements

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