MSACL 2024 – Scientific Session 1

Pilot Study on the Prototype of a Fully Automated Mass-Spectrometry Based Clinical Laboratory Analyzer System

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Disclosure

The Institute of Laboratory Medicine receives research funding from Roche Diagnostics.

Prof. Vogeser receives honoraria for scientific lectures from Roche Diagnostics.

Dr. Christian Schneider-Thauern and Dr. Antje Reuter are employees of Roche Diagnostics and hold shares in F. Hoffmann-La Roche Ltd

This presentation contains information about products in development.

The mass spectrometry prototype (PT) and the assays are in development, not approved by regulatory bodies, and not commercially available.

Not all parameters may be available in all countries.

Environment and background

University Hospital, Ludwig-Maximilians University (LMU), Munich

LMU and medical faculty founded in 1472

>10,000 employees
> 1,700 physicians

Best-ranked university in the EU
14 Nobel laureates

Institute of Laboratory Medicine: approx. 9 Mio analyses per year

History of Mass Spectrometry in the LMU Hospital

1974

Implementation of ***GC-MS***

Prof. Karl Jacob, PhD

2000

Implementation of ***LC-MS/MS***

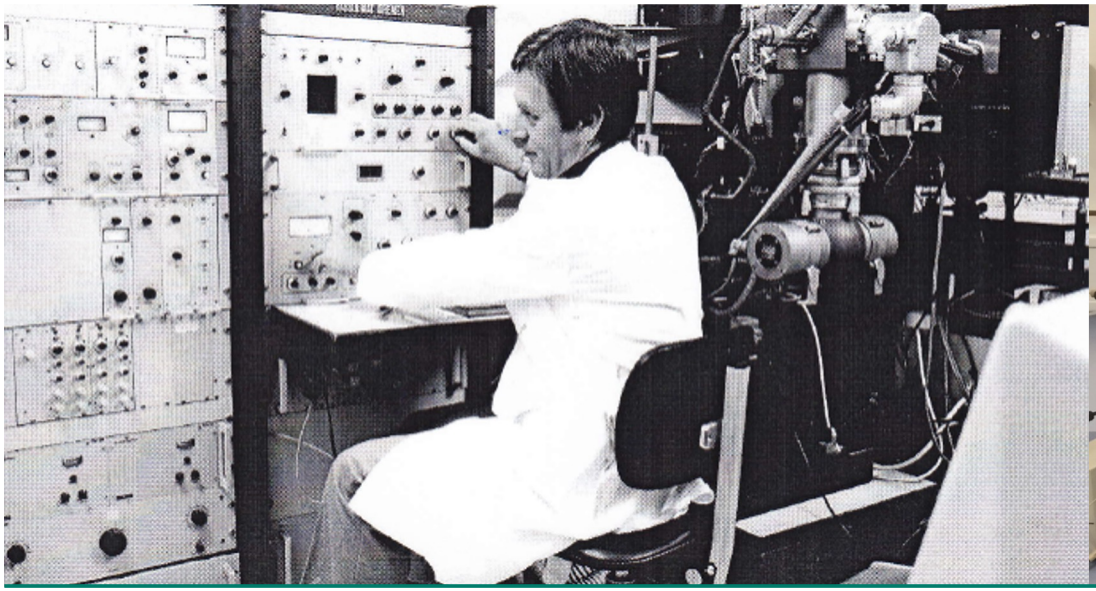
Prof. Michael Vogeser, M.D.

Present day

8 systems in use

10 bench technicians trained

Diagnostic operation 7 days per week



Prof. Dr. rer. nat. Karl Jacob with the first mass spectrometer in the LMU-Lab, 1974

Waters Quattro LC, 2000, first LC-MS/MS system in the LMU-Lab

Commitment and experience of the Institute for the systematic validation of IVD instruments prior to market launch in public-private partnership since the foundation of the Institute in the 1970s

The Prototype MS-Analyzer System

The system under study is designed to be a fully automated, integrated and standardized LC-MS solution with a broad test menu designed as an end-to-end solution for the core lab. The test menu is planned to be CE marked /IVD.

Only this complete automation will make the enormous potential of mass spectrometry for patient care accessible to patients worldwide

These potentials lie above all in:

- Wide analyte spectrum
- Highest analytical specificity (molecular detection)
- Simultaneous quantification of a range of analytes
- Very high analytical reliability (isotope dilution technique)

Future integration
Connection to existing core lab

Ready for use reagents
Loading on-the-fly

Analyte quantification
Automated data processing

Result reporting & flagging

Sample purification
Paramagnetic particle based sample preparation

Analyte separation
Multi-stream liquid chromatography

Analyte detection
Mass spectrometer MS/MS

Key element of automation: Sample preparation is based on the principle of ferromagnetic particles with modified surfaces

ELSEVIER

Available online at www.sciencedirect.com
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CLINICAL BIOCHEMISTRY

Case Report

Sample preparation for liquid chromatography-tandem mass spectrometry using functionalized ferromagnetic micro-particles

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The Association for Mass Spectrometry: Applications to the Clinical Lab

MSACL 2014

The 6th Annual Conference & Exhibits of MSACL

Wednesday @ 9:20 AM in Harbor 2

Deproteination of Serum Samples for LC-MS/MS Analyses Applying Magnetic Micro-particles

Michael Vogeser - *Hospital of the University of Munich, Germany* (michael.vogeser@med.uni-muenchen.de)

‣ A novel, micro-particle based approach for sample preparation in LC-MS/MS was evaluated. In a commercially available kit, a proprietary protein denaturation reagent is combined with ferromagnetic particles which capture and remove denatured proteins from the sample. The principle was tested for amiodarone as an exemplary analyte. On-line solid phase extraction was applied as a second clean-up step. This set-up was found highly efficient and convenient. The principle competes with protein precipitation and seems highly attractive for automation, since no centrifugation or application of positive or negative pressure is required.

Prototype Pilot Study Mass Spec Analyzer: Study design

Setting

First evaluation of a fully automated MS-analyzer system under intended user conditions in a routine clinical laboratory setting

Q3 & Q4 2022

Aims

- *Assessment of the system functionality as the interaction between software, hardware, reagents, auxiliaries and biological samples*
- *Assessment of practicability*
- *Assessment of robustness*
- *Assessment of sample throughput under intended user / real world / random access conditions*
- *Identify potential technical failures at an early stage before performance evaluation and market launch.*

Not within the scope of the prototype study:
Assessment of analytical performance data

Study design I

- *Stand-alone Mass Spec instrument with a laboratory automation system sample management module upfront (core unit)*
- *Training of two operators (routine bench technicians) by manufacturer training expert*
- *One operator from the MS lab, one from the automated lab*
- *Supervision by manufacturer's experts with several on-site visits and remote dialogue*
- *Familiarization program*
- *Addressed analytes: Tacrolimus, Cyclosporine A, Sirolimus, Everolimus, MPA, Voriconazole, Lamotrigine, Meropenem, Estradiol, Testosterone, 25-OH-Vitamin D2/3 – wide range of molecular weight and polarity*
- *Use of anonymized left-over samples from our routine service*

Study design II

- *All analyses controlled via host-instrument interaction with request download and result upload*
- *Daily start-up and QCs*
- *Pre-defined daily plan of experiments, daily log*
- *Assessment of precision study according to CLSI EP5*
- *Routine simulation in random access working mode with assessment of throughput and TAT*
- *Stress testing (e.g., carry-over tests)*
- *HPLC stream comparability studies*
- *Workflow-analysis, assessment of throughput*
- *Remote data analysis with validated data acquisition tool*

Results and findings

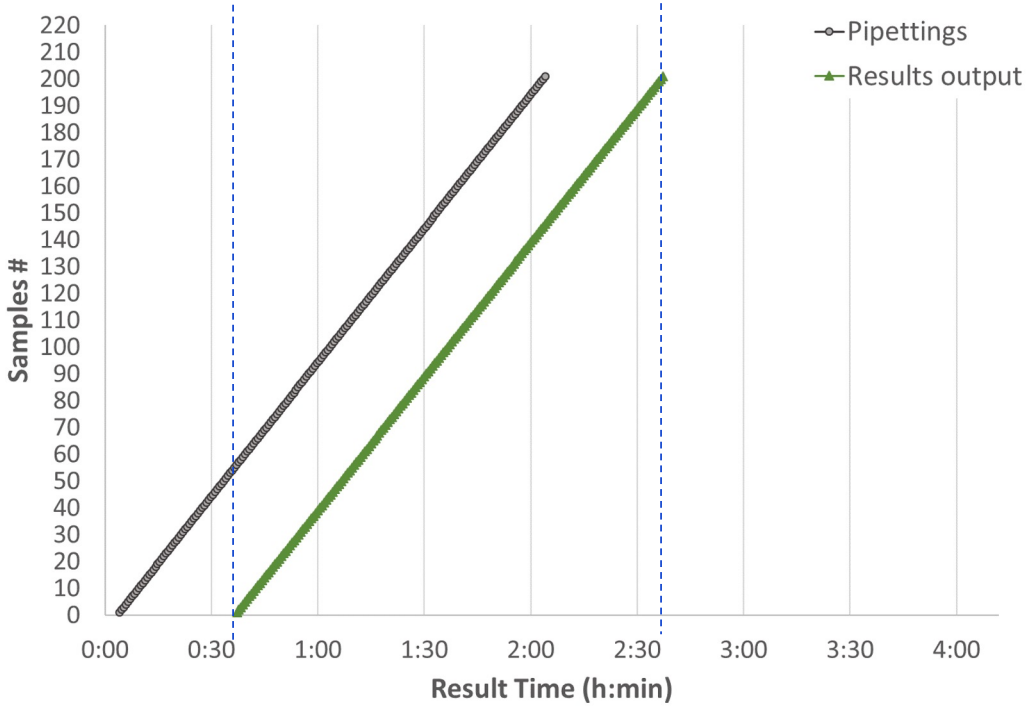
Related to operators

- *3-day training was sufficient*
- *No need for previous MS / chromatography skills*
- *Handling of reagents very convenient*
- *Maintenance convenient*
- *Data management* identical to an existing analyzer platform*

  **download of requests / upload of results*
- *Trouble shooting worked efficiently*
- *Run-interruptions were observed – causes was identified in all cases and could be addressed*

Analytical unit workflow efficiency

Mycophenolic acid measurement of 200 samples

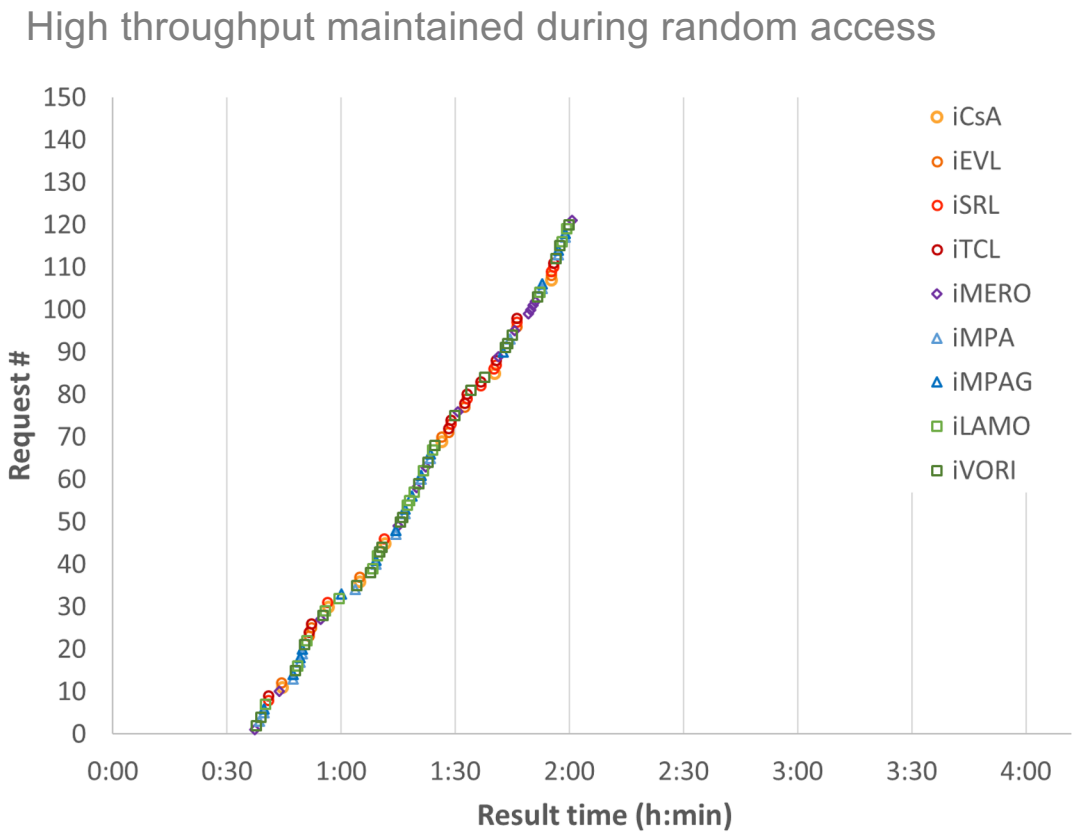


Time to first result:
0:37 (h:min)

Time to last result:
2:37 (h:min)

up to100 samples/hour

Random access workflow



Conclusions

Based on our results, observations, and handling experience, we believe that further development and maturation of the system under study will most likely result in the first MS/MS-based analytical system that can be seamlessly integrated into comprehensive high-throughput, multi-technology laboratory solutions.

Outlook

Multicenter Evaluation with respect to analytical performance of launch panel assays in 2024

LMU University Hospital, Munich

LMU HOSPITAL Munich

Thank you

for your attention