

Rapid and cost-efficient analysis of pharmaceutical and clinical samples by TXRF



Bruker Nano Analytics, Berlin
Webinar, September 21st, 2016

A blue-toned graphic illustrating TXRF technology. It features a central X-ray tube emitting a beam towards a sample on a turntable. The background is filled with a periodic table of elements, with some elements highlighted in larger boxes. A spectral plot with peaks is visible in the lower-left quadrant. The text "XFlash® Technology" and "TXRF" are prominently displayed. At the bottom, the slogan "Innovation with Integrity" is written in white on a dark blue background.

Ca Sc Ti
Sr Y Zr
Ba La Hf
Ra Ac

XFlash®
Technology

V Cr Mn Fe Co Ni Cu Zn Ga Ge As Se Br Kr
Nb Mo Tc Ru Rh Pd Ag Cd In Sn Sb Te W Pt Au Hg Tl Pb Bi Po At Rn
Ta W Re Os Ir Pt Au Hg Tl Pb Bi Po At Rn

Ce Pr Nd Pm Sm Eu Gd Tb Dy Ho Er Tm Yb Lu
Th Pa U Np Pu Am Cm Bk Cf Es Fm Md No Lr

K α K β L α L β M α M β

TXRF

Innovation with Integrity

Welcome



Speakers

Dr. Hagen Stosnach
Applications Scientist TXRF
Berlin, Germany



Dr. Armin Gross
Global Product Manager TXRF
Berlin, Germany



Itinerary



-
- Introduction
 - Next Generation TXRF Concept
 - Application example
Quantification of catalyst elements
 - Comparison with Atomic
Spectroscopy methods
 - Summary and Outlook

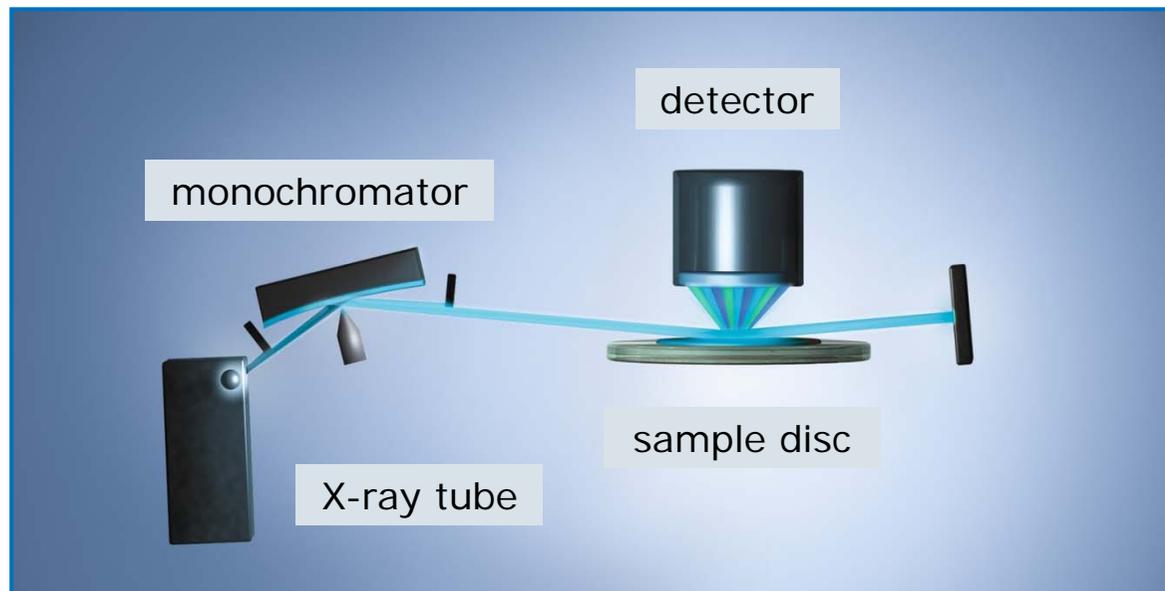


Introduction

Principles of total reflection X-ray fluorescence (TXRF) spectroscopy



Total reflection X-ray fluorescence spectroscopy



Beam angle: 0° / 90°

- Samples must be prepared on a reflective media
- Polished quartz glass or polyacrylic glass disc
- Dried to a thin layer, or as a thin film or microparticle

Product Portfolio

S2 PICOFOX



S2 PICOFOX - Unique benefits

- Most compact design portable, for on-site analysis
- Fixed excitation mode easy to use,
most suitable for teaching
- >200 installations
world wide well established technology
- Attractive pricing most valuable TXRF solution



Second Generation TXRF Spectrometer S4 TStar



S4 TStar - **Unique benefits**

- Multiple excitation modes to detect most elements of the PSE
- Large area detectors improved sensitivity for lowest limits of detection
- Sample geometry flexibility measurement of discs, microscopy slides, wafers etc.
- Motorized beam path automatic beam adjustment and QC procedures
- Large sample capacity up to 90 sample discs, multi-user operation
- Most modern software instrument/measurement status display, statistical functions



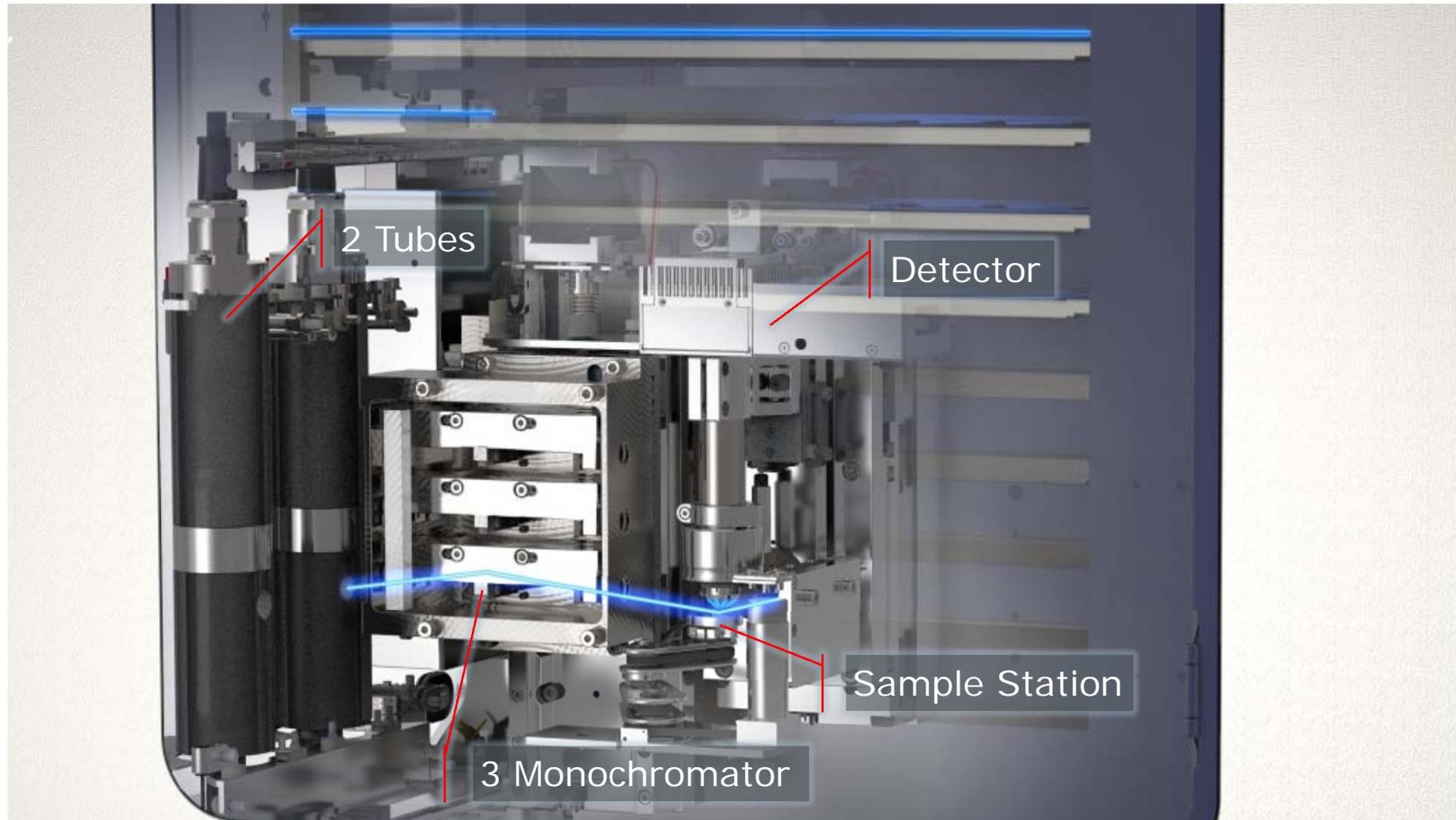


Next Generation TXRF Concept

Next Gen TXRF Excitation and Detection Module



Next Gen TXRF Excitation and Detection Module



Next Gen TXRF Excitation and Detection Module



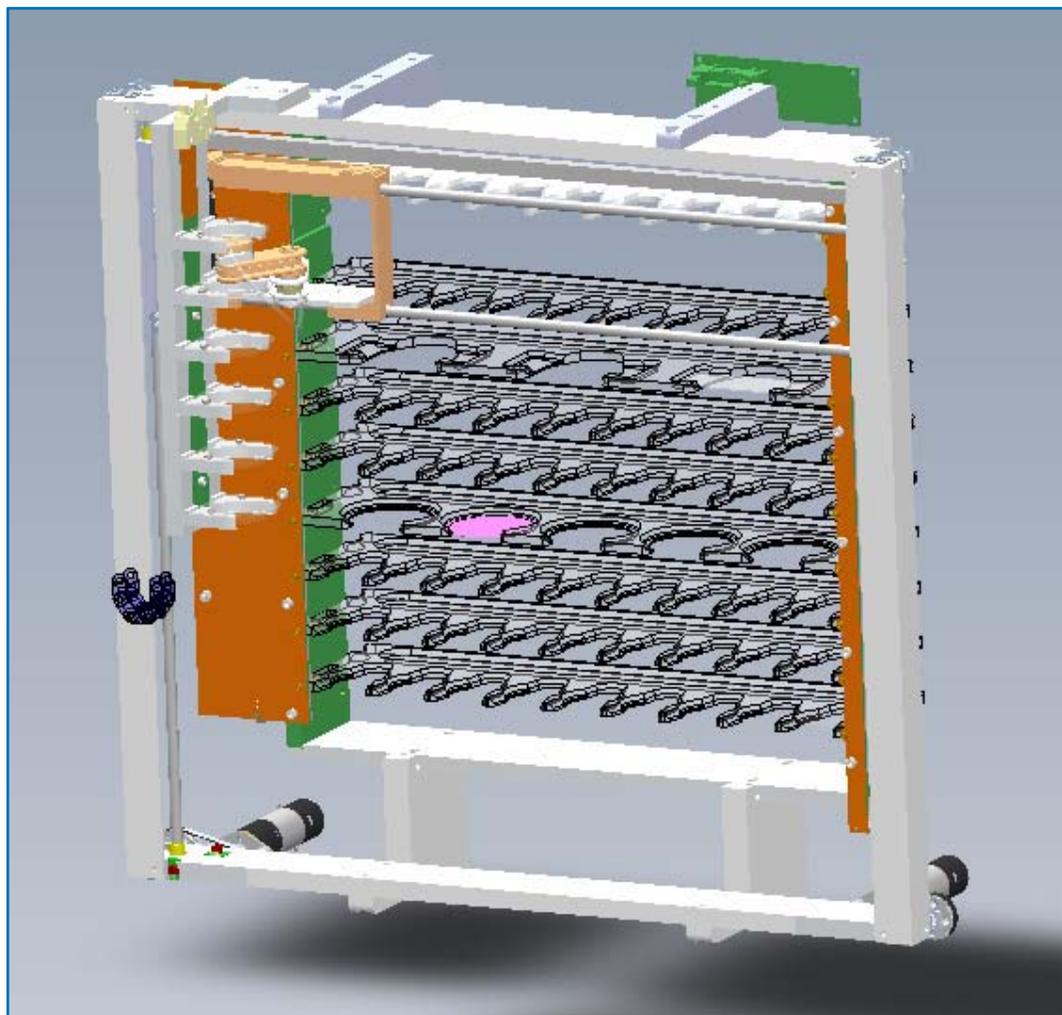
Feature	S4 TStar	Benefit
Tubes	2 tubes (Mo and W) Ag, Cu, Cr planned	Best performance in one instrument only
Excitations	Up to 3 W-Brems and W-L	Low detection limits for Na – Ca: W-L Ca – Y, Cs – U: Mo Zr – I: W-Brems
Detectors	60 mm ² (100 mm ² option)	Doubles sensitivity

Next Gen TXRF Samples and Sample Changer



Autosampler

- Horizontal sample orientation
- 90 quartz discs (30 mm)
- 2" wafer
- Microscopy slides
- Rectangular samples max. 54 mm

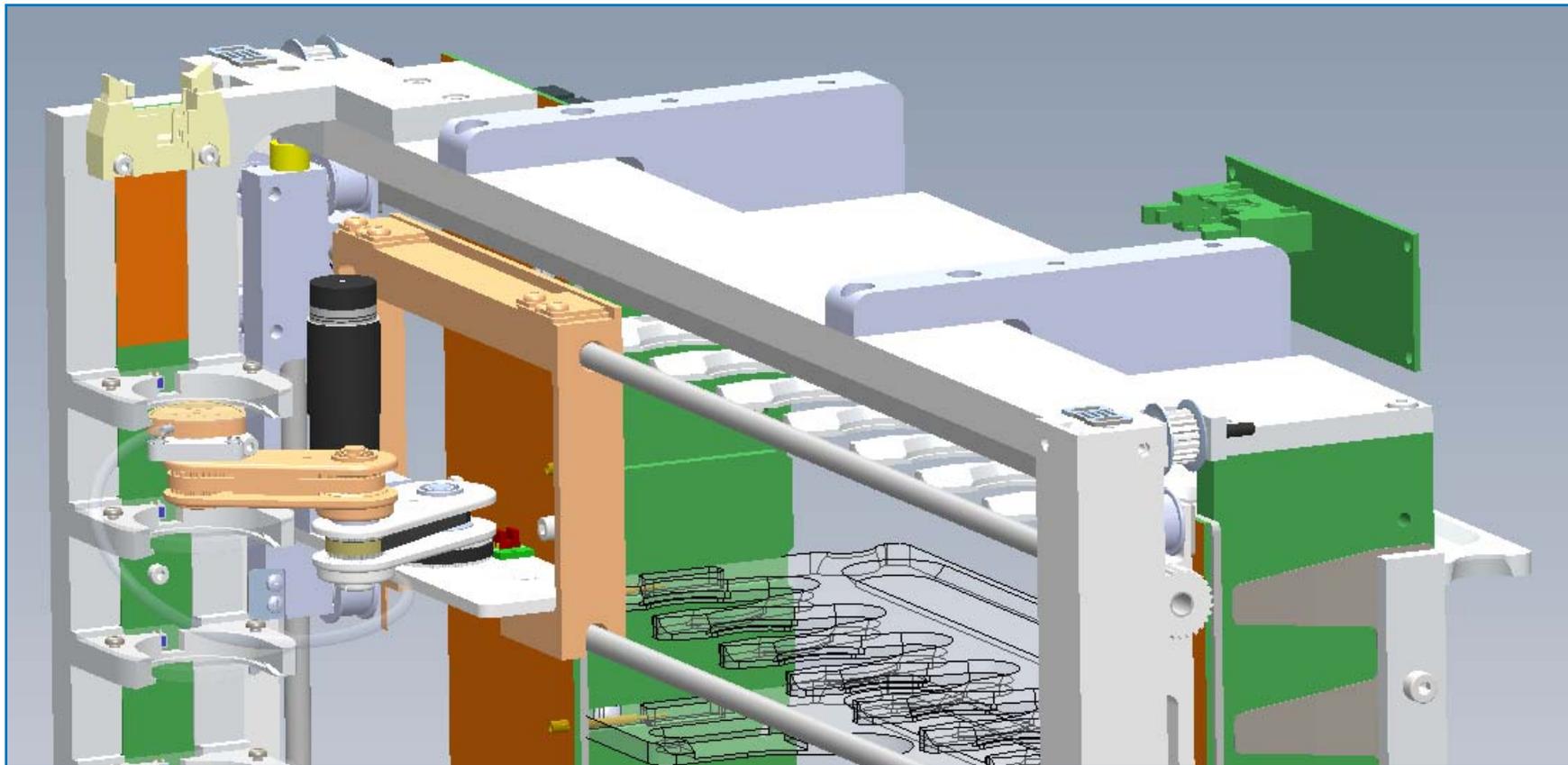


Next Gen TXRF Samples and Sample Changer



Autosampler

- 6 internal instrument quality standards



Next Gen TXRF Samples and Sample Changer



Automatic tray recognition

- Recognizes different tray types (disc / wafer / ...)
- „Ownership“ for trays
- Automatic loading and starting of measurement jobs possible

Next Gen TXRF Samples and Sample Changer



Automatic tray recognition

- Recognizes different tray types (disc / wafer / ...)
- „Ownership“ for trays
- Automatic loading and starting of measurement jobs possible

LED light provides status information



Tray identified, no job

Tray and job identified

Job running

Job finished

Next Gen TXRF

Valuable accessories



Offer solution including peripheral tools

- Storage box
 - Safe storage of trays and discs after cleaning
 - Stackable
 - Direct sample preparation avoids contamination
- Drying station
 - Fits to tray dimensions
 - One button operation

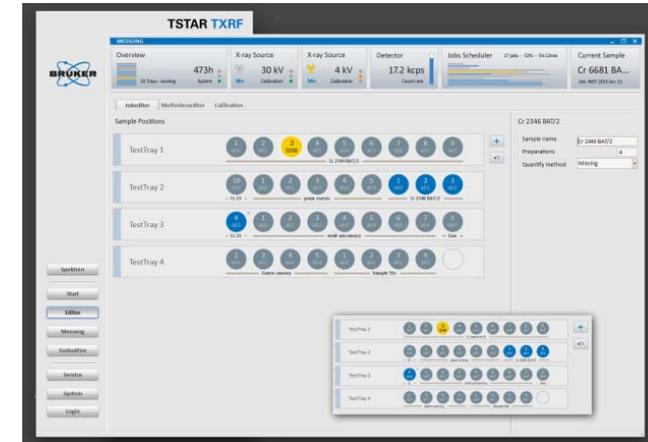


Next Gen TXRF Software



Modern User Interface

- Intuitive, easy to use SW interface
- Fresh, modern look and feel
- Esprit based SW platform (2.1)
- Multi user interface – capability to manage jobs of multiple users
- Job management – automated workflow optimization
- Better serviceability – remote control, sophisticated performance and error log function



Next Gen TXRF Software



Modern User Interface

- Advanced data evaluation
- Statistics, recoveries
- Threshold levels incl. warnings in case of deviations

The screenshot displays the 'EVALUATION' software interface. At the top, there are control panels for 'X-ray Source' (0,0 kV) and 'Detector' (0 cps). Below this is a 'Measured jobs' tree on the left, showing a hierarchy of folders like 'Nachweisgrenzen', 'Referenzspektren M K 2 - Plant Soil', and 'Abwassertest 1'. A specific job '2926' is highlighted. On the right, a 'Statistics' table shows results for various elements. A box labeled 'Statistical results' highlights the row for Chromium (24). Below the statistics table is a 'Concentration for each preparation' table, with a box labeled 'Results of single preparations' highlighting the data for preparations 2919, 2904, and 2926. A 'Job tree' box also points to the left-hand navigation area.

Element	Name	Average	Median	RSD
22	Titanium	0,196	0,194	0,003
23	Vanadium	1,036	1,012	0,046
24	Chromium	0,926	0,917	0,017
25	Manganese	0,986	0,986	0,004
26	Iron	1,004	1,002	0,007
27	Cobalt	0,971	0,973	0,004
28	Nickel	0,990	0,990	0,005
29	Copper	0,992	0,994	0,004
30	Zinc	1,030	1,032	0,009
31	Gallium	0,910	0,910	0,000
33	Arsenic	0,954	0,952	0,005

	Titanium	Vanadium	Manganese	Iron	Cobalt	Nickel	Copper	Zinc
Used								
Prep.								
	Error	Error	Error	Error	Error	Error	Error	Error
<input checked="" type="checkbox"/> 2919	0,199 0,024	1,012 0,084	0,986 0,023 1,012 0,021	0,973 0,020	0,994 0,020	0,994 0,020 1,039 0		
<input checked="" type="checkbox"/> 2904	0,194 0,023	1,090 0,076	0,981 0,020 0,999 0,018	0,966 0,017	0,985 0,017	0,986 0,018 1,020 0		
<input checked="" type="checkbox"/> 2926	0,194 0,023	1,007 0,079	0,989 0,021 1,002 0,019	0,973 0,019	0,990 0,019	0,994 0,019 1,032 0		



Application of Next Generation TXRF

Quantification of catalyst elements

Catalyst elements

S2 PICOFOX



First studies

- Practical course of a pharmacist student at the Institut of Pharmaceutical Chemistry in Braunschweig, Germany
- Analysis of catalyst elements in different matrices
 - 5% and diluted Glucose
 - 0,9% NaCl
 - Placebo pills
 - Distilled water
- Spectrometer S2 PICOFOX
Mo excitation (17,5 keV)
50 kV, 600 μ A, 1000s



Catalyst elements

S2 PICOFOX



Sample preparation

- Direct analysis after addition of internal standard possible
- Pills prepared as suspension after grinding
- No time-consuming digestion required

Catalyst elements

S2 PICOFOX

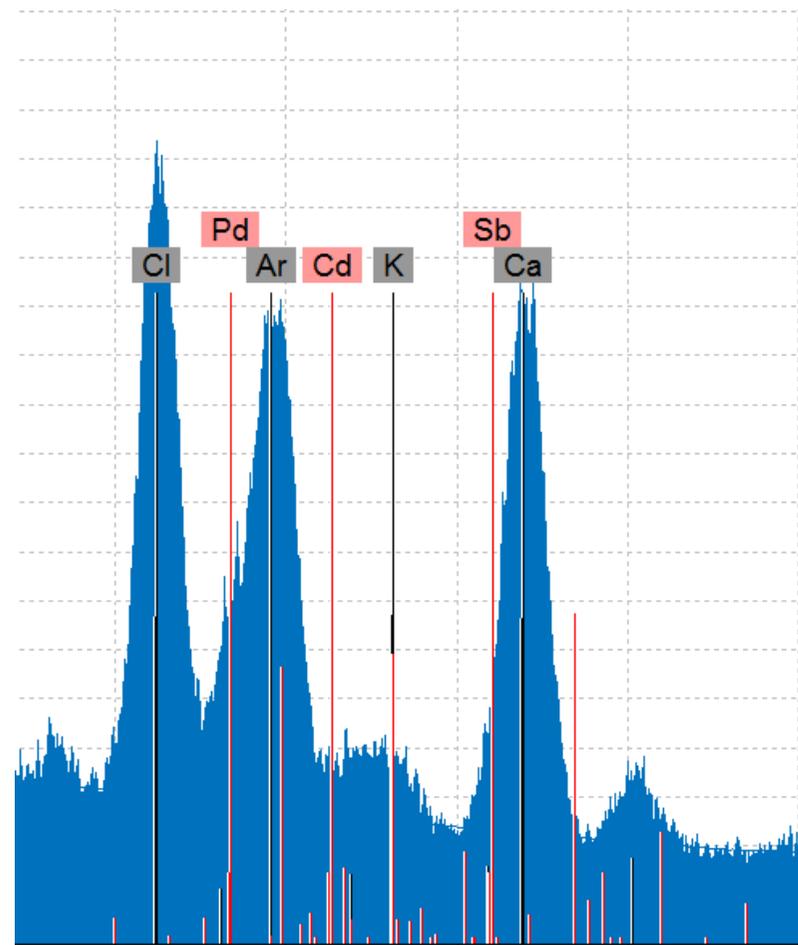


Sample preparation

- Direct analysis after addition of internal standard possible
- Pills prepared as suspension after grinding
- No time-consuming digestion required

Issues

- Mo tube excites only L lines of many catalysts
- Ar can be removed by nitrogen purge
- Strong line overlap with e.g. Cl, K, Ca

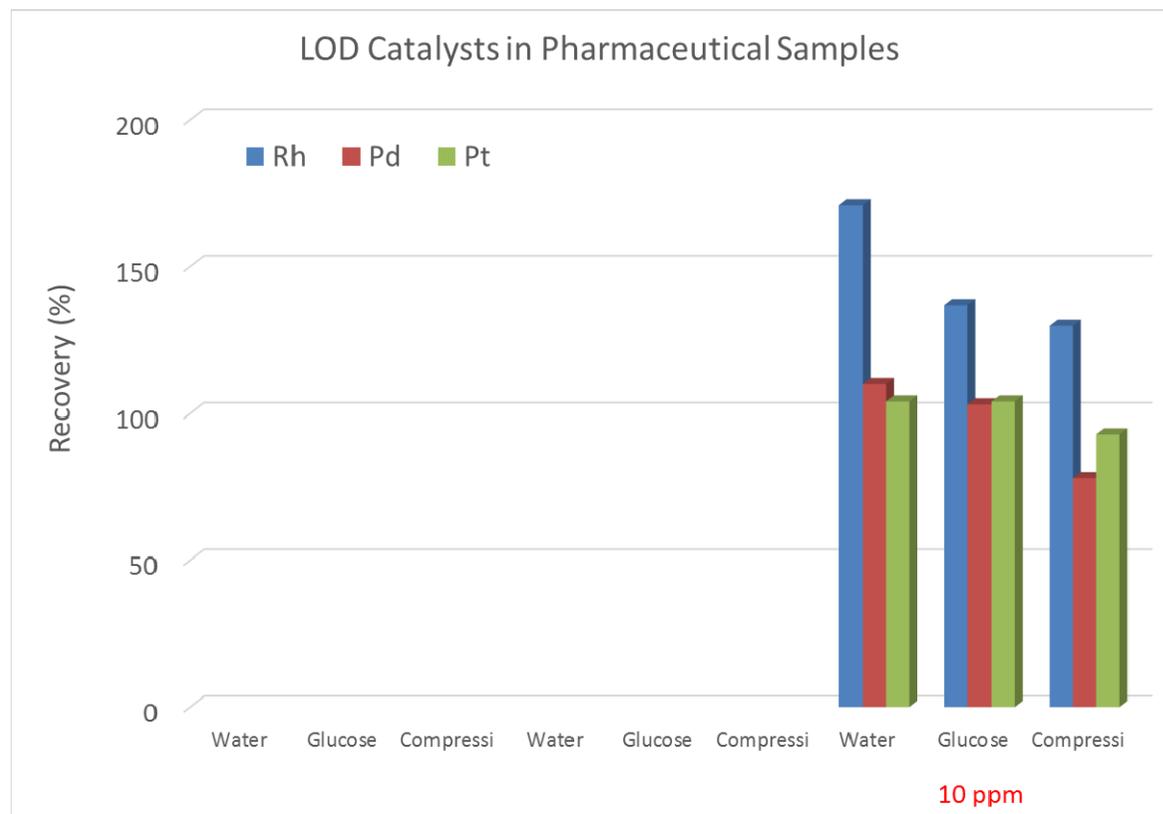


Catalyst elements S2 PICOFOX



10 ppm catalyst

- good recovery for most catalysts

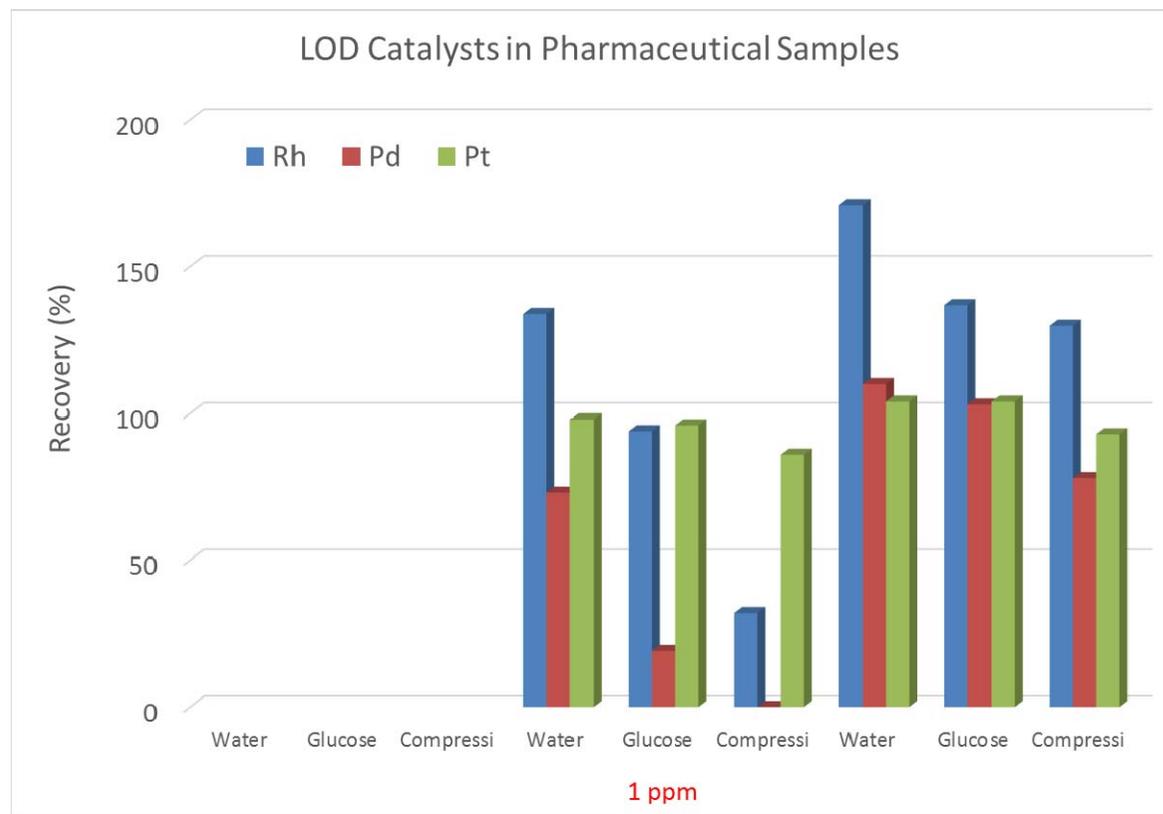


Catalyst elements S2 PICOFOX



1 ppm catalyst

- Rh, Pd „o.k.“ in water
- Good recovery in all matrices for Pt only

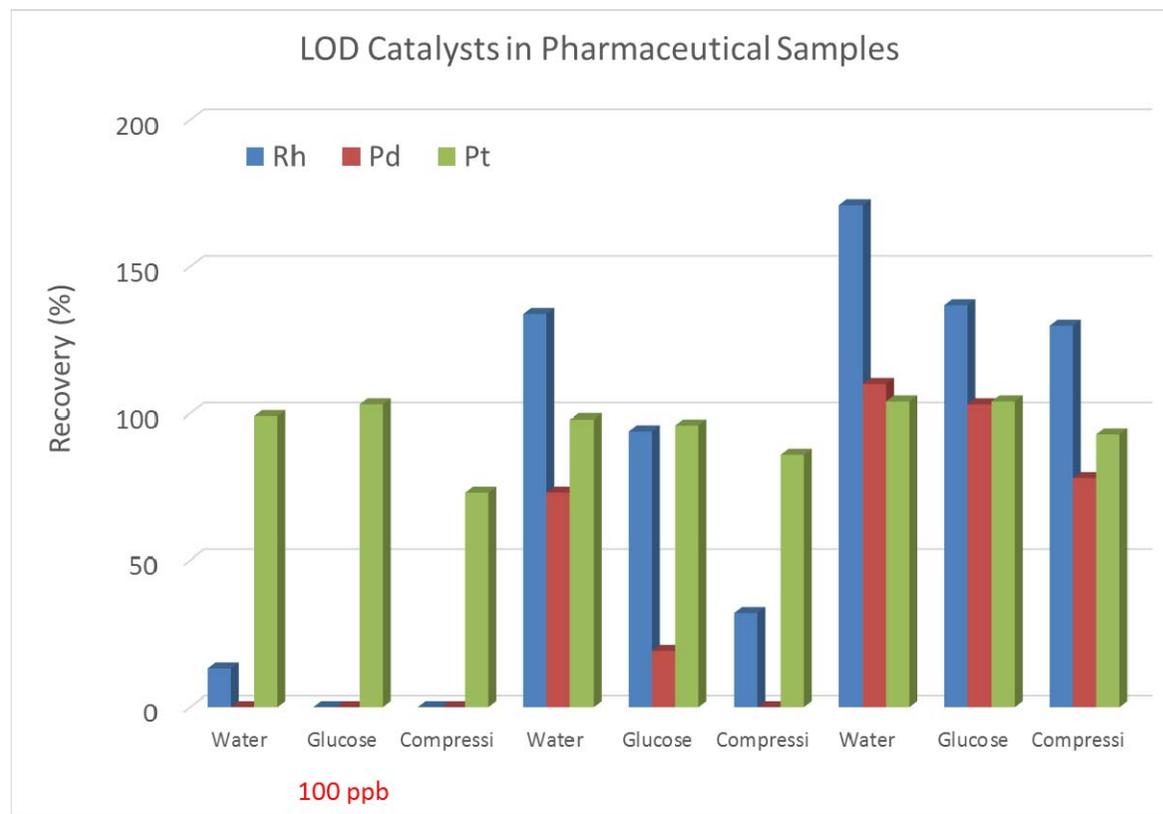


Catalyst elements S2 PICOFOX



100 ppb catalyst

- Pt good in most matrices
- Rh, Pd not detectable

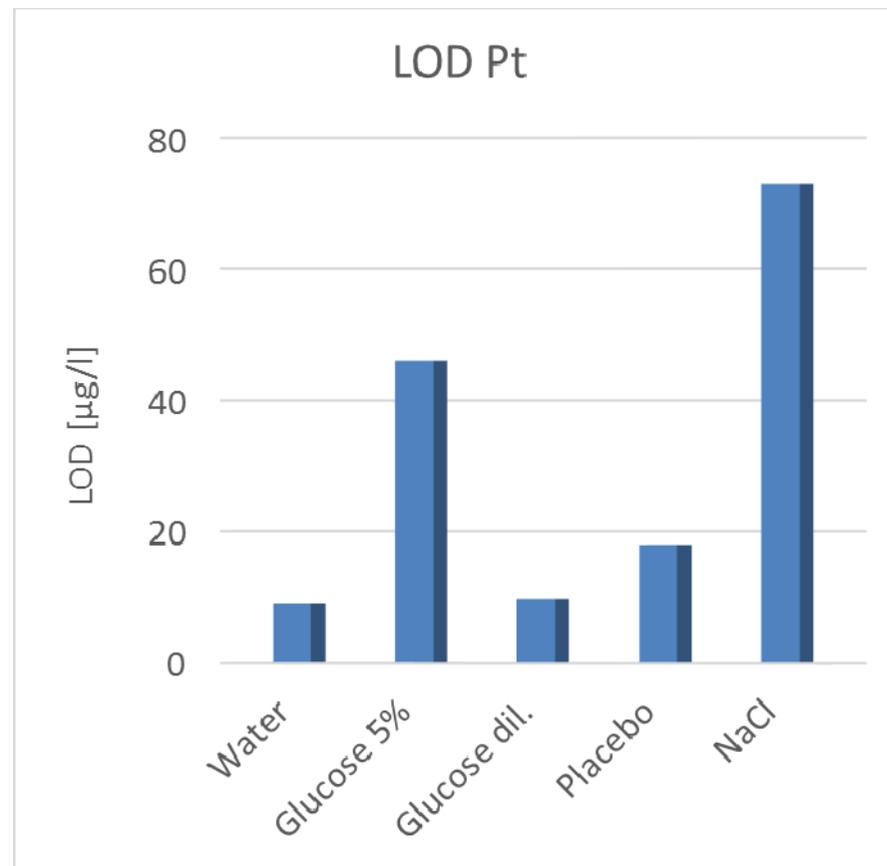


Catalyst elements S2 PICOFOX



Platinum

- LOD depend on matrix
- Vary from 9 to 70 ppb



Catalyst elements

S4 TStar



Catalyst analysis applying other excitation energies

- Spectrometer S4 TStar
- More powerful tubes (30W to 50W)
- New large area detector 60 mm²
- 3 excitation energies
 - Mo-K, 17,5 keV
 - W Bremsstrahlung, 35 keV
 - W-L, 8,4 keV



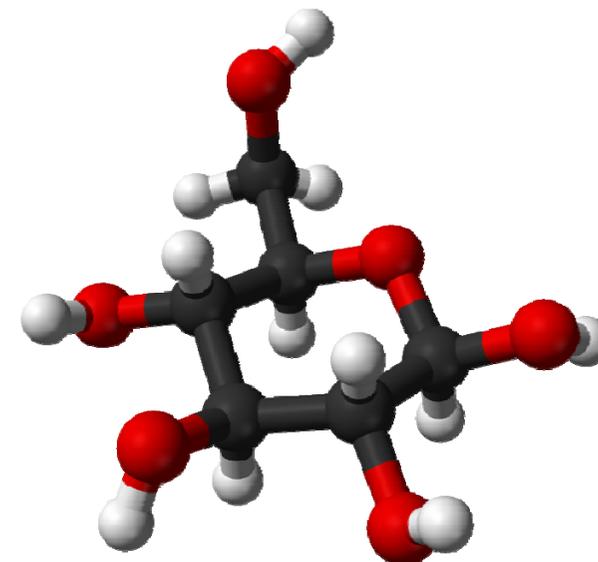
Catalyst elements

S4 TStar



Samples

- Glucose at different concentrations (0,1%, 0,5%, 1%, 5%)
- Spike with 2 ppm metal concentration (Cr, As, Pd, Cd, Sb)



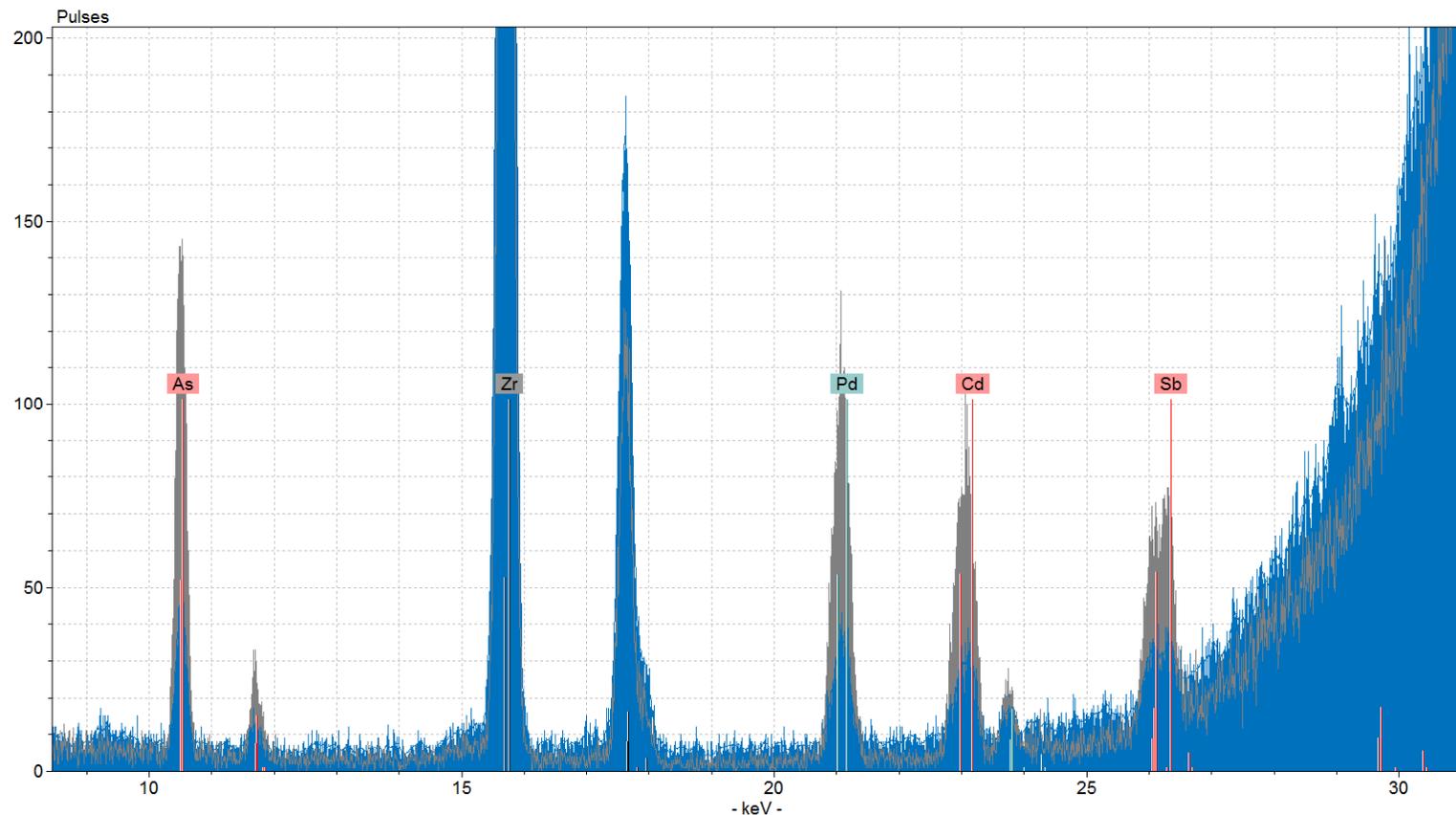
Catalyst elements

S4 TStar W-Brems excitation



Spectrum W-Brems excitation

- Well separated peaks of Pd, Cd, Sb



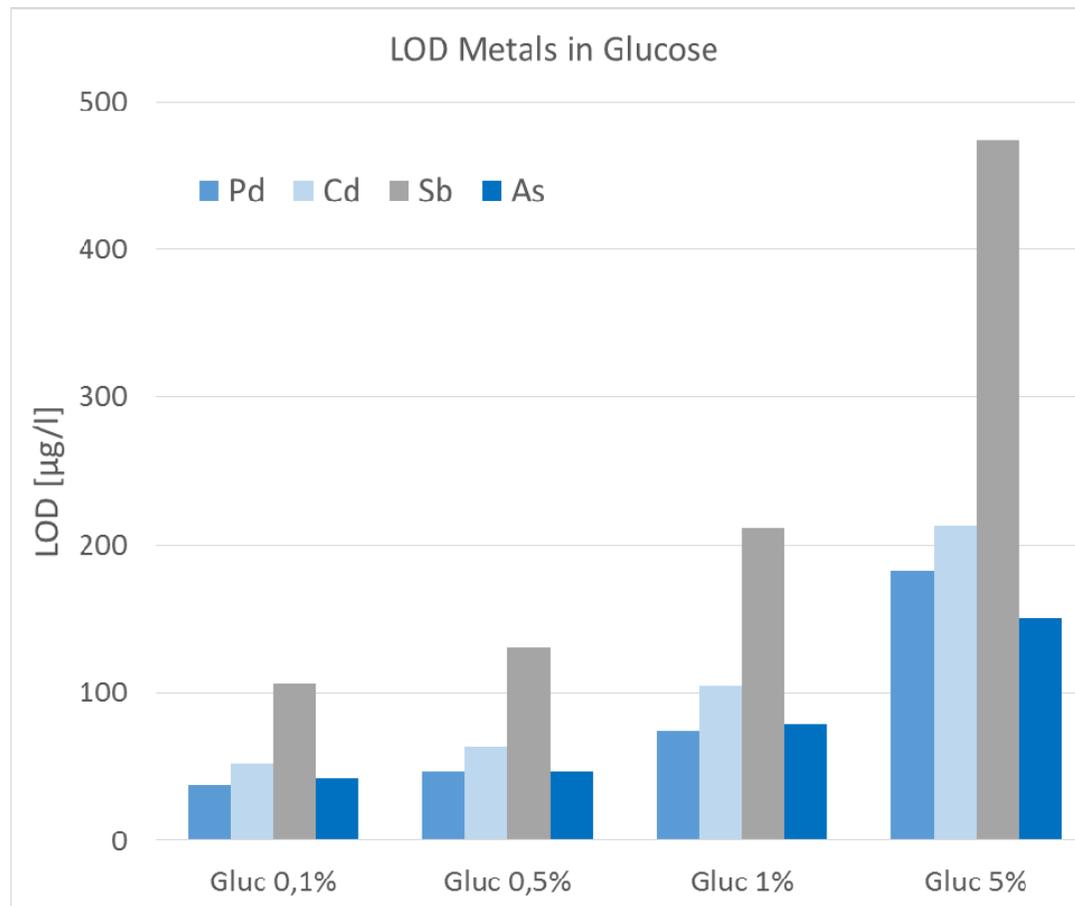
Catalyst elements

S4 TStar W-Brems excitation



Results

- Count rates of W-Brems excitation below Mo excitation (40% for Pd)
- No critical line overlaps!
- LOD of typical catalyst elements at about 200 ppb in high matrix samples



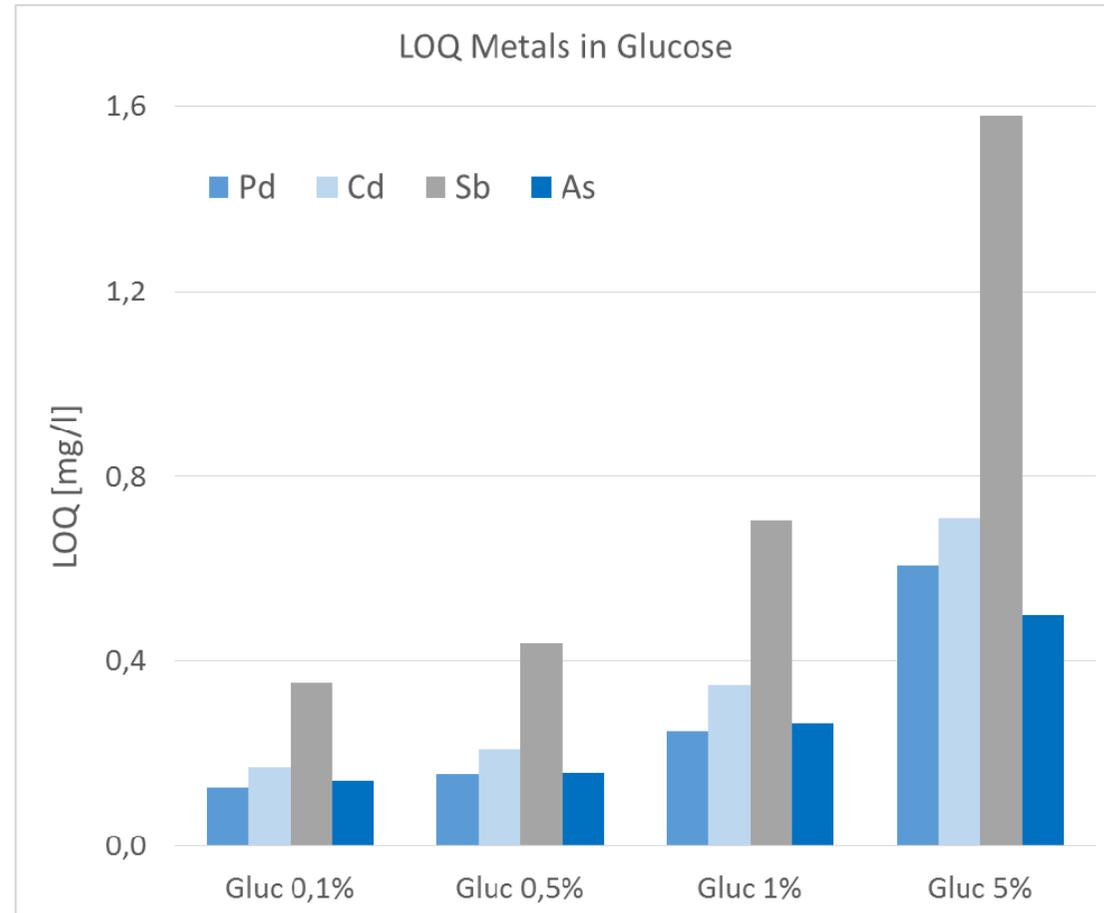
Catalyst elements

S4 TStar W-Brems excitation



Results

- LOQ typically in the sub-ppm range
- Dilution of high matrix samples strictly recommended
- More uniform sample layer
- Improved reproducibility



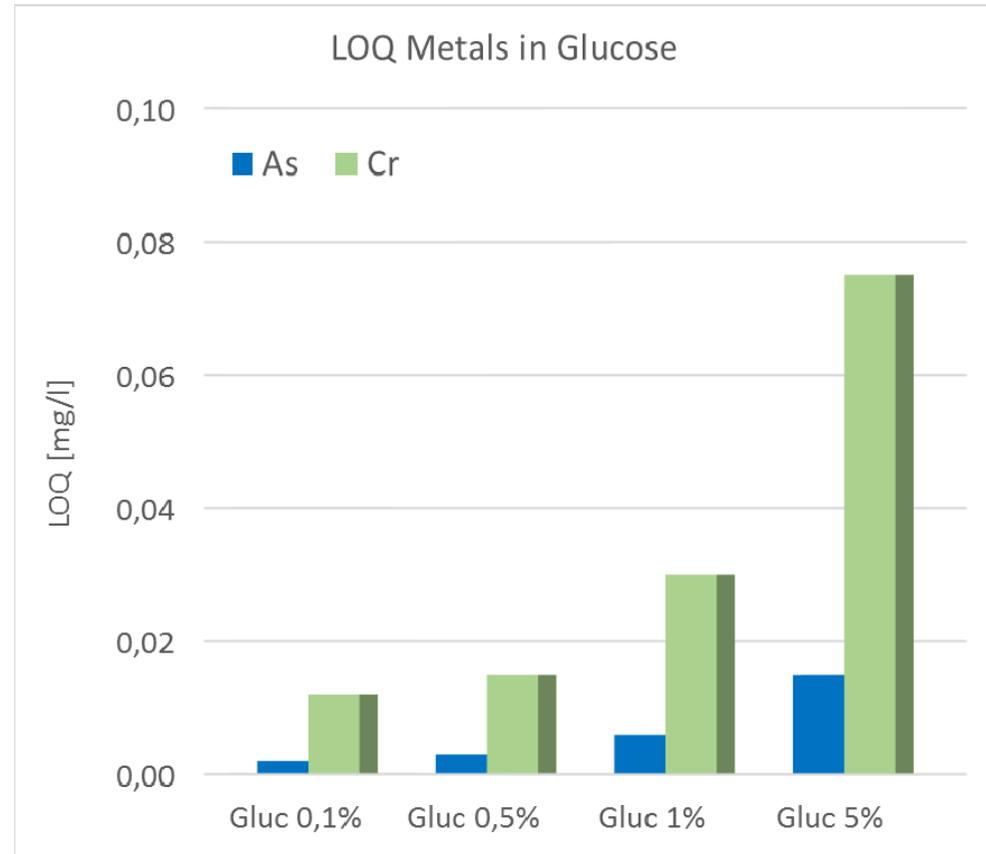
Catalyst elements

S4 TStar Mo excitation



Outstanding performance

- Low ppb quantification limits for As and Cr
- Similar performance for V, Co, Se, Pt etc. (not shown)



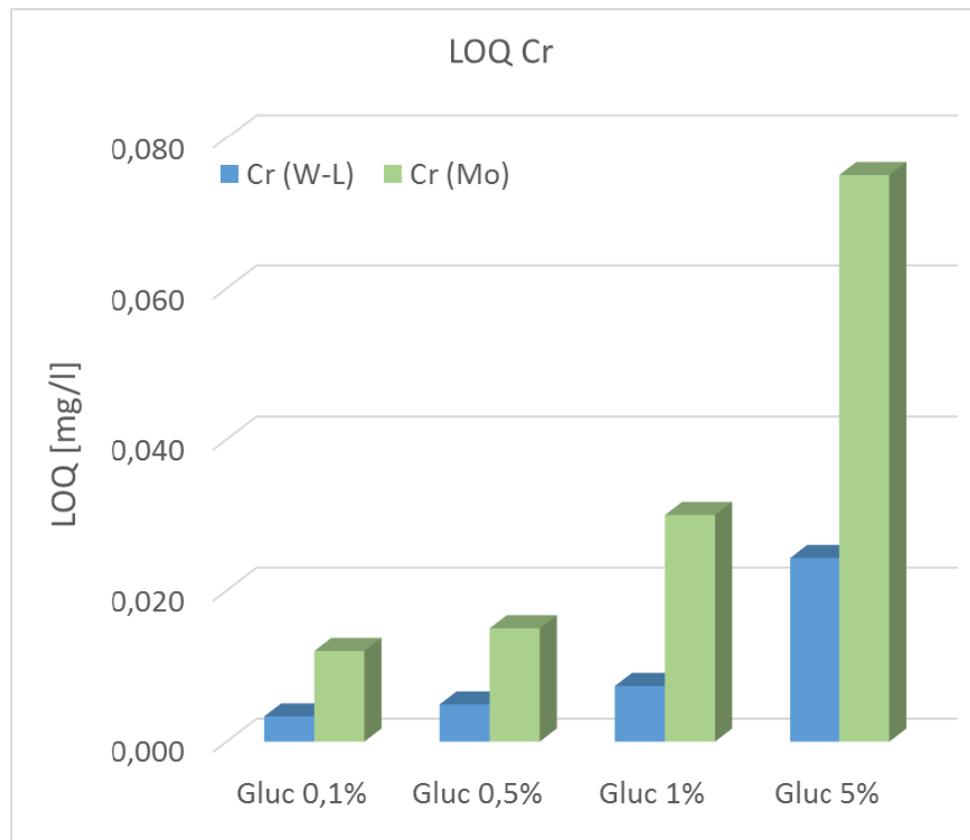
Catalyst elements

S4 TStar W-L excitation



Light elements

- W-L excitation for quantification of light elements (Na to V)
- Improvement by a factor of 3 or more
- LOQ for Cr down to 3 ppb
- Quantification of Na, Mg, Al to be tested soon



Catalyst elements

Recommended excitations



Element classes

- Most important elements are quantifiable by TXRF applying Mo and W-Brems excitation

Class	Element	Recommended excitation
1	As, Pb, Hg Cd	Mo W-Brems
2A	V, Se, Co Mo	Mo W-Brems
2B	Au, Tl, Pt, Ir, Os Ag, Pd, Rh, Ru	Mo W-Brems
3	Ba, Cu, Ni Sb, Sn Cr	Mo W-Brems W-L
4	Fe, Zn, K, Ca, Mn, W Na, Mg, Al	Mo W-L
	B, Li	Not possible



Comparison with Atomic Spectroscopy

AAS, ICP-MS, ICP-OES

TXRF

Normative Work



EUPh / USP

- ICP-OES/MS already listed as validated method in Pharmacopeia
- Validation of TXRF planned with external cooperation partner

Other norms

- ISO TS 18507: „Technical Specification for the use of Total Reflection X-ray Fluorescence spectroscopy in biological and environmental analysis“
- ISO NWIP: „Total Reflection X-Ray fluorescence analysis of water samples

Cost comparison TXRF versus ICP-MS



Installation	S4 TStar	ICP-MS	Remarks
Instrument price	123.500 €	130.000 €	
Validated installation	8.300 €	10.000 €	IQ/OQ/PQ
Training	4.900 €	9.000 €	2 days onsite + courses for 2 users
Gas supplies	0 €	8.000 €	Argon, He, H ₂
Electrical supplies	0 €	600 €	
Exhaust	0 €	3.500 €	if exhaust system already exists in building
Peripheral devices	(12.000 €)	28.000 €	Disc cleaning, microwave
Sum	148.700 €	189.100 €	

Cost comparison TXRF versus ICP-MS



Operation / year	S4 TStar	ICP-MS	Remarks
Service contract (std)*	9.483 €	10.000 €	
Gas	0 €	7.000 €	
Standards	100 €	4.000 €	
Electrical power	200 €	2.000 €	
Spare parts	1.965 €	3.300 €	TXRF: X-ray tube, carriers ICP: detector, torch, cones, injector
Sum	11.748 €	26.300 €	

*) Bruker standard care contract
incl. 1 preventive maintenance per year

Cost comparison TXRF versus ICP-MS



Total (5 years)	S4 TStar	ICP-MS	Remarks
Installation	148.700 €	189.100 €	
Operation costs	58.740 €	131.500 €	
Man hours	120.000 €	185.000 €	100 k€/a, 220 working days, 50 samples/d
Total	327.440 €	505.600 €	
Costs / sample	5,95 €	9,19 €	

Sources: Automotive study 2015
 EPA study 2007
 ICP-OES cost calculator
 Discussion forums
 Bruker data

Summary and outlook



- The S4 TStar TXRF spectrometer using multiple excitation energies allows the quantification of almost all elements listed in USP/EUPh
- LOQ values are typically below 1 ppm, for certain elements in the low ppb range

Next steps

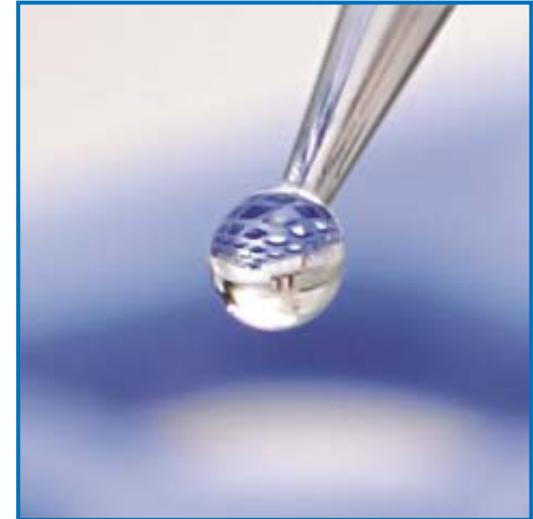
- Studies showing the accuracy and precision of TXRF for metal analysis in different matrices will be continued
- A program for validation of TXRF for pharmaceutical applications is planned
- Software, which will fulfill GMP guidelines and CRF21 part 11 is in development

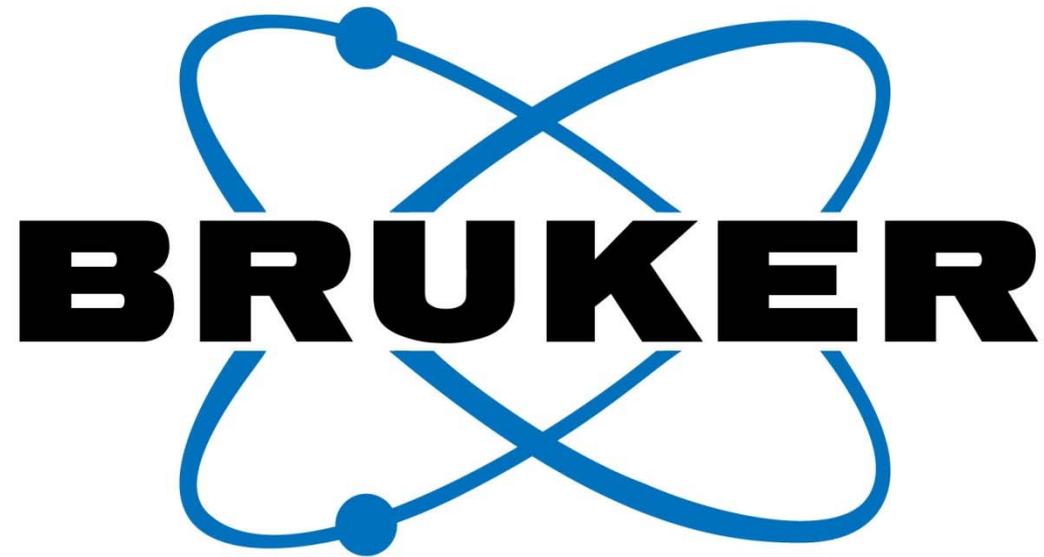
Q & A



Any Questions?

Please **type in** the questions you may have for our speakers in the **Questions Box** and click **Submit**





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Thank you for your attention!

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