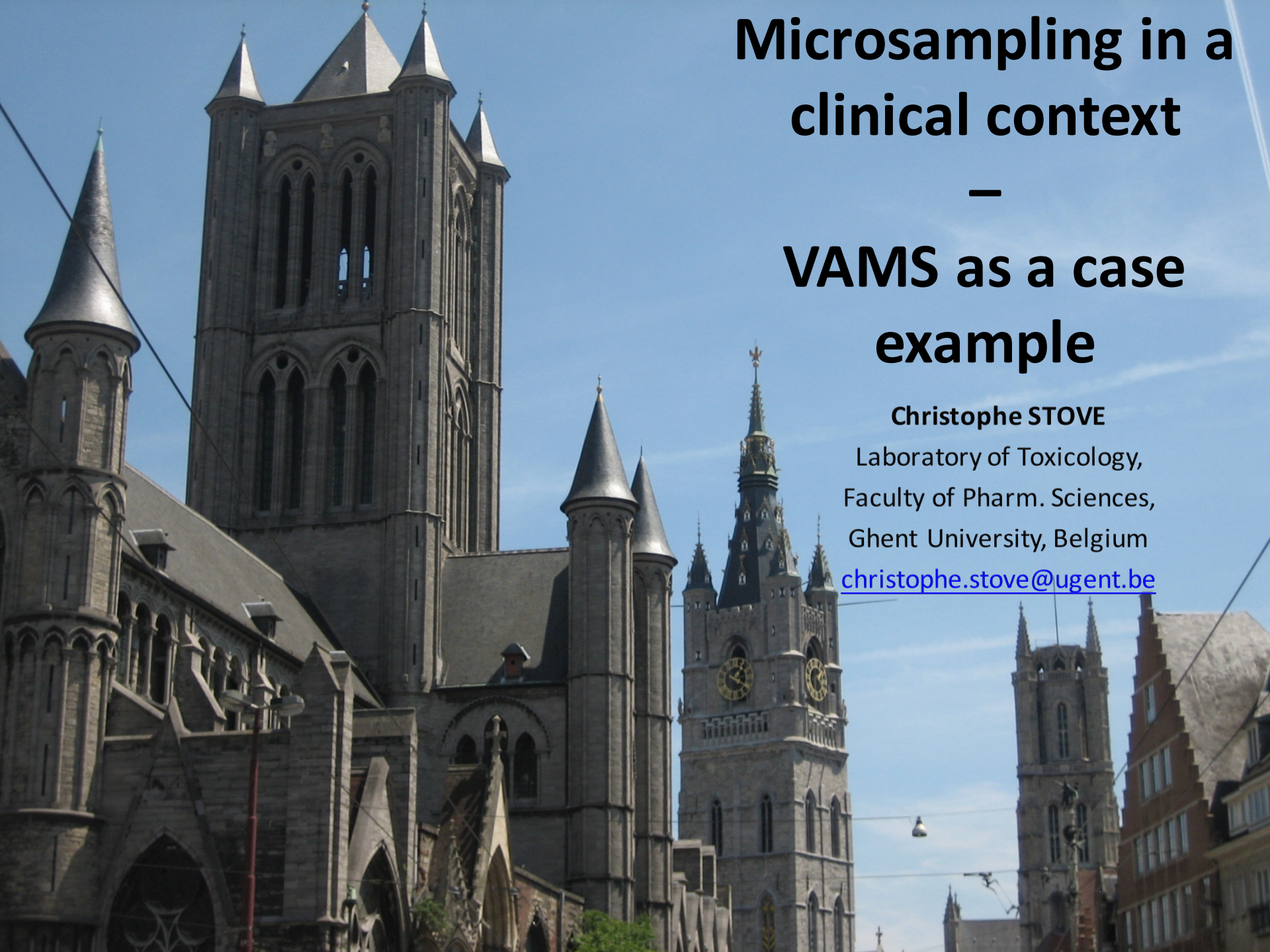
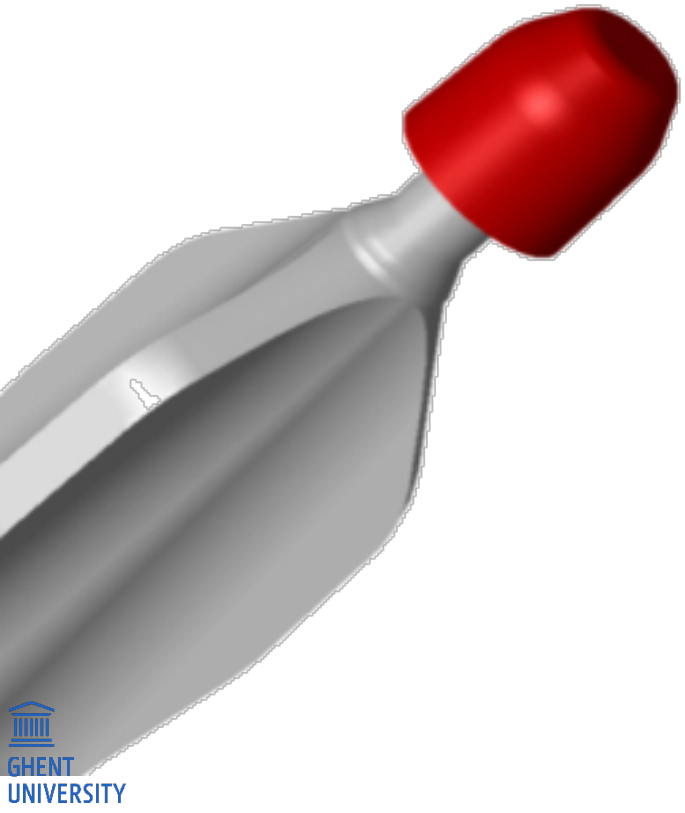


Microsampling in a clinical context – VAMS as a case example

Christophe STOVE
Laboratory of Toxicology,
Faculty of Pharm. Sciences,
Ghent University, Belgium
christophe.stove@ugent.be

PRESENTATION OVERVIEW



- General
- Hct independence of VAMS
- VAMS for anti-epileptic TDM
- VAMS for Co monitoring
- VAMS for HbA1c monitoring

INTRO: Challenges of Volumetric Absorptive Microsampling

- Limited amount of sample & analyte available
- Sample quality (+ contamination risk)
- Recovery issues (hematocrit!)
- Stability issues
- ~~Volume Issues (related to paper saturation)~~
- ~~Spot inhomogeneity ('chromatography effect')~~
- ~~Hematocrit effect (spreading)~~
- Possible differences between capillary & venous blood
- Interpretation (blood [ ] *vs.* plasma [ ])

More extensive validation required

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De Kesel, Sadones & Capiau *et al.*, Bioanalysis, 2013

Volumetric Absorptive Microsampling: Hct independence

analytical chemistry

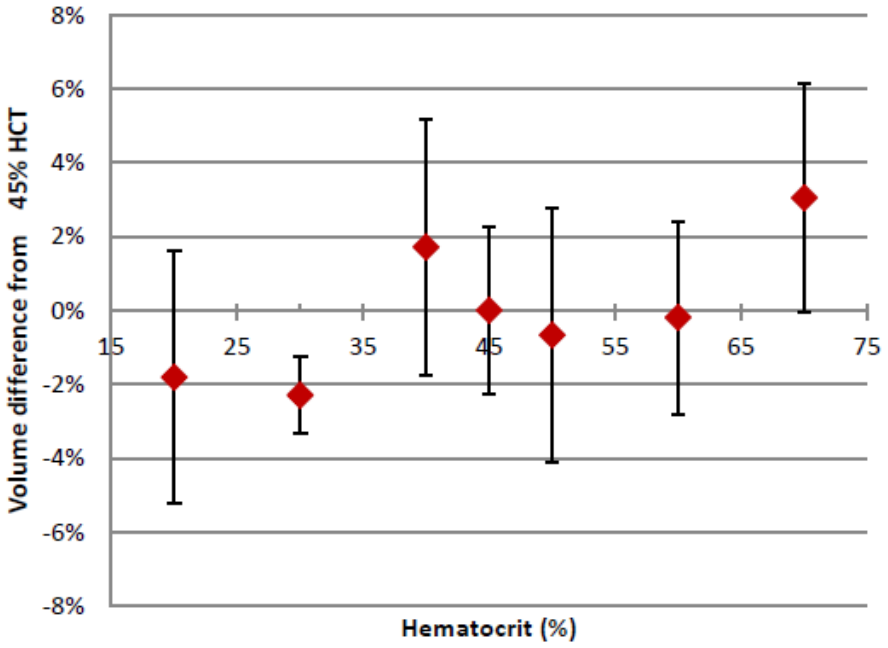
Article

pubs.acs.org/ac

Volumetric Absorptive Microsampling: A Dried Sample Collection Technique for Quantitative Bioanalysis

Philip Denniff and Neil Spooner*

Bioanalytical Science and Toxicokinetics, Drug Metabolism and Pharmacokinetics, GlaxoSmithKline Research and Development, Ware, Hertfordshire SG12 0DP, United Kingdom



Artificial samples: ≠ Hct by adding or removing plasma

What about real (clinical) samples?

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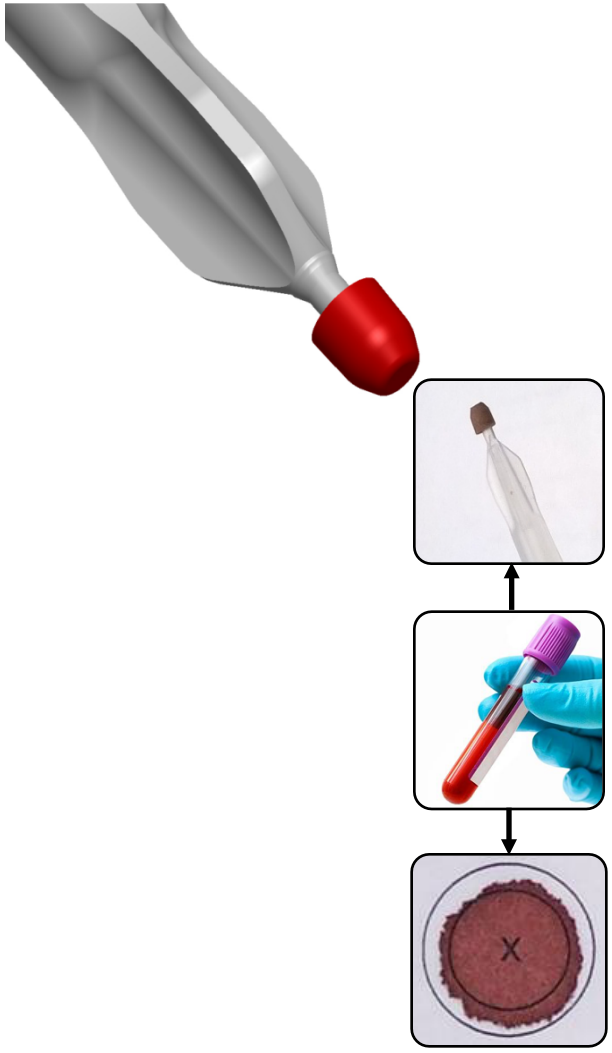
Volumetric Absorptive Microsampling: Hct independence



Study Set-up:

- Use left-over EDTA-anticoagulated blood from patients (≠ hospital departments)
- Compare liquid blood – VAMS – DBS
- Analytes: caffeine & paraxanthine

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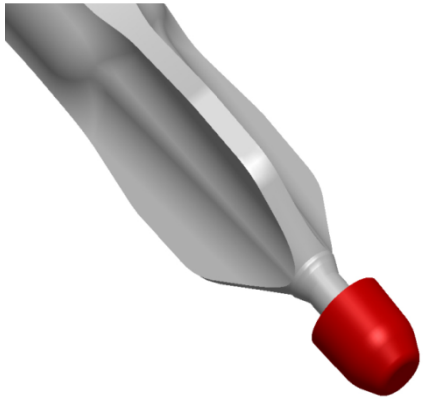
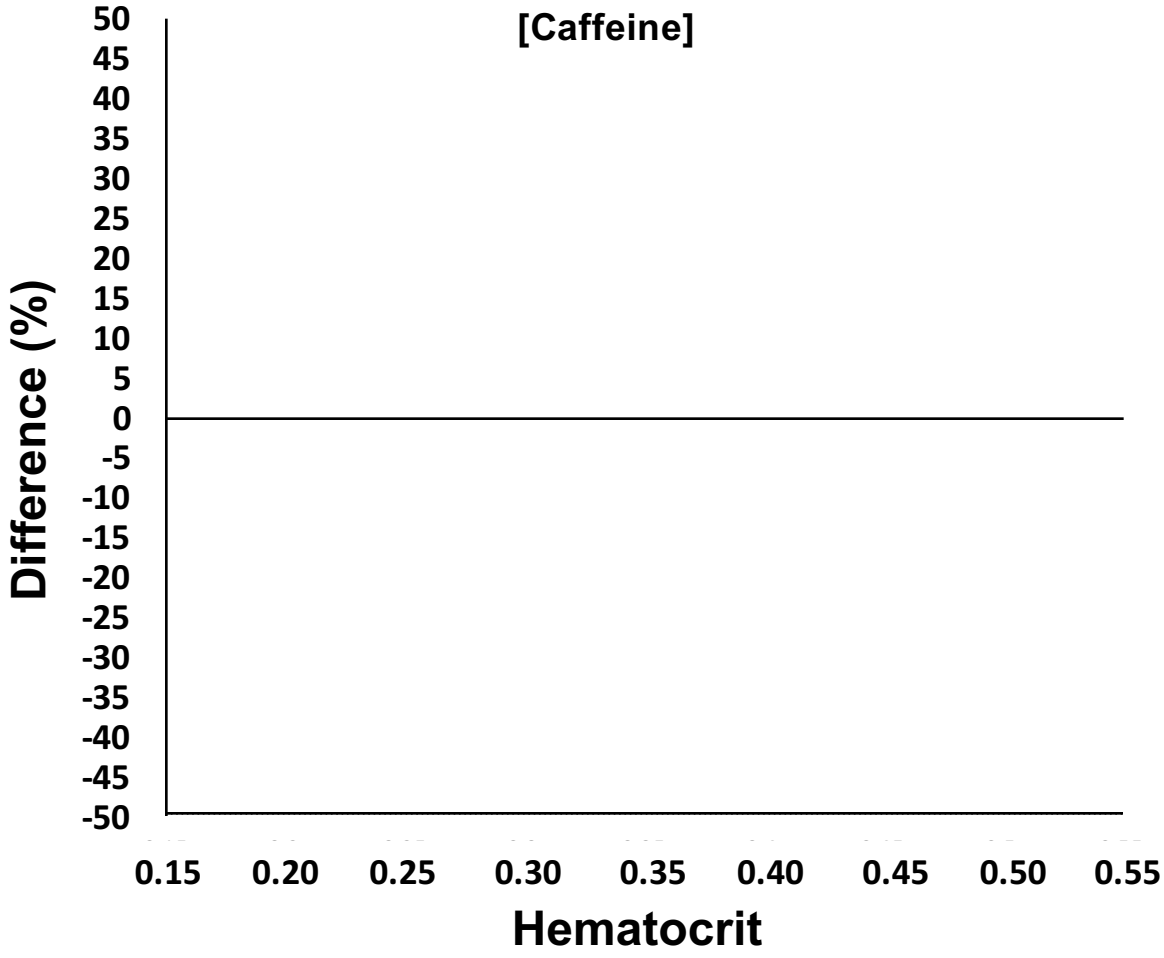
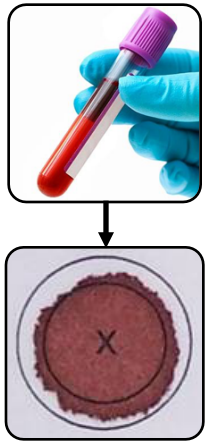
De Kesel et al., Anal Chim Acta, 2015

Volumetric Absorptive Microsampling: Hct independence







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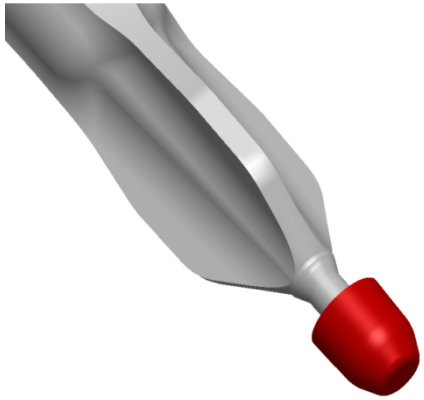
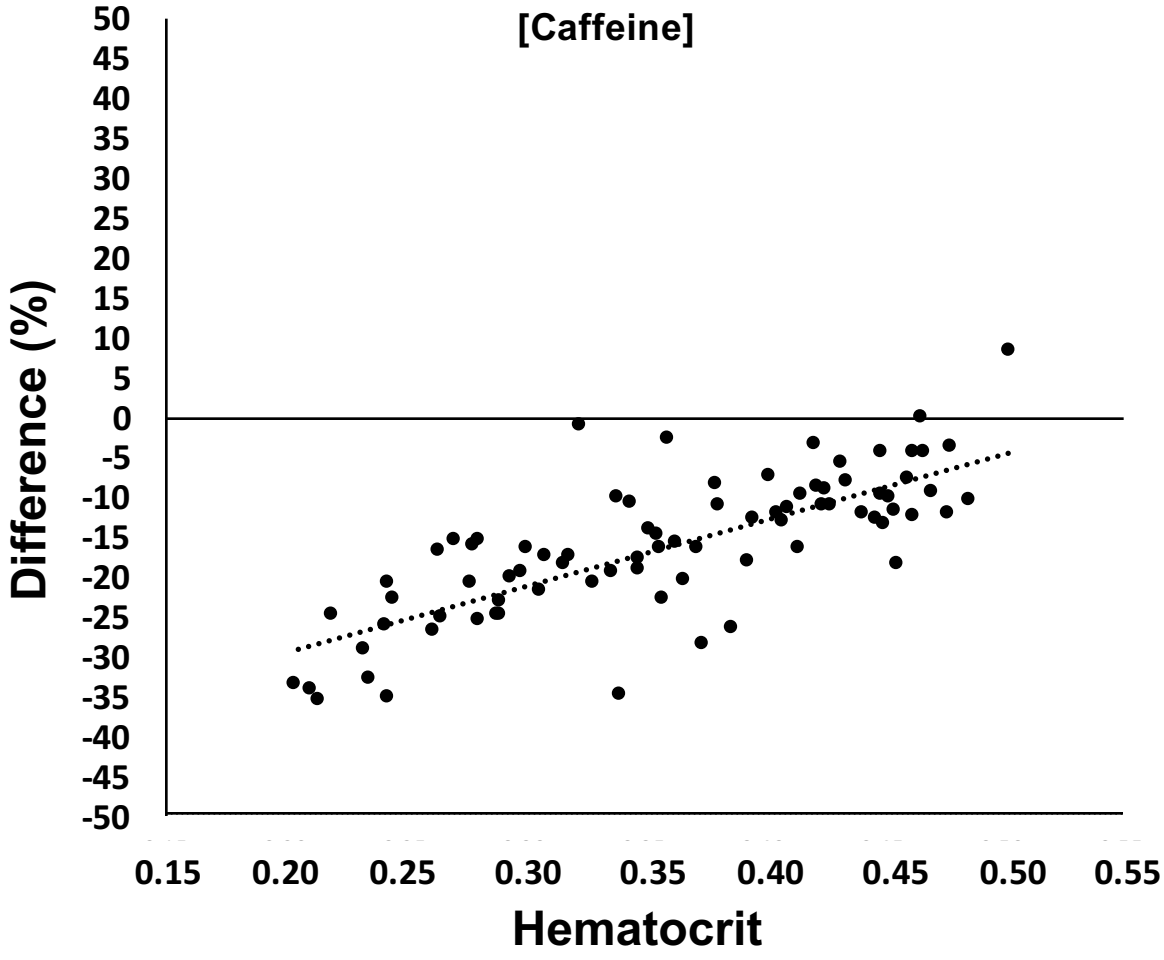
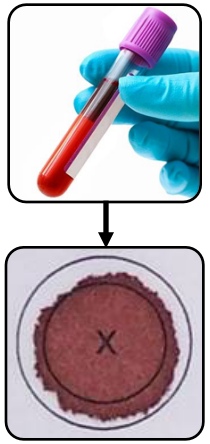
De Kesel et al., Anal Chim Acta, 2015

Volumetric Absorptive Microsampling: Hct independence







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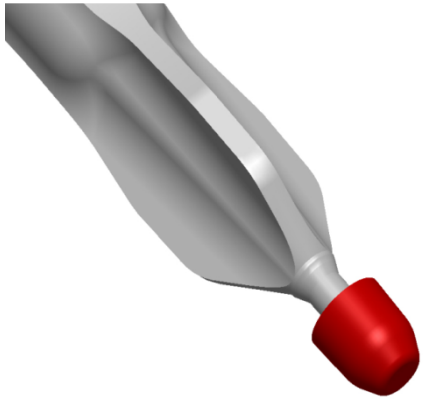
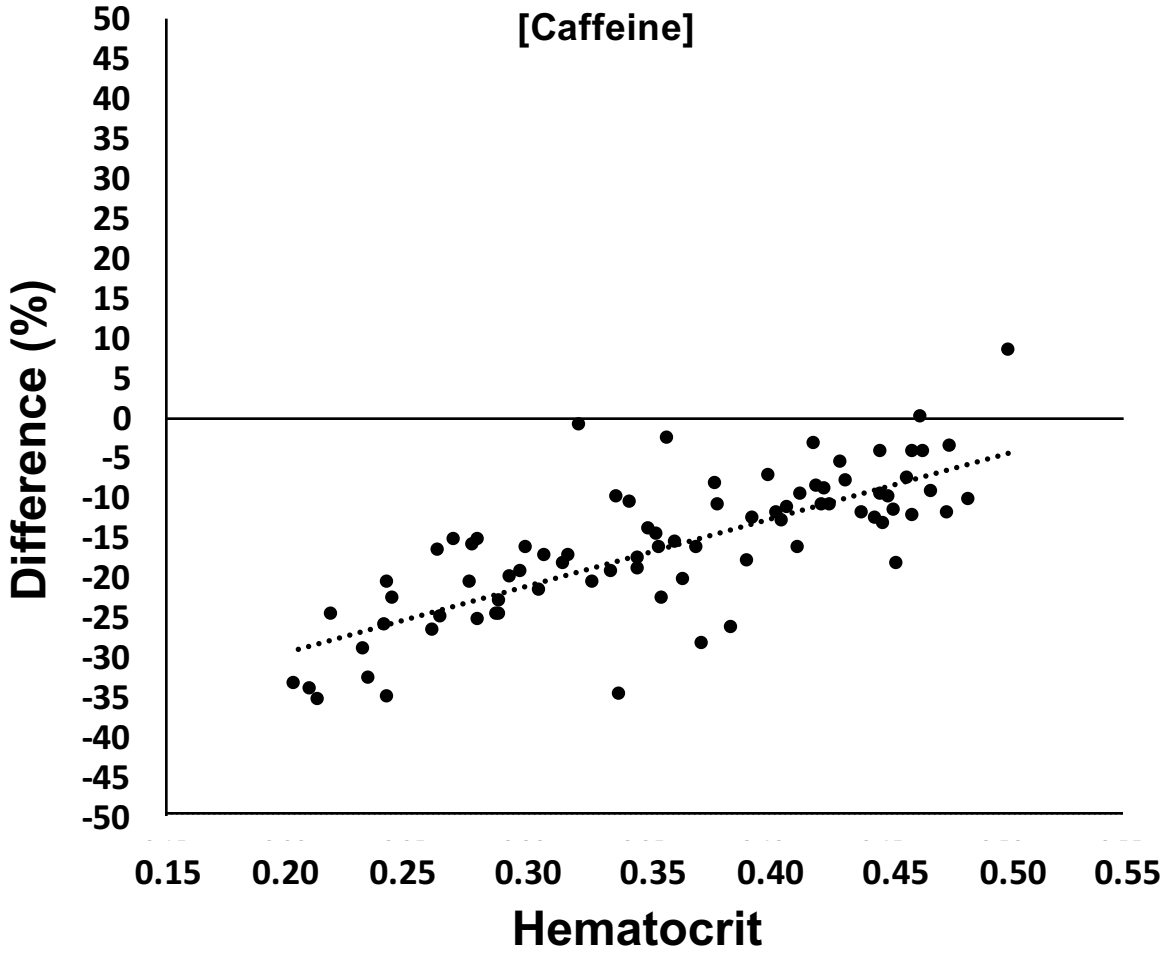
Volumetric Absorptive Microsampling: Hct independence





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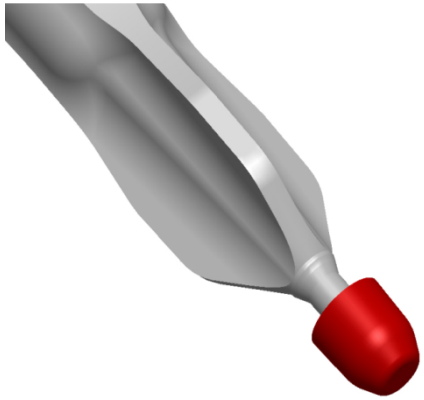
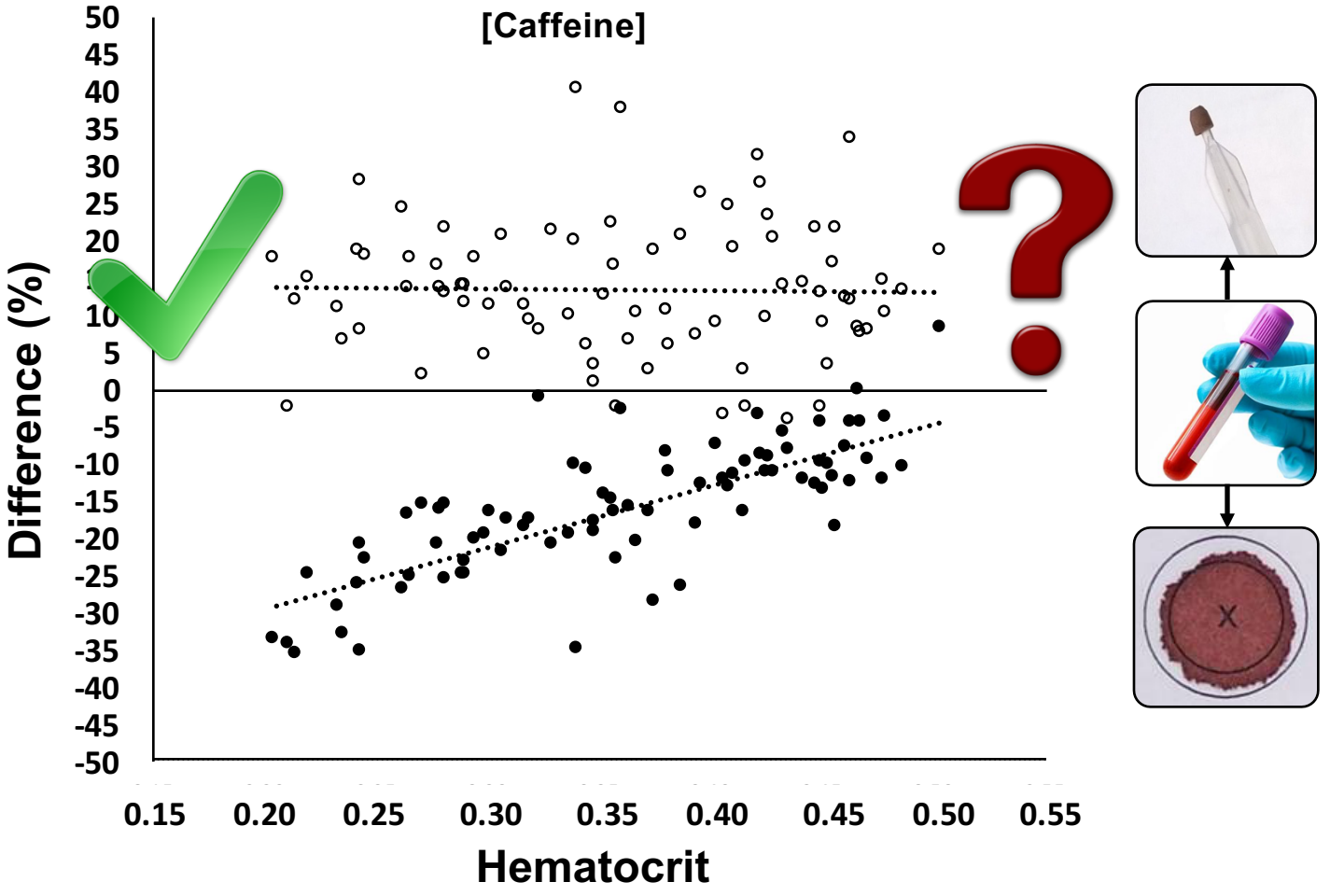
De Kesel et al., Anal Chim Acta, 2015

Volumetric Absorptive Microsampling: Hct independence





De Kesel et al., Anal Chim Acta, 2015

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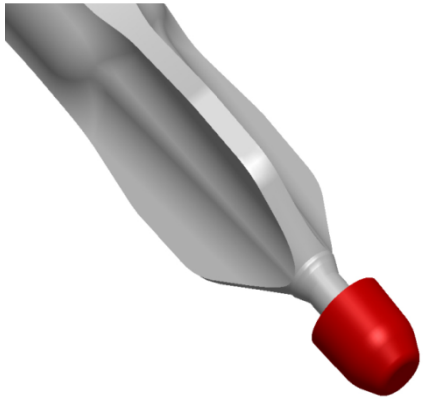

Evaluation of impact of hematocrit on recovery:

- VAMS: Similar extraction procedure as for DBS
- ↓ recovery at higher hematocrits

Absolute recovery and matrix effect data (n = 3) for caffeine and paraxanthine at two concentration levels in VAMS samples prepared using whole blood with varying Hct values.

	Hct	Caffeine		Paraxanthine	
		Low QC	High QC	Low QC	High QC
Absolute recovery (mean ± SD, %)	0.21	101.45 ± 2.26	101.79 ± 0.67	86.98 ± 1.52	87.14 ± 1.75
	0.42	101.30 ± 1.28	100.53 ± 2.67	84.70 ± 3.53	84.33 ± 1.38
	0.48	93.86 ± 0.89	91.08 ± 2.03	75.48 ± 0.60	75.93 ± 1.09
	0.62	92.01 ± 4.80	92.91 ± 4.74	73.51 ± 1.60	77.72 ± 5.69

The calibration line had been set up at a relative high Ht;

⇒ because of the impact of the Ht, recovery of the vast majority of the samples will be slightly higher than that of the calib.'s

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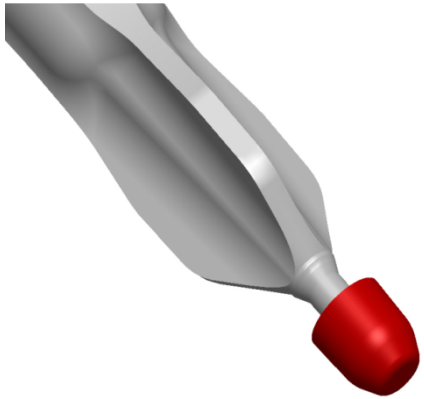
De Kesel et al., Anal Chim Acta, 2015

Volumetric Absorptive Microsampling: Hct independence



Evaluation of impact of hematocrit on recovery:

- VAMS: Similar extraction procedure as for DBS
- ↓ recovery at higher hematocrits
- No impact on matrix effect

Absolute recovery and matrix effect data (n = 3) for caffeine and paraxanthine at two concentration levels in VAMS samples prepared using whole blood with varying Hct values.

	Hct	Caffeine		Paraxanthine	
		Low QC	High QC	Low QC	High QC
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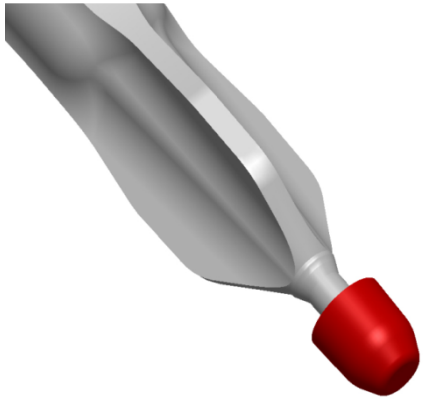
	0.62	92.01 ± 4.80	92.91 ± 4.74	73.51 ± 1.60	77.72 ± 5.69
Absolute matrix effect (mean ± SD, %)	0.21	104.29 ± 3.37	100.49 ± 1.54	101.46 ± 2.49	99.69 ± 2.01
	0.42	101.16 ± 0.53	99.52 ± 1.71	98.28 ± 3.28	99.48 ± 0.34
	0.48	97.46 ± 0.50	97.48 ± 0.99	99.03 ± 2.73	99.10 ± 1.31
	0.62	103.07 ± 2.09	98.36 ± 0.31	100.58 ± 4.26	99.48 ± 1.78

De Kesel et al., Anal Chim Acta, 2015

Volumetric Absorptive Microsampling: Hct independence



Might there be a blood-VAMS difference between real samples & spiked samples?:

→ Determine concentrations in a spiked sample and a real sample (following caffeine consumption) (n=3)

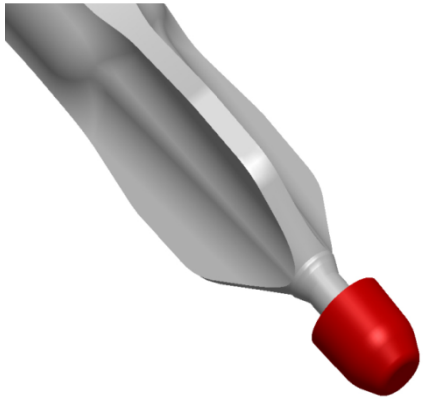
		VAMS (µg mL^{-1}) mean ± SD [% CV]	Whole blood (µg mL^{-1}) mean ± SD; [CV]	Difference VAMS-whole blood (%)
Caffeine	Spiked samples	1.03 ± 0.01 [1.36]	1.01 ± 0.01 [1.31]	1.49
	Incurred samples	1.12 ± 0.01 [1.07]	1.04 ± 0.02 [1.74]	6.86*
Paraxanthine	Spiked samples	0.81 ± 0.01 [1.45]	0.81 ± 0.01 [0.62]	0.35
	Incurred samples	0.82 ± 0.02 [1.95]	0.77 ± 0.01 [0.88]	6.35*

* significant difference ($p < 0.05$)

⇒ **Incurred (real) samples show a slight overestimation with VAMS, as compared to liquid blood**

De Kesel et al., Anal Chim Acta, 2015

Volumetric Absorptive Microsampling: Hct independence



Conclusions of our evaluation of VAMS:

- Sampling is straightforward (even more than with DBS)
- VAMS overcomes the hematocrit bias that is seen in DBS analysis
- For the analytes investigated (caffeine & paraxanthine), a slight positive bias (i.e. overestimation) was observed

  This positive bias may be accounted for by 2 factors:

  - VAMS are more subject to a hematocrit effect on recovery than DBS (our calibr. line being set up at a higher Ht than that of most samples)
  - VAMS resulted in a slight overestimation of incurred but not spiked samples, when compared with blood

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De Kesel et al., Anal Chim Acta, 2015

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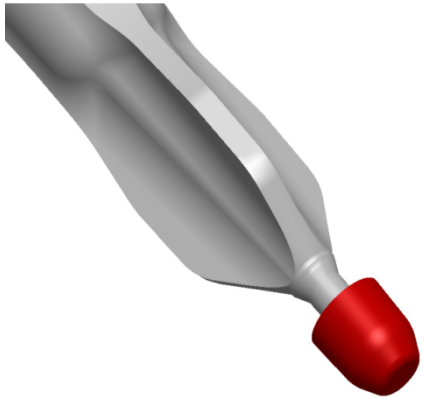

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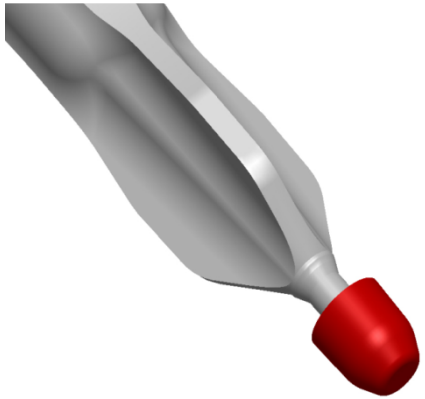

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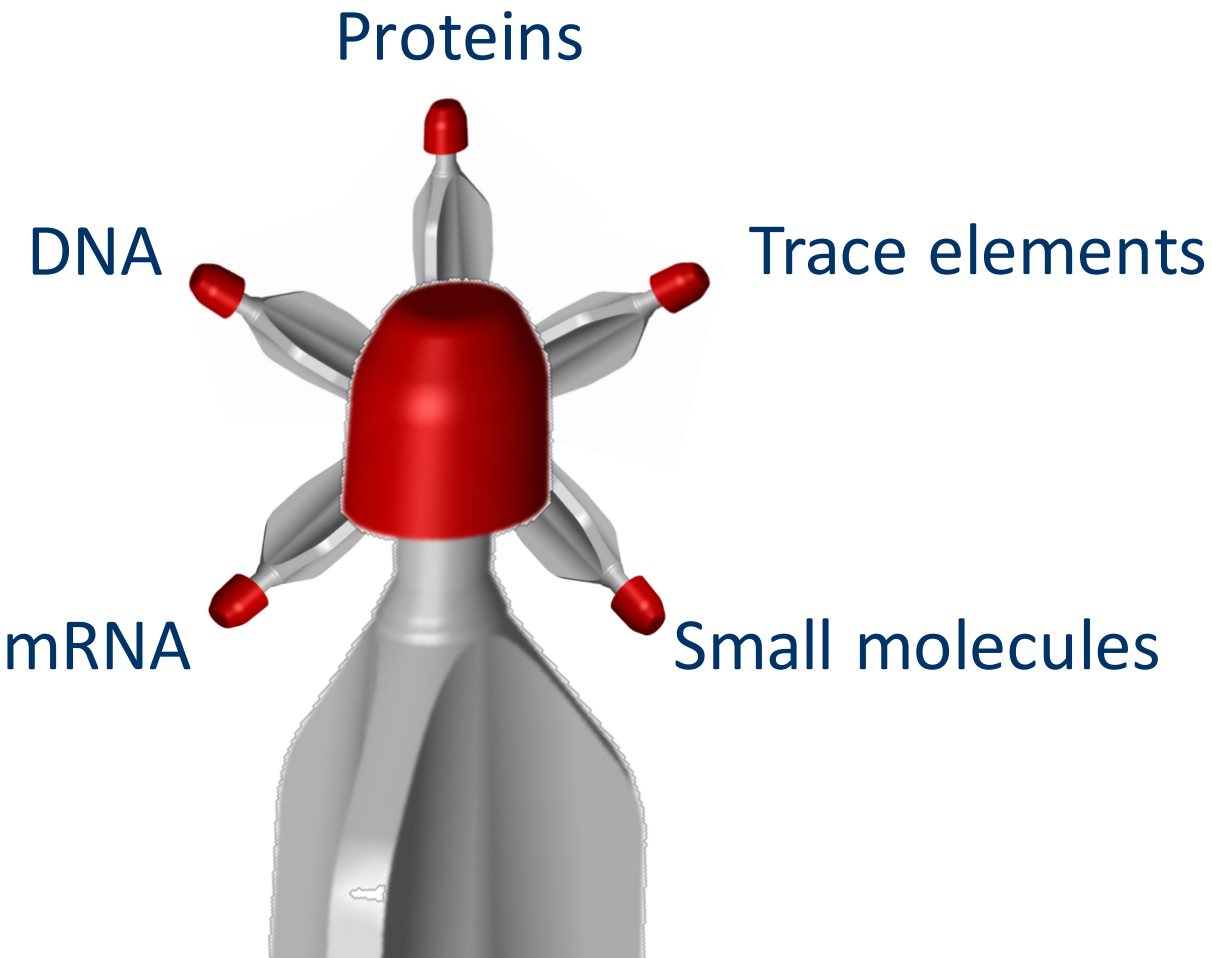
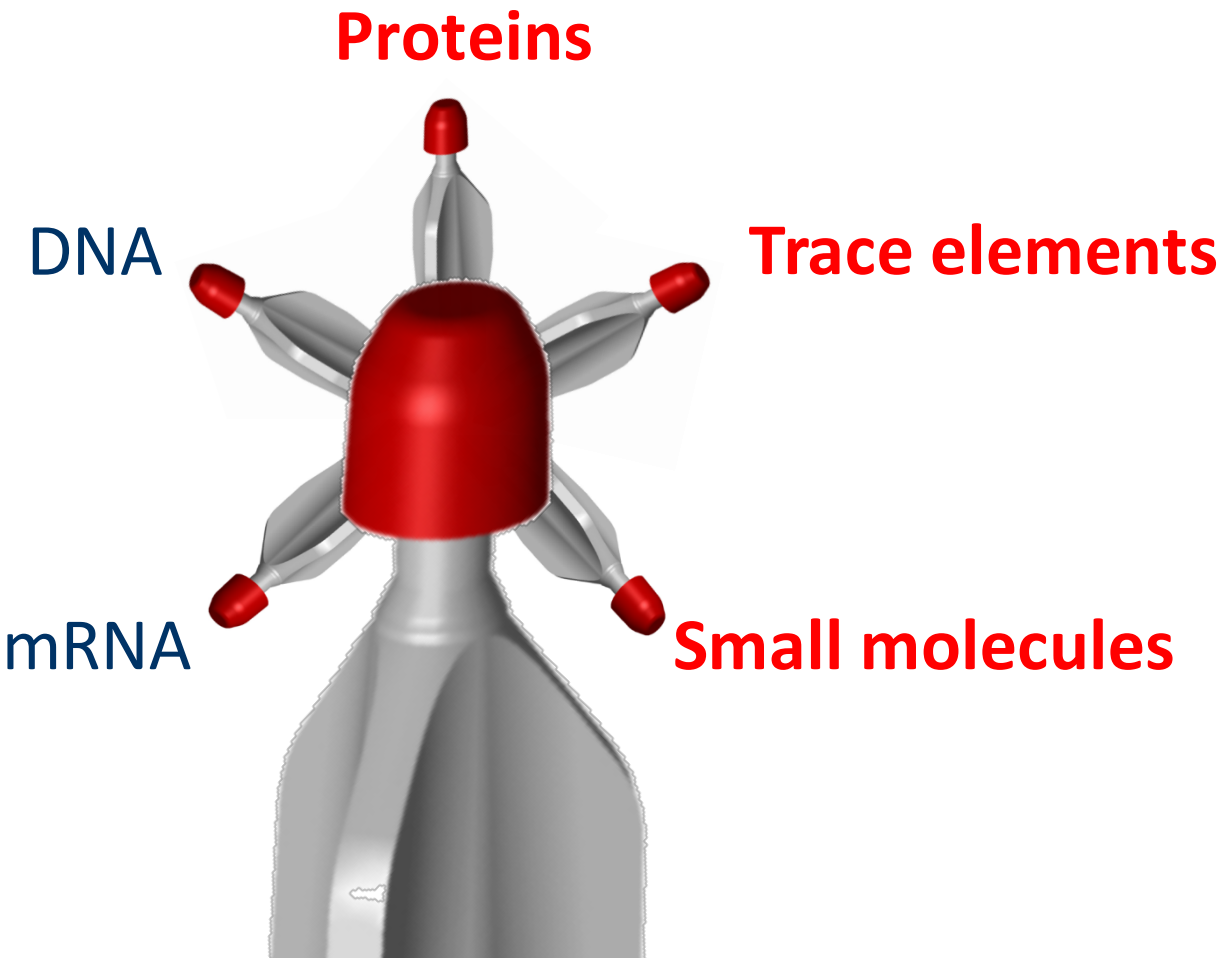
De Kesel et al., Anal Chim Acta, 2015

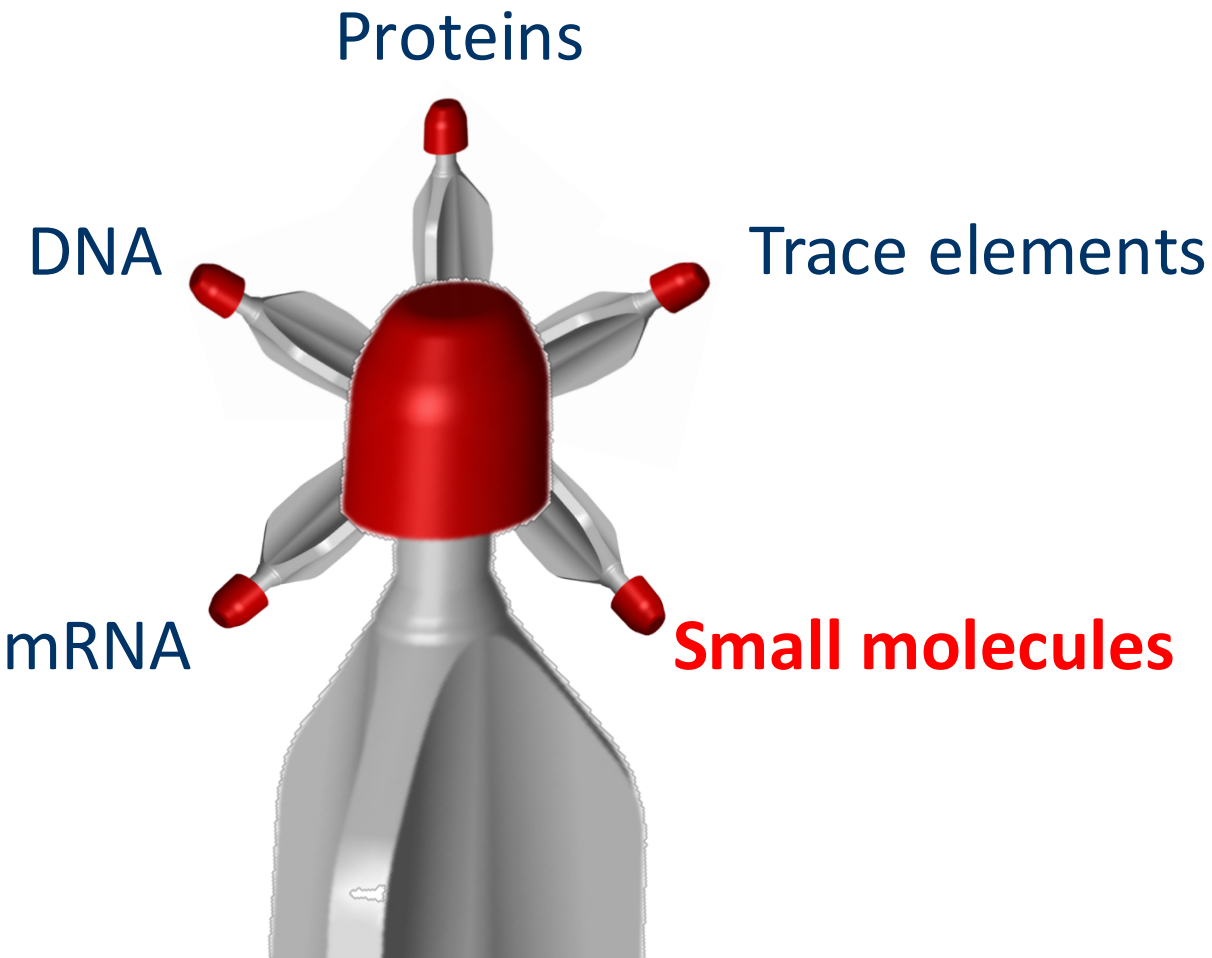
Volumetric Absorptive Microsampling: (potential) analytes



Volumetric Absorptive Microsampling: (potential) analytes



Volumetric Absorptive Microsampling: (potential) analytes



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Volumetric Absorptive Microsampling: small molecules

- Antihypertensives
- Antiretrovirals
- Antimalarials
- Antibiotics
- Antidiabetics
- Analgesics
- Immunosuppressants
- Anticonvulsants
- Antipsychotics
- …

TDM

- Phosphatidylethanol
- Cotinine
- Benzodiazepines
- Heroin, Morphine, 6-Monoacetylmorphine
- Methadone, Buprenorphine
- Fentanyl
- Cocaine, benzoylecgonine, cocaethylene
- MDMA (ecstasy), MDA
- Cannabinoids
- Gamma-hydroxybutyric acid (GHB)
- …

CLIN TOX

Volumetric Absorptive Microsampling: small molecules

- Antihypertensives
- Antiretrovirals
- Antimalarials
- **Antibiotics**
- Antidiabetics
- **Analgesics**
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- …

TDM

- **Phosphatidylethanol**
- Cotinine
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- MDMA (ecstasy), MDA
- **Cannabinoids**
- Gamma-hydroxybutyric acid (GHB)
- **…**

CLIN TOX

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VAMS for TDM of conventional anti-epileptics

Anti-epileptic drugs

Classical or First-generation AEDs	New-generation AEDs
Valproic acid, phenobarbital, phenytoin, carbamazepine, primidone and ethosuximide	Gabapentin, lamotrigine, oxcarbazepine, topiramate, vigabatrine, … .
→ Narrow therapeutic ranges → inter-individual variability in PK (ADME) ⇩ Therapy optimization and individualization quite challenging	→ Wider therapeutic ranges → Fewer serious adverse effects

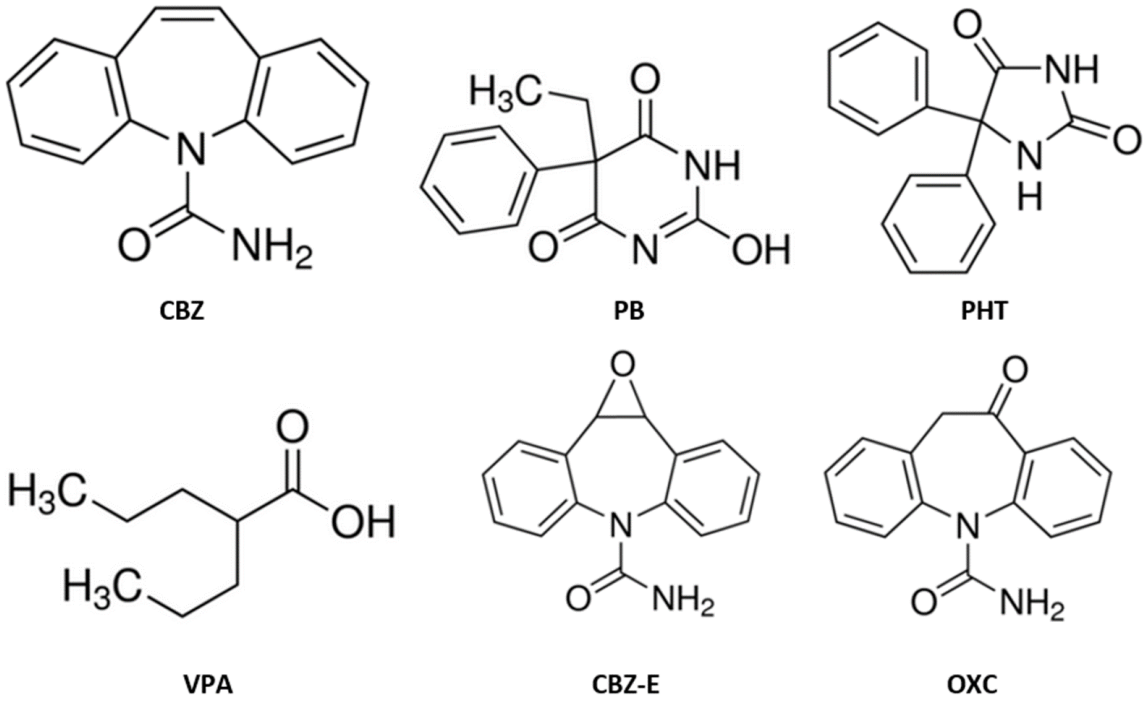
TDM of AEDs:

- **Excellent tool for therapy optimization & individualization**
- **Helpful in maximizing safety and benefits**

VAMS for TDM of conventional anti-epileptics

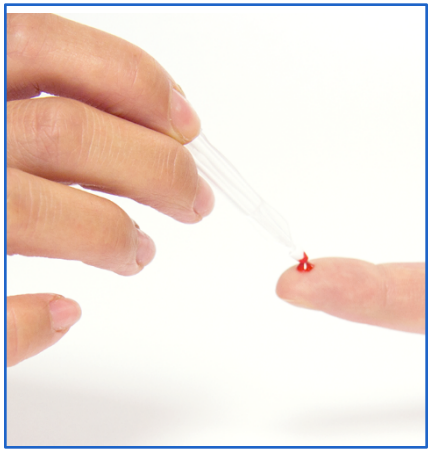
Study objective

Determination and quantification of 5 AEDs and 1 active metabolite

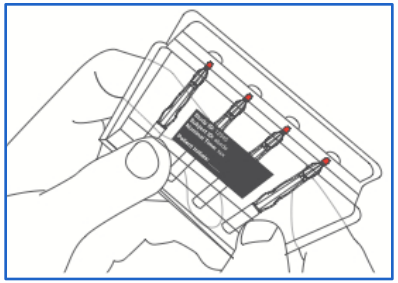


VAMS for TDM of conventional anti-epileptics

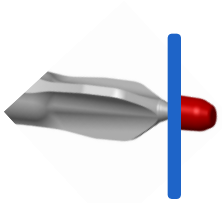
Sample preparation



Preparing the VAMS



Drying for 2 hours



Removing of VAMS tip

Extraction with 100 µL 80/20 ACN/H_2O + IS + 5mM amm.acet

Thermomixer: 10min; 60°C; 1000 rpm

Centrifugation: 10min; 10 000 g

70 µL supernatant + 70 µL H_2O + 5mM amm.acet

LC-MS/MS

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VAMS for TDM of conventional anti-epileptics

LC-MS/MS

Chromatography (Waters Acquity UPLC®)

- Column: Chromolith® reversed phase (RP)-18 endcapped (100x4.60 mm; 5 µm)
- Mobile phase: 5mM ammonium acetate in H_2O (A) and in ACN/H_2O 95/5 (B)
- Flow: 1.4 mL/min
- Column temperature: 45°C
- Gradient elution
- Total runtime: 10 min (including negative, positive run, washing and equilibrating)

Mass spectrometry (Sciex API 4000™)

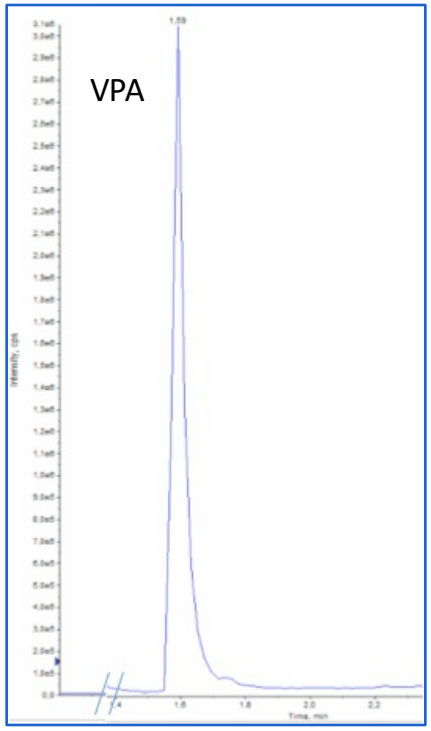
- TurboIonSpray® probe (ESI)
- MRM™ mode
- Positive ion mode: CBZ, CBZ-E, OXC
- Negative ion mode: VPA, PB, PHT

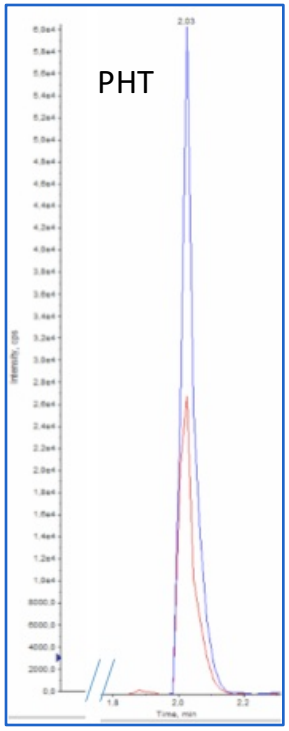
Use of deuterium-labeled internal standards: CBZ-d10, CBZ-E-d10, OXC-d4, VPA-d6, PB-d5, PHT-d10

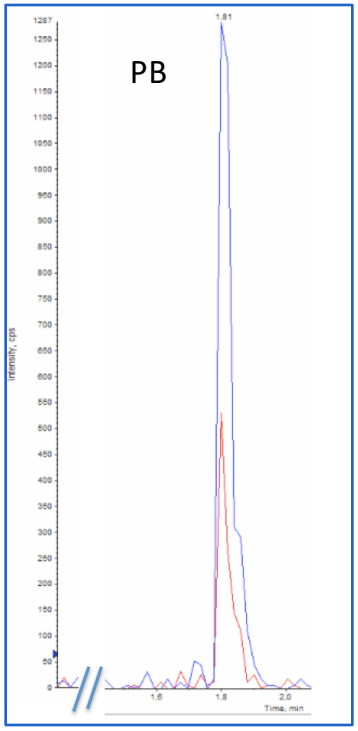
VAMS for TDM of conventional anti-epileptics

Chromatogram

Negative ion mode (LLOQ)



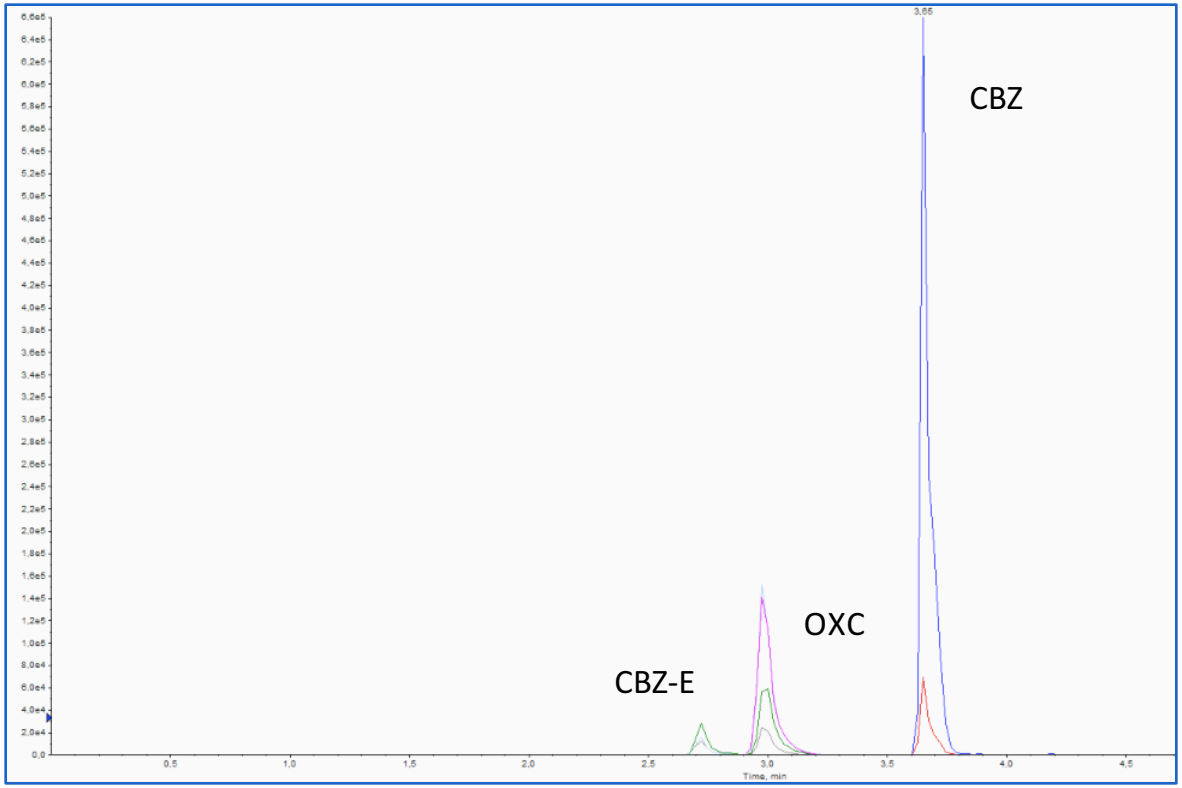




VAMS for TDM of conventional anti-epileptics

Chromatogram

Positive ion mode (LLOQ)



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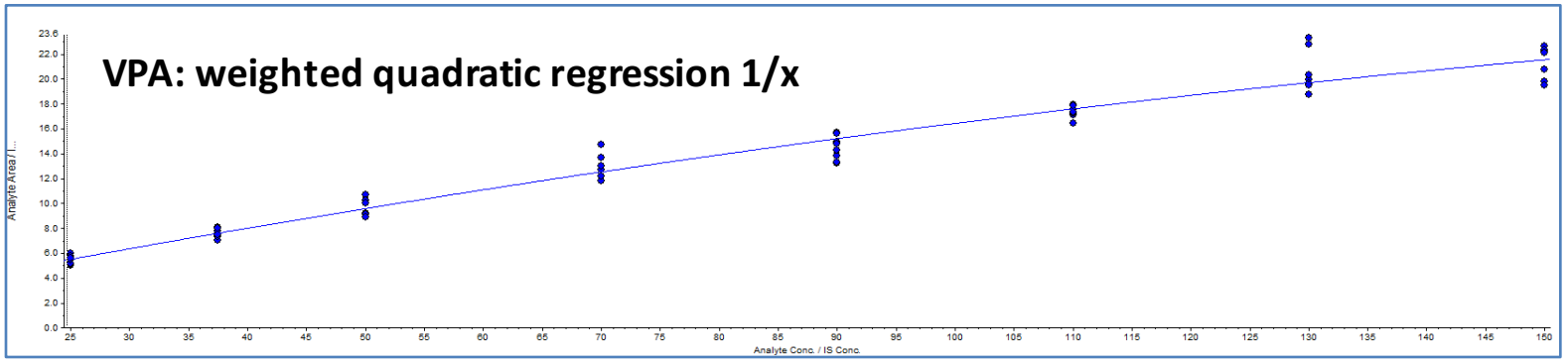
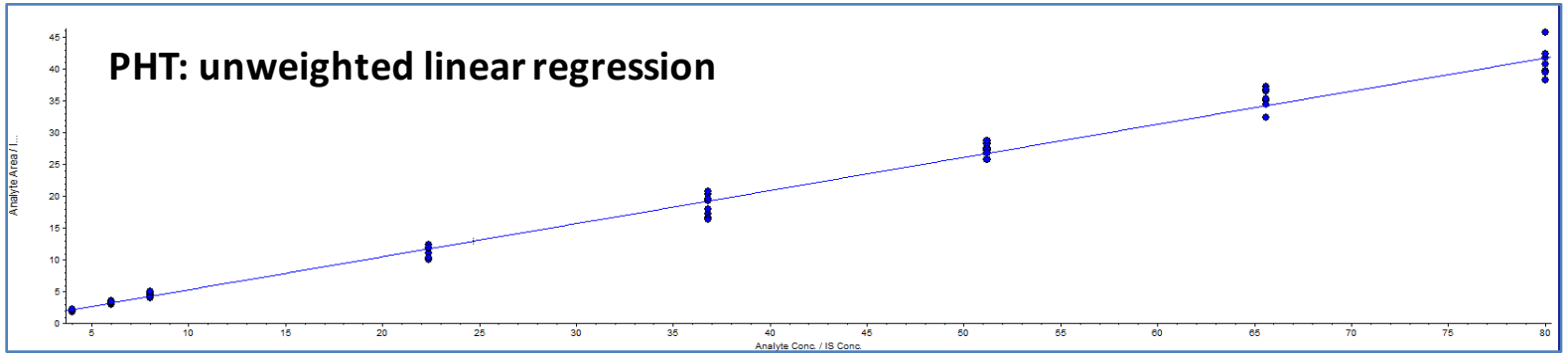
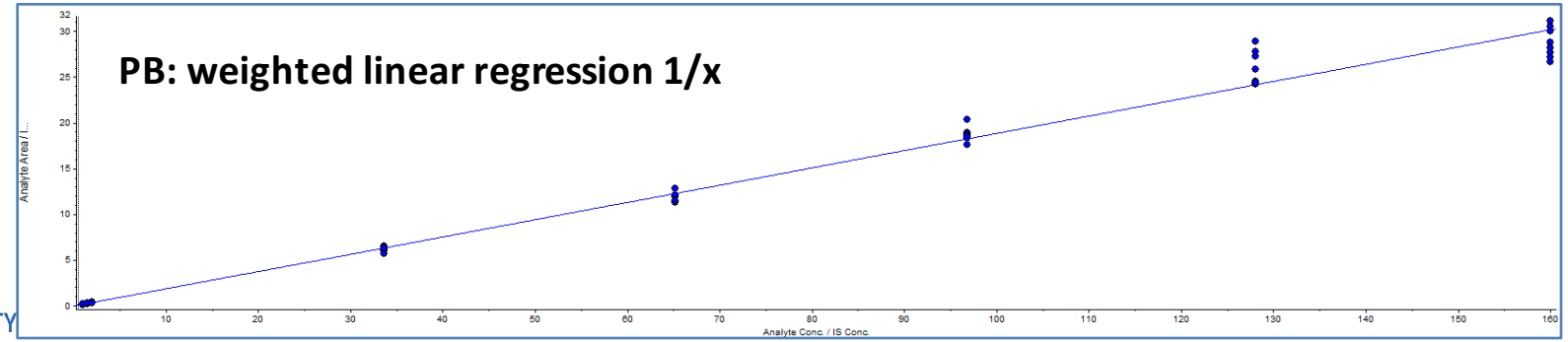
VAMS for TDM of conventional anti-epileptics

Validation: calibration model







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VAMS for TDM of conventional anti-epileptics

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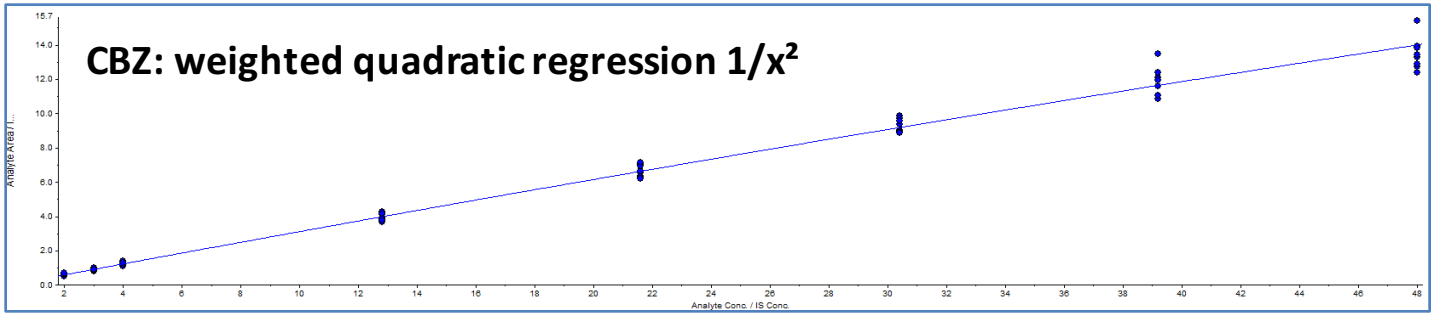

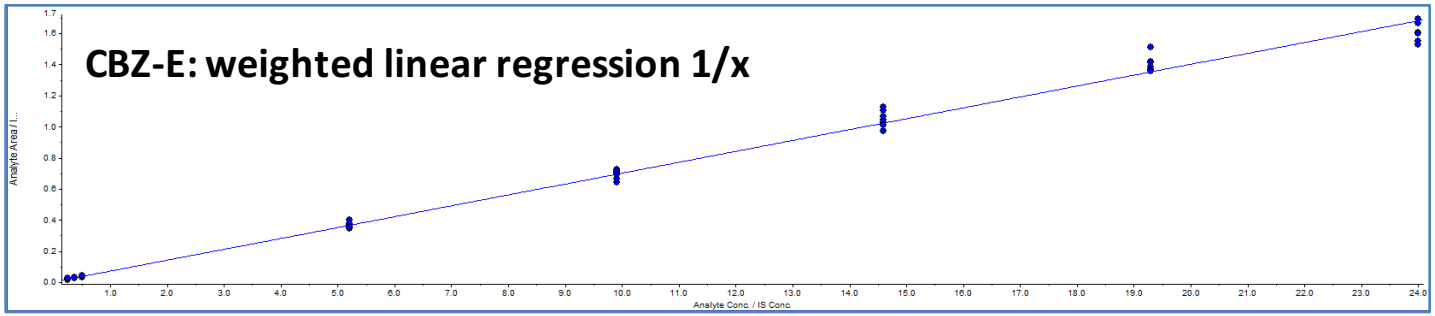

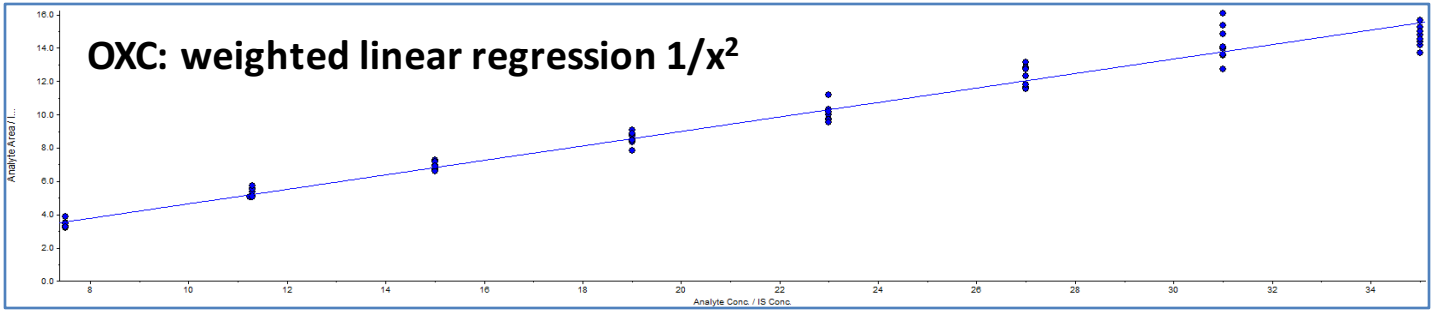

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VAMS for TDM of conventional anti-epileptics

Validation: accuracy and precision

VPA	Accuracy %	Within run precision %	Between run precision %
LLOQ	-15	7.5	7.5
Low QC	18	3.8	8.2
Mid QC	-1	5.6	5.6
High QC	-1	8.3	8.3

PHT	Accuracy %	Within run precision %	Between run precision %
LLOQ	4	8.6	8.6
Low QC	1	6.6	6.6
Mid QC	4	7.9	7.9
High QC	5	4.1	7.7

PB	Accuracy %	Within run precision %	Between run precision %
LLOQ	-1	9.8	9.8
Low QC	-1	7.3	7.8
Mid QC	-3	4.5	4.5
High QC	2	3.9	6.2

VAMS for TDM of conventional anti-epileptics

Validation: accuracy and precision

CBZ	Accuracy %	Within run precision %	Between run precision %
LLOQ	10	8.8	8.8
Low QC	1	7.5	7.5
Mid QC	8	6.0	6.0
High QC	2	9.0	9.0

CBZ-E	Accuracy %	Within run precision %	Between run precision
LLOQ	4	7.7	7.7
Low QC	14	6.5	6.6
Mid QC	8	5.3	5.3
High QC	5	5.1	5.1

OXC	Accuracy %	Within run precision %	Between run precision %
LLOQ	-40	6.4	6.4
Low QC	5	5.2	6.3
Mid QC	1	4.1	5.6
High QC	11	6.4	6.4

VAMS for TDM of conventional anti-epileptics

Validation: matrix effects

Hct range: 0.335 – 0.495

VPA

IS corrected matrix effect	Low QC %	High QC %
Matrix 1	103	101
Matrix 2	103	102
Matrix 3	104	102
Matrix 4	100	99
Matrix 5	103	104
Matrix 6	103	99
Average	103	101
CV%	1.21	1.83

PHT

IS corrected matrix effect	Low QC %	High QC %
Matrix 1	96	98
Matrix 2	94	96
Matrix 3	97	91
Matrix 4	104	93
Matrix 5	97	99
Matrix 6	102	95
Average	99	95
CV%	3.91	3.01

PB

IS corrected matrix effect	Low QC %	High QC %
Matrix 1	98	98
Matrix 2	96	95
Matrix 3	99	96
Matrix 4	101	94
Matrix 5	98	97
Matrix 6	97	95
Average	98	96
CV%	1.92	1.58

VAMS for TDM of conventional anti-epileptics

Validation: matrix effects

Hct range: 0.335 – 0.495

CBZ

IS corrected matrix effect	Low QC %	High QC %
Matrix 1	91	91
Matrix 2	96	89
Matrix 3	92	91
Matrix 4	94	91
Matrix 5	93	90
Matrix 6	92	90
Average	93	90
CV%	1.67	0.93

CBZ-E

IS corrected matrix effect	Low QC %	High QC %
Matrix 1	96	97
Matrix 2	93	100
Matrix 3	98	96
Matrix 4	96	96
Matrix 5	95	99
Matrix 6	96	106
Average	95	99
CV%	1.70	3.97

OXC

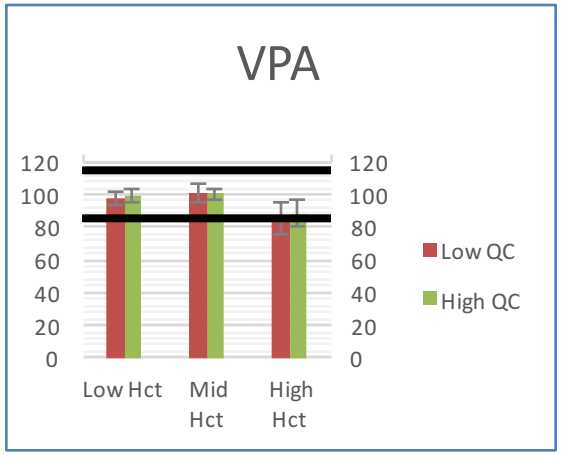
IS corrected matrix effect	Low QC %	High QC %
Matrix 1	116	83
Matrix 2	117	86
Matrix 3	116	88
Matrix 4	120	89
Matrix 5	119	89
Matrix 6	120	91
Average	118	88
CV%	1.46	3.15

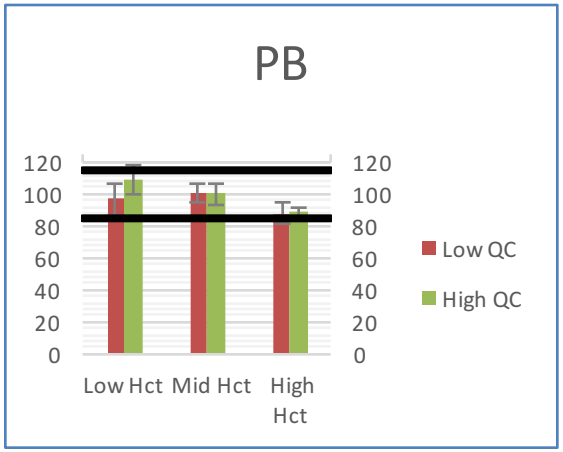
=> Fulfills acceptance criteria, except for Low QC of OXC

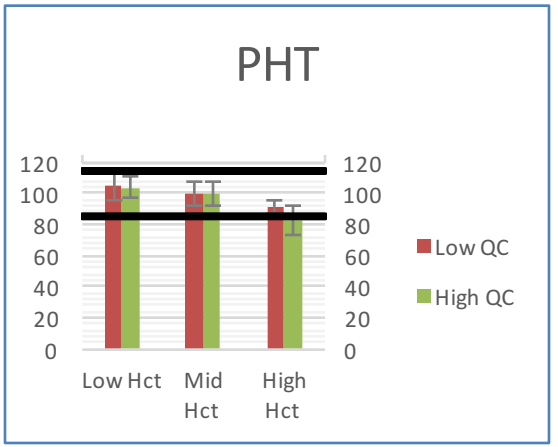
VAMS for TDM of conventional anti-epileptics

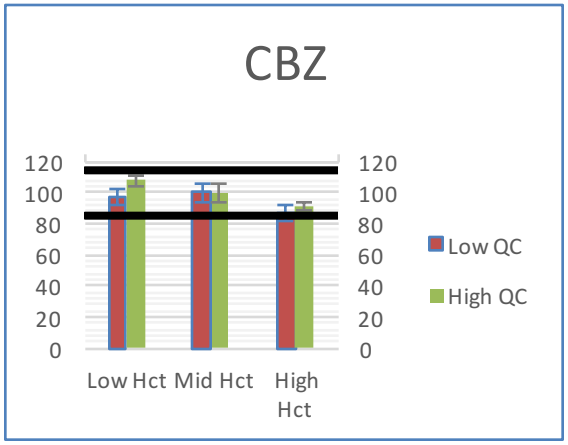
Validation: haematocrit effect

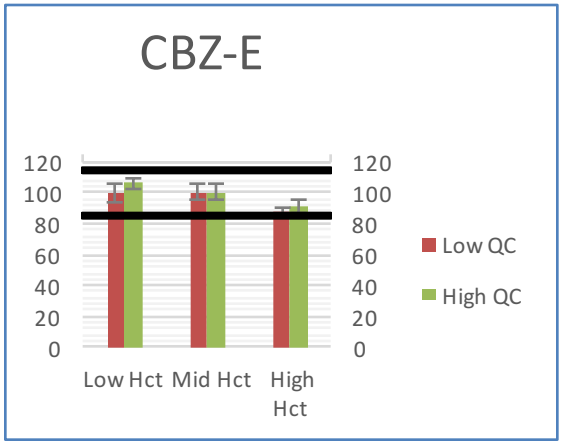
Low Hct: 0.21
Mid Hct: 0.42
High Hct: 0.62

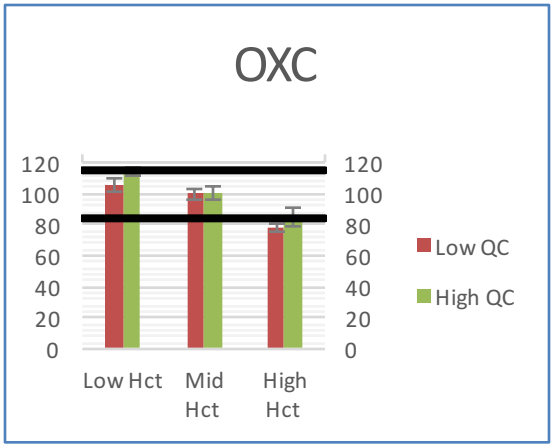












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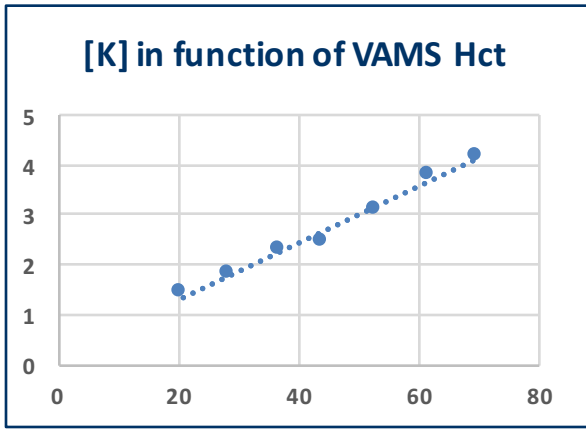
VAMS for TDM of conventional anti-epileptics

Conclusion and future perspectives

- A method for the quantification of conventional anti-epileptics was succesfully set up
- The calibration lines cover relevant concentration ranges
- Accuracy and precision overall fulfilled acceptance criteria
- Matrix effects (evaluated at different hematocrits) overall fulfilled acceptance criteria
- At elevated Hct levels there was a slight Hct effect (in terms of somewhat ↓ recovery)
- The method has already been applied succesfully on reference samples
- This method will be applied on patients

  K-based Hct may be used to calculate serum[ ]



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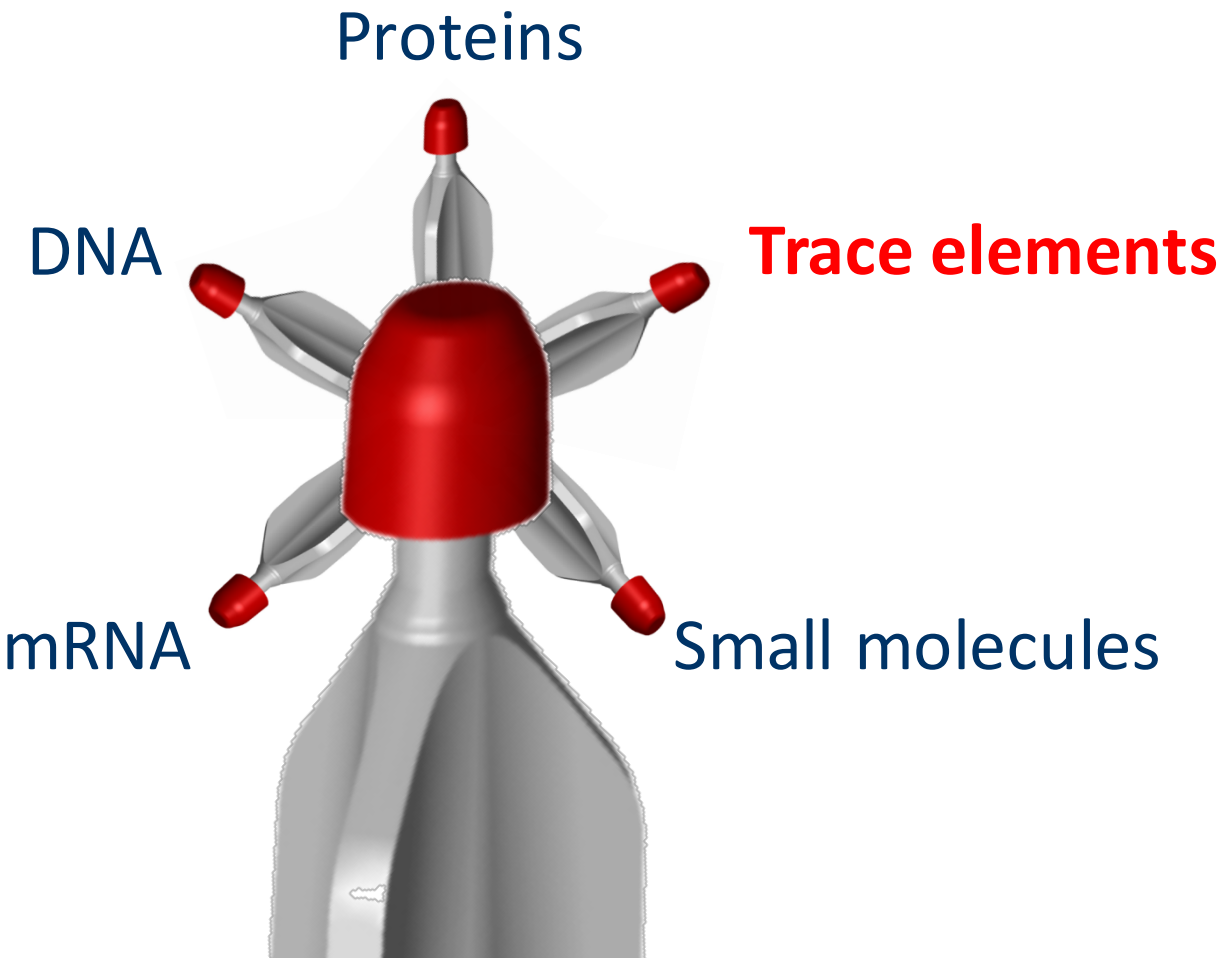
Volumetric Absorptive Microsampling: (potential) analytes



Trace elements in VAMS: Co

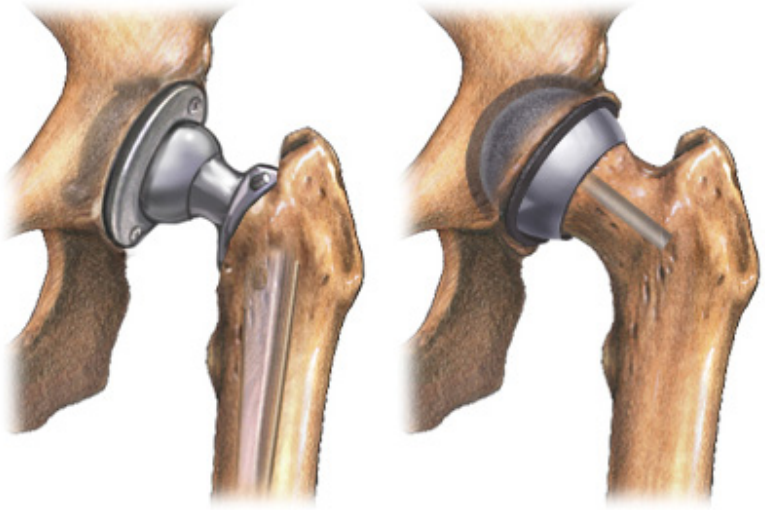
Introduction

- MoM prosthesis

  = metal ball + metal cup

- Total hip replacement
- Hip resurfacing

- High prevalence



Trace elements in VAMS: Co

Introduction

- Wear and corrosion → debris (Co & Cr)

=> Adverse local tissue reaction

= soft tissue damage, implant loosening,
implant failure, need for revision

=> Systemic toxicity (Co):

= thyroid dysfunction, cardiomyopathy, neurological changes

= arthroprosthetic cobaltism

Trace elements in VAMS: Co

Introduction

- Co-level ~ implant wear

  => Determination of Co in whole blood or plasma (400 µL)

- Cut offs used:

  4 µg/L: Upper limit acceptable for unilateral HP
  5 µg/L: Upper limit acceptable for bilateral HP
  10 µg/L: More pronounced wear
  20 µg/L: Substantial wear & systemic toxicity possible
  Revision should be considered

Trace elements in VAMS: Co

Introduction

- Goals:
  - Home-based patient sampling
  - Easier sample transfer to the lab/between labs

- Collaboration:
  - Ghent University Hospital → routine Co analysis
  - Department of Analytical Chemistry → ICP-MS
  - Laboratory of Toxicology → microsampling

Trace elements in VAMS: Co

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Determination of ultra-trace amounts of prosthesis-related metals in whole blood using volumetric absorptive micro-sampling and tandem ICP – Mass spectrometry

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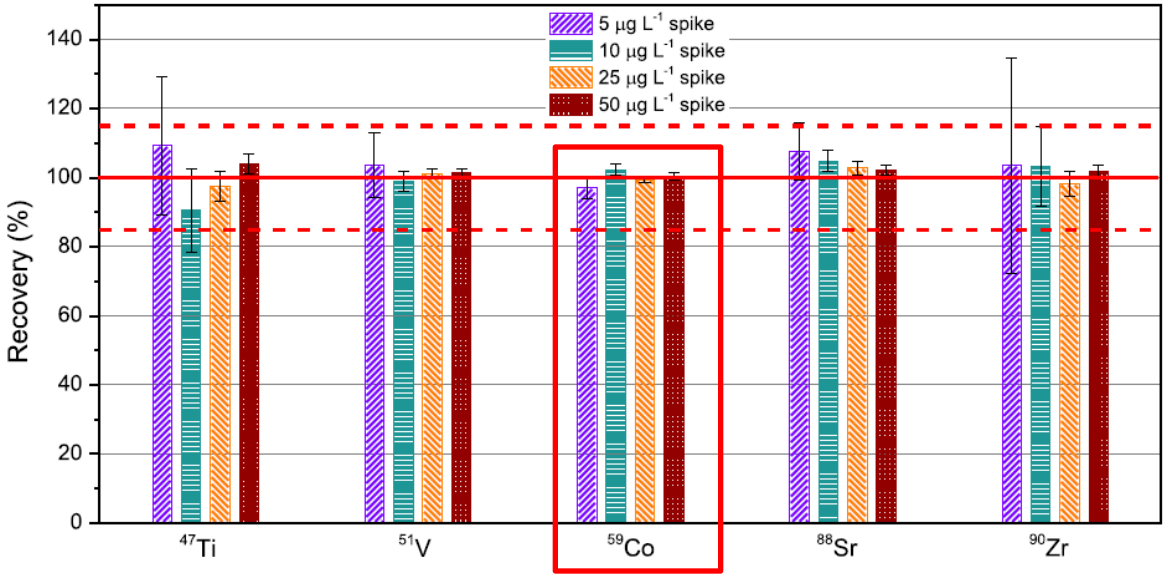

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Trace elements in VAMS: Co

Materials and methods

- ICP-MS: Agilent 7900
- Co 59 & Rh 103
- 10 measurements of 1 sec per element → average

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Trace elements in VAMS: Co

Materials and methods

- VAMS vs. DBS
  - Background lower in VAMS

- VAMS
  - No Hct effect
    = fixed sample volume
  - Cave: Hct effect on extraction

Trace elements in VAMS: Co

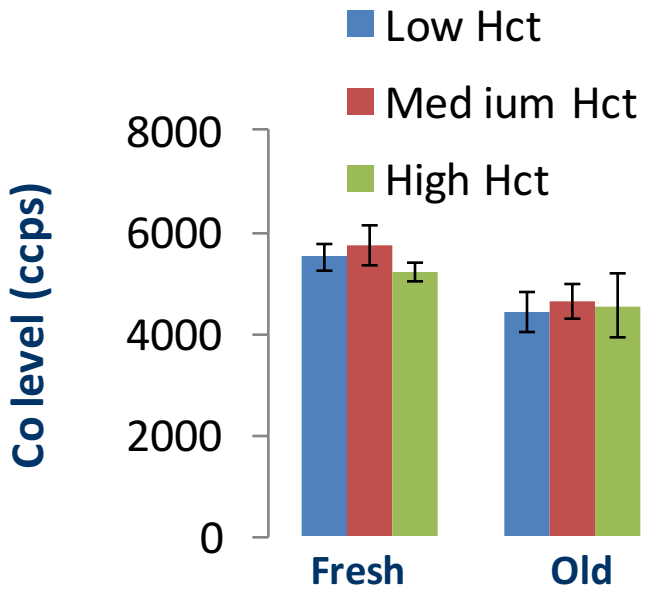
Materials and methods

- Sample prep: acidic extraction

  - 1% HCl: still coloured

  - 5% HCl: clear

    However: not age independent



Trace elements in VAMS: Co

Materials and methods

- Final method:
  1) Remove VAMS tip with pipet tip
  2) Add 300 µL of H_2O (containing 0.75 ppb Rh)
  3) 15 min in thermomixer @ 60°C & 1000 rpm
  4) Transfer 250 µL of extract
  5) Add 40 µL of subboiled HCl + vortex 1 sec
  6) Centrifuge 3 min @ 3000g
  7) Transfer 270 µL of supernatant
  8) Add 1400 µL of H_2O

Trace elements in VAMS: Co

Validation

- Calibration model
- LLOQ – ULOQ
- Accuracy & precision
- Carry-over
- Stability
- Recovery
- Hct effect

Trace elements in VAMS: Co

Validation

- Calibration model

Based on sum %RE: weighted linear regression $1/X^2$

Conc. (µg/L)	Curve 1	Curve 2	Curve 3	Curve 4	Curve 5	Curve 6
3	13.85%	-16.90%	3.02%	-21.27%	-6.74%	0.03%
4	-12.84%	17.90%	-10.77%	-0.28%	7.05%	-3.09%
10	10.92%	-4.91%	31.08%	-0.11%	4.61%	10.66%
20	1.88%	9.32%	-0.84%	1.52%	-3.42%	-9.88%
30	-4.71%	-0.09%	4.12%	5.88%	-1.60%	6.79%
40	2.94%	-7.65%	-10.58%	-7.54%	-0.73%	-3.94%

=> Acceptable based on backcalculated values

=> LLOQ: 3 µg/L & ULOQ: 40 µg/L

Trace elements in VAMS: Co

Validation

- Accuracy and precision:

QC	Conc (µg/L)	Accuracy	Intraday precision	Interday precision
LLOQ	**3**	-5.82%	11.06%	18.80%
LOW	**4**	-5.48%	14.36%	14.36%
MID	**20**	1.50%	10.33%	11.21%
HIGH	**30**	0.37%	4.93%	4.93%
DIL	**300**	7.04%	14.61%	16.88%

=> Accuracy and precision within 15% (20% for LLOQ)

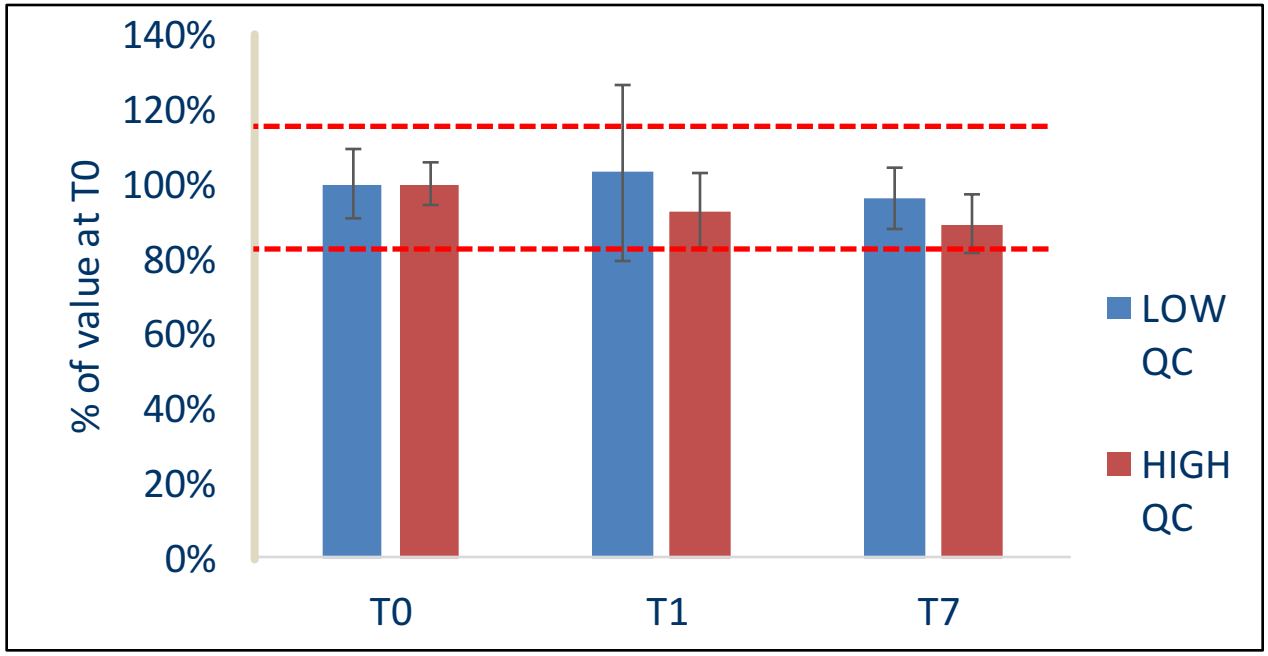
=> Exception: dilution QC

However, still acceptable from a clinical point of view (extremely elevated)

Trace elements in VAMS: Co

Validation

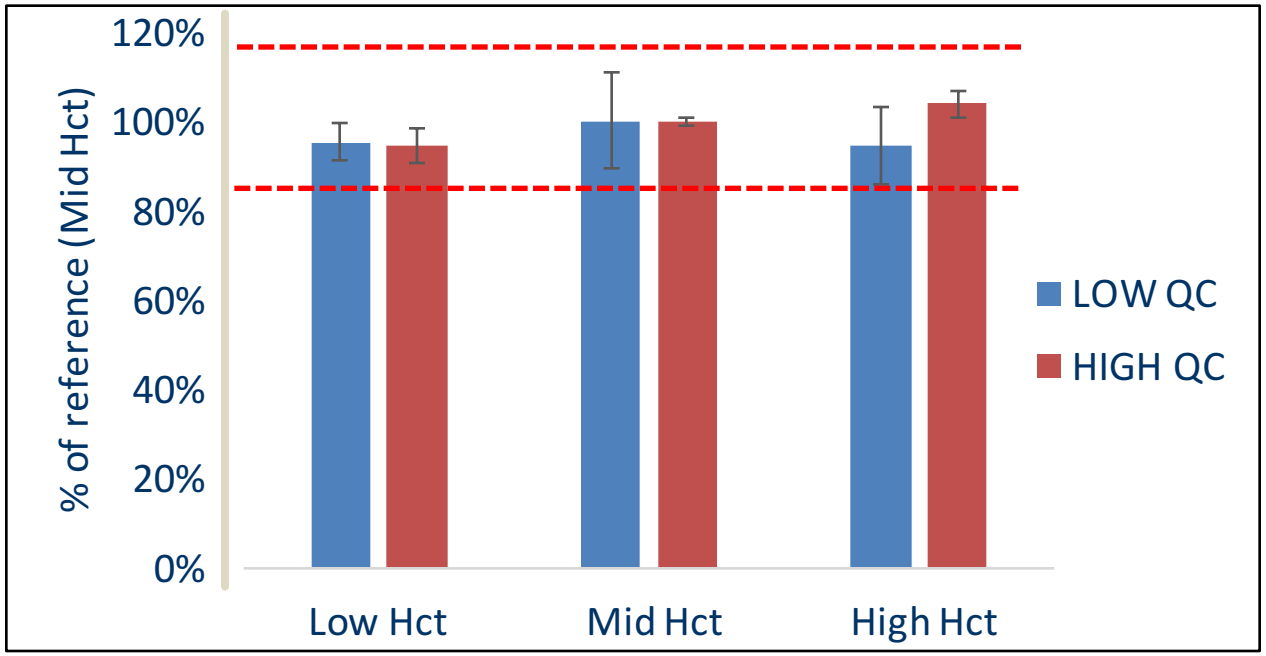
- Stability: RT at least 1 week



Trace elements in VAMS: Co

Validation

- Recovery: high & Hct independent

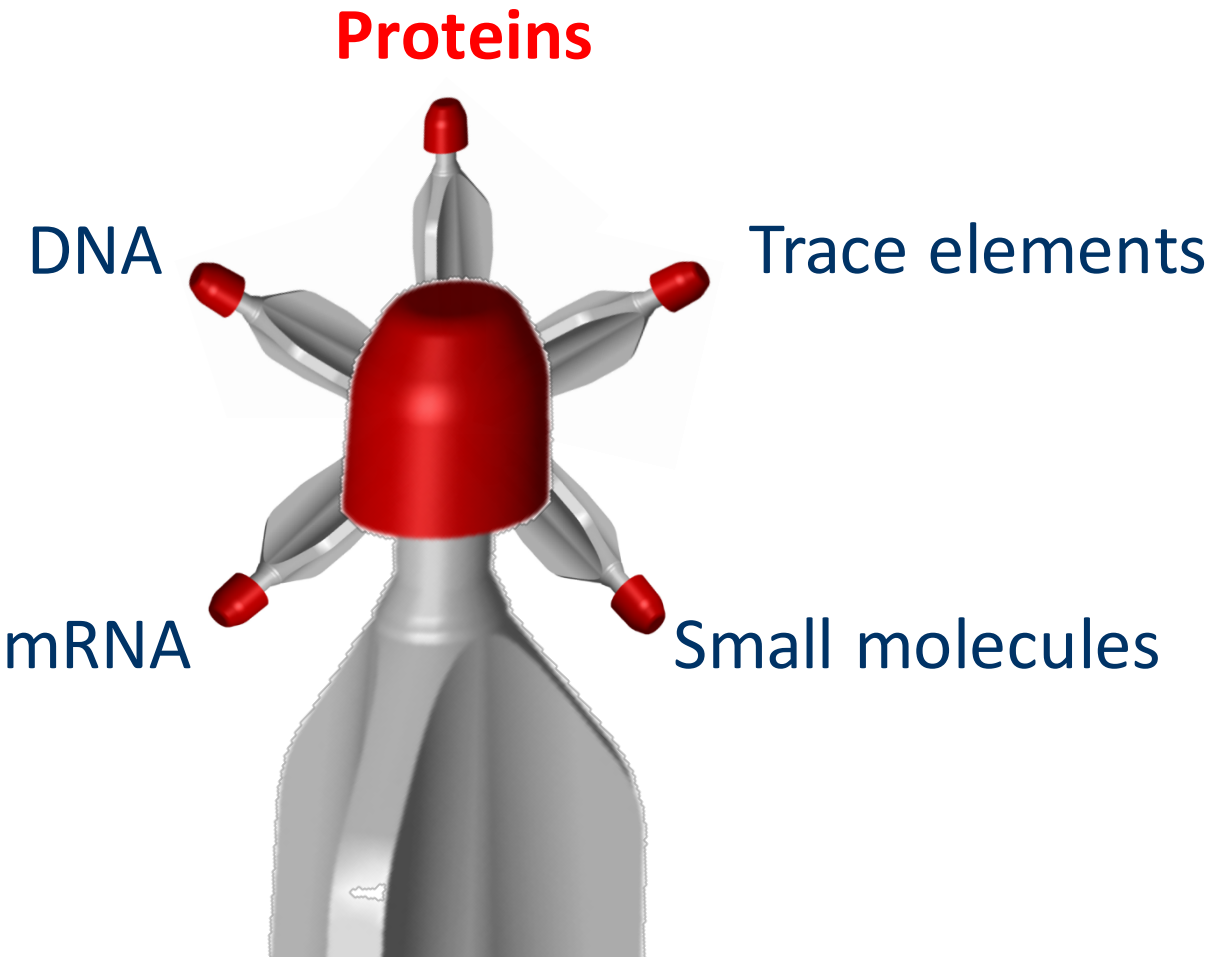


Trace elements in VAMS: Co

Conclusion

- Sample prep optimized
- Method validated
  - → Sufficiently sensitive
  - → No Hct effect, also not on extraction efficiency
  - → Stability OK
- Method still has to be applied to patient VAMS
  - Comparison with data from venous blood
  - Comparison venous-capillary blood
- Real home-based sampling to be performed

Volumetric Absorptive Microsampling: (potential) analytes



Proteins in VAMS: HbA1c

HbA1c monitoring in diabetics via sampling @ home via volumetric absorptive microsampling

- HbA1c reflects average glycaemia of last 100-120 days and is predictive for development of vascular complications
- Study with comparison of home sampling (VAMS & DBS) & regular sampling in adults & children

	All	Adults	Children
n	84	40	44
Age (years) median (IQR)[a]	16.5 (12.0-51.8)	54.0 (43.0-64.0)	12.0 (10.0-16.0)
Gender (males/females)	57 M/ 27 F	28 M/ 12 F	29 M/ 15 F
Hospital sampled HbA1c[b] (mmol/mol) median (IQR)	56.3 (49.2-65.7)	58.7 (48.8-66.8)	55.6 (49.7-63.3)

[a] IQR=interquartile range

[b] Hospital sampled: for adults a venous K_2-EDTA-blood sample and for the children a capillary blood sample in a heparinized capillary tube

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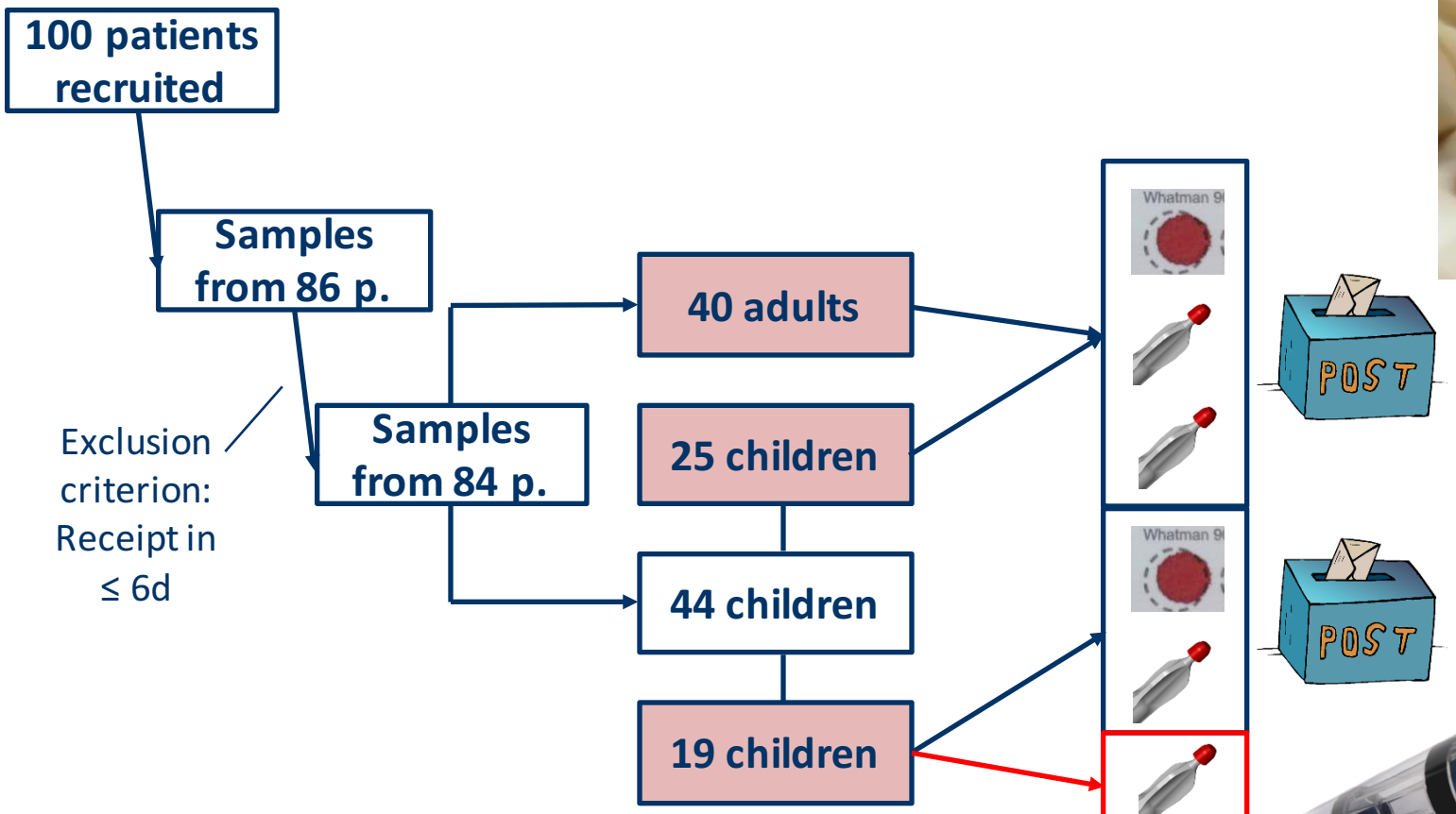
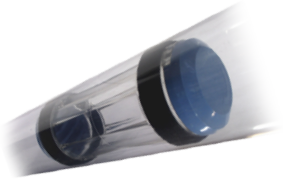
Proteins in VAMS: HbA1c

- Sampling protocol:



Analysis on the day of receipt



Analysis within 1h

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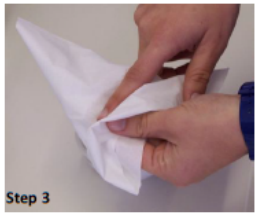
Proteins in VAMS: HbA1c

- Information folder

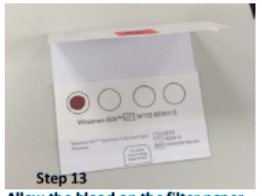
Uncover the VAMS devices by pulling apart the clamshell and fold over the cover to create a handle for easy sample collection + keep within reach

Wash hands with warm water for 1 minute and keep the arm down for another minute.



Dry fingertip with a clean tissue.

Wipe the fingertip clean.

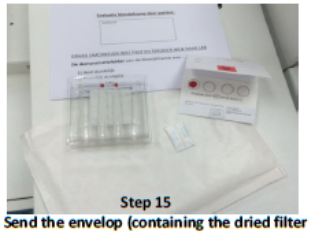


Allow the blood on the filter paper to dry for 2 hours at room temperature, and then put in the envelop.

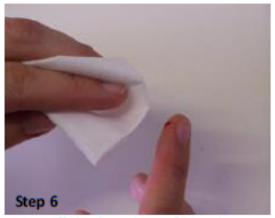
Add the closed clamshell with the 2 VAMS devices to the envelop (picture shows only one VAMS device).

Take the lancet.

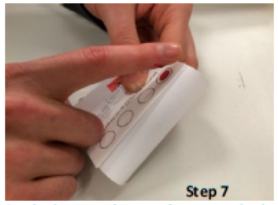

Push it to the side of the fingertip. The finger will be automatically pierced.



Send the envelop (containing the dried filter paper, the clamshell, the absorbent packet and the filled in questionnaire) to the lab.

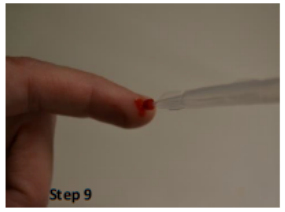


Wipe off the first drop of blood with a clean tissue.



Apply the next drop to the premarked circle on the filter paper (fingertip may not touch the paper).

Apply the sampler tip of the VAMS device to the surface of the third blood drop (make no contact with the skin).



Once you see the sampler tip go fully red, count an additional 2 seconds and then remove the sampler tip from the blood.

Apply the sampler tip of the second VAMS device to the surface of the fourth drop of blood (picture shows only one VAMS device).

Fold the clamshell back together and press closed.

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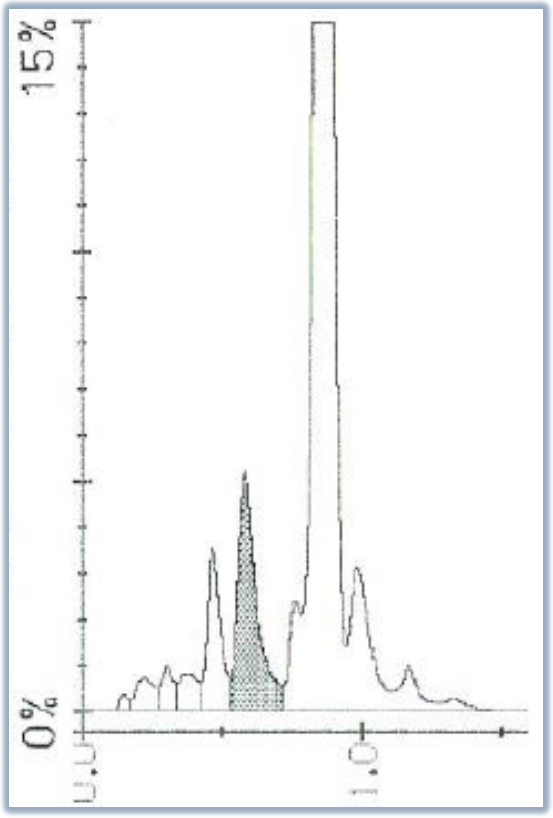
Proteins in VAMS: HbA1c

- Prerequisite: technology readily available at the clinical lab should be used for analysis

Tosoh HLC-723 G8 automated ion-exchange HPLC



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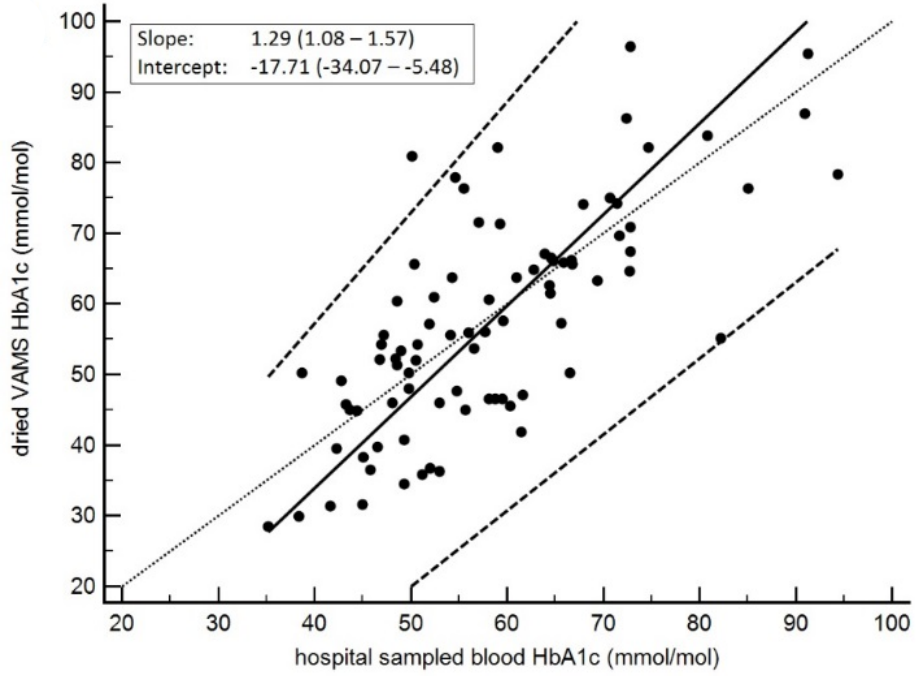
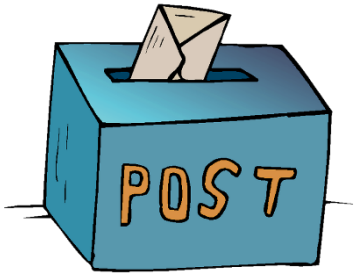
Proteins in VAMS: HbA1c

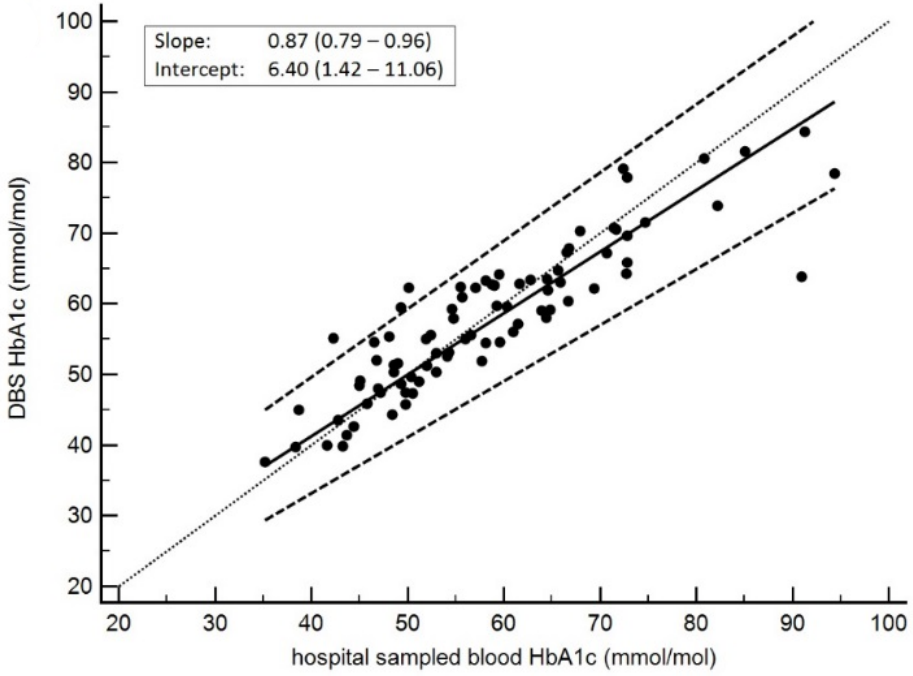
Passing-Bablok plots relative to the capillary/venous hospital blood samples

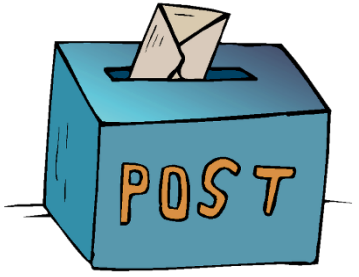
VAMS (dried & sent)





DBS (dried & sent)





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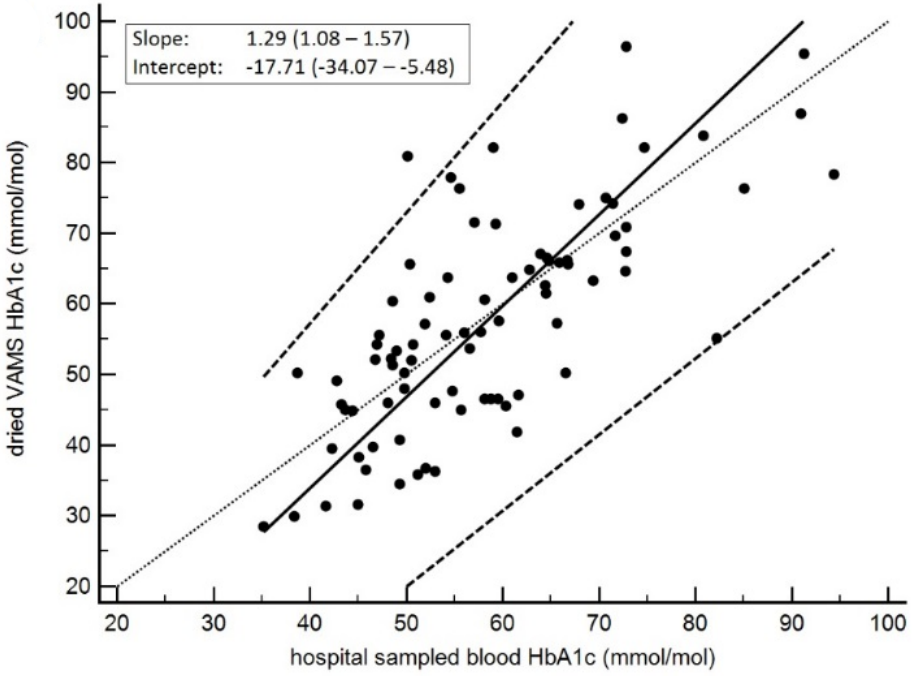
Proteins in VAMS: HbA1c

Passing-Bablok plots relative to the capillary/venous hospital blood samples

VAMS (dried & sent)



VAMS (wet)

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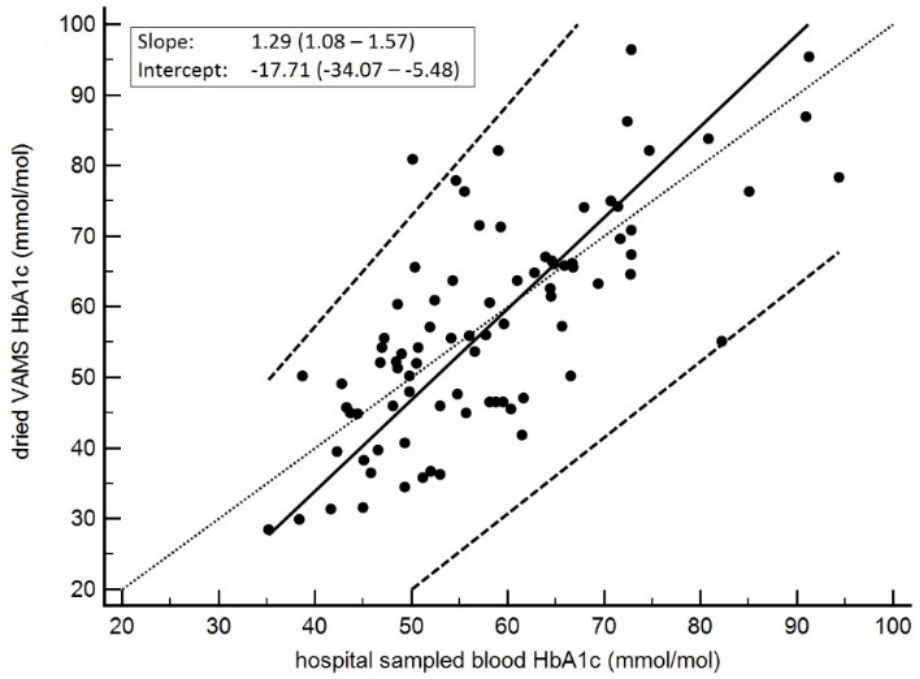
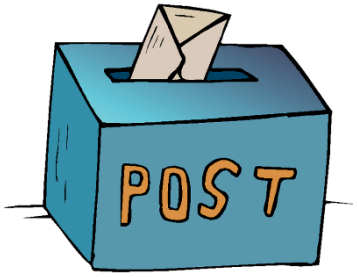
Proteins in VAMS: HbA1c

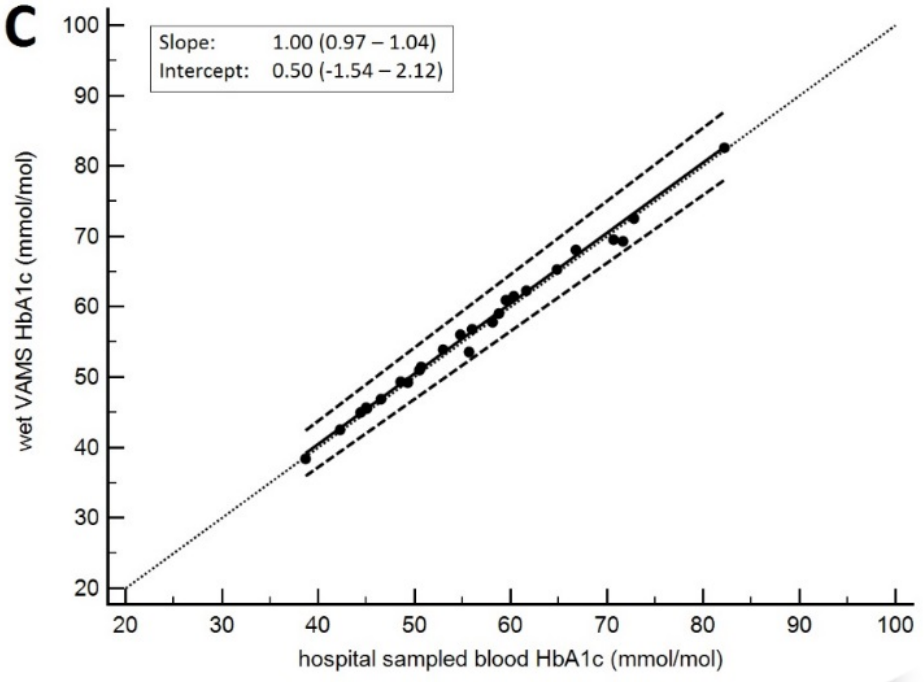
Passing-Bablok plots relative to the capillary/venous hospital blood samples

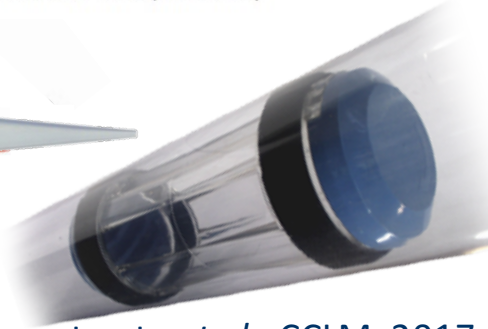
VAMS (dried & sent)





VAMS (wet)





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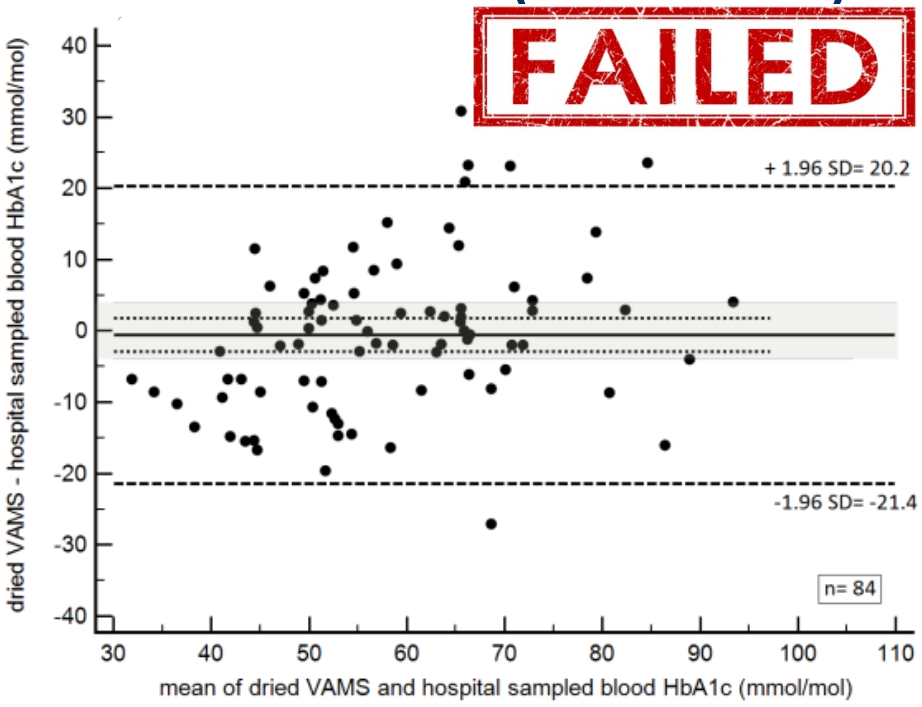
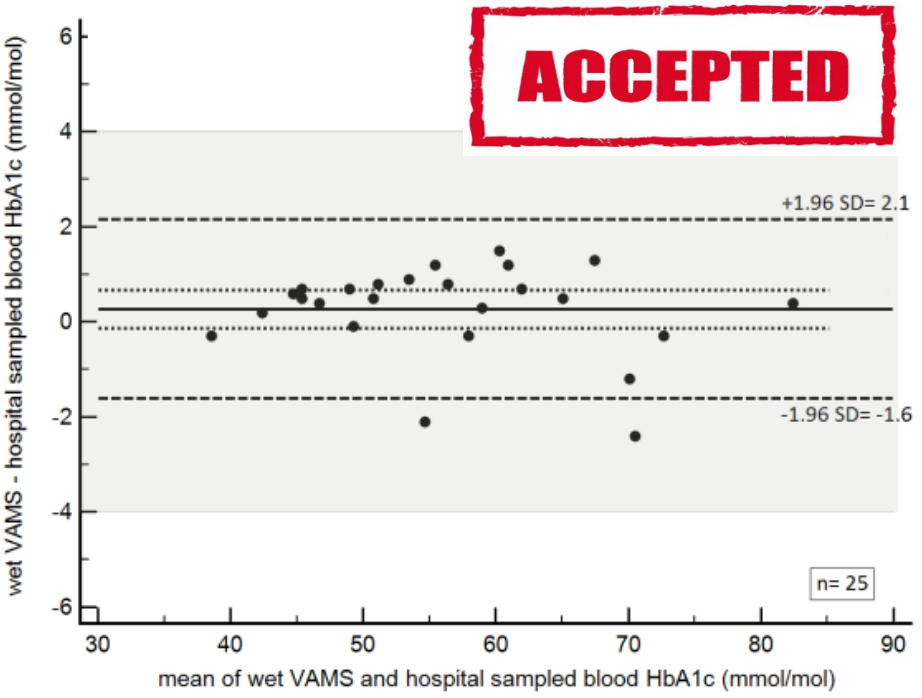
Proteins in VAMS: HbA1c

Bland-Altman plots relative to the capillary/venous hospital blood samples

VAMS (dried & sent)



VAMS (wet)



Solid line: average difference, with its 95% CI indicated as dotted lines
Dashed lines: lower and upper limit of agreement (±1.96 SD)
Grey area: allowable error according to RCPA Quality Requirements (± 4 mmol/mol)

Note the difference in scale!

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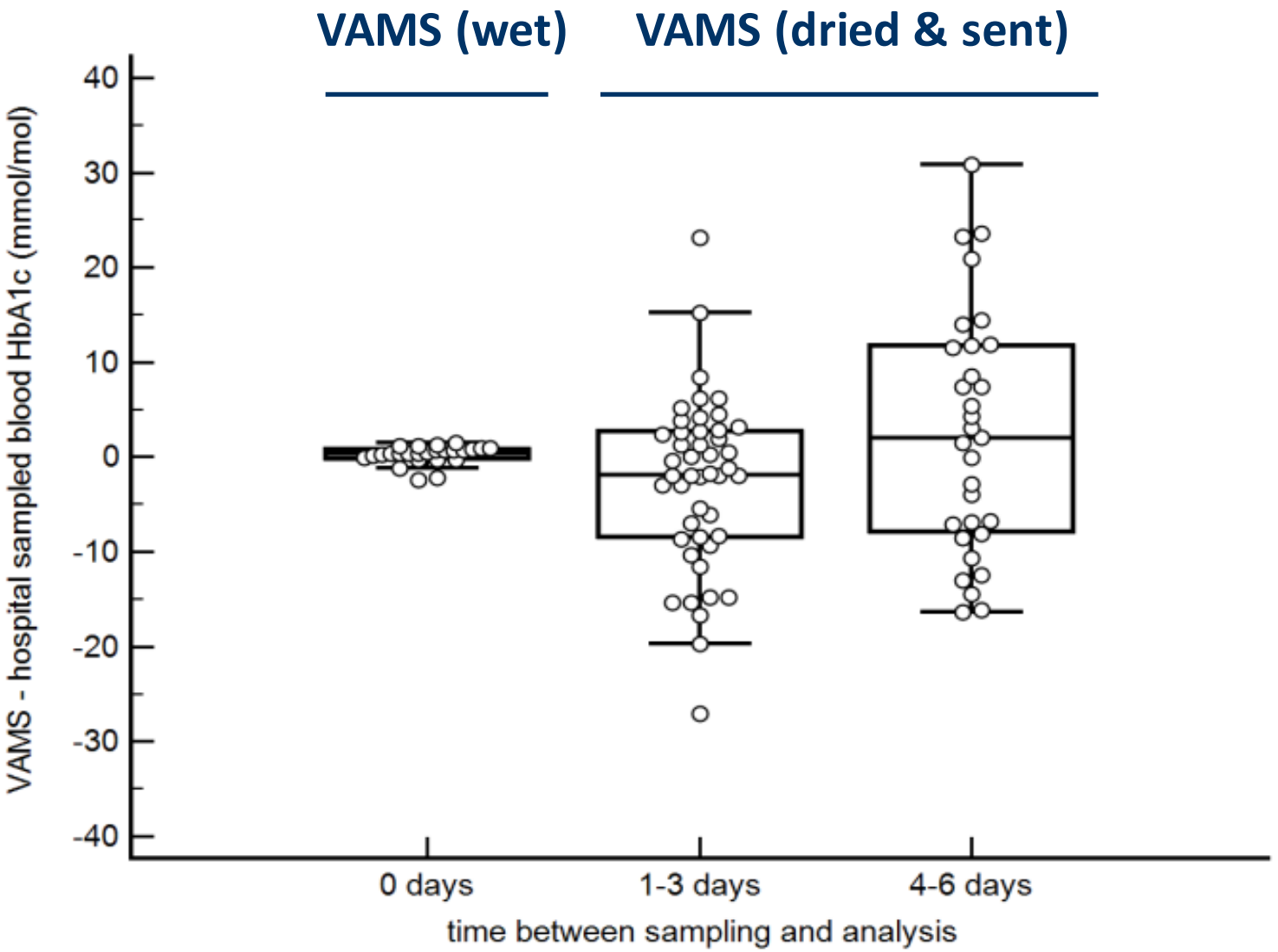
Proteins in VAMS: HbA1c



Box and whisker plots indicating the distribution and influence of time between sampling and analysis on HbA1c results in VAMS

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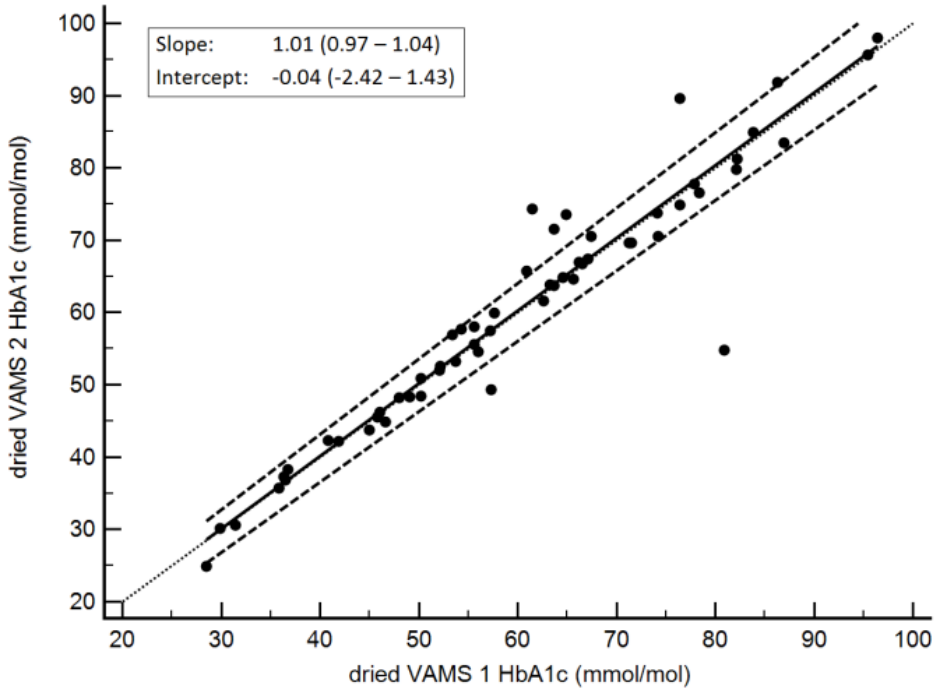
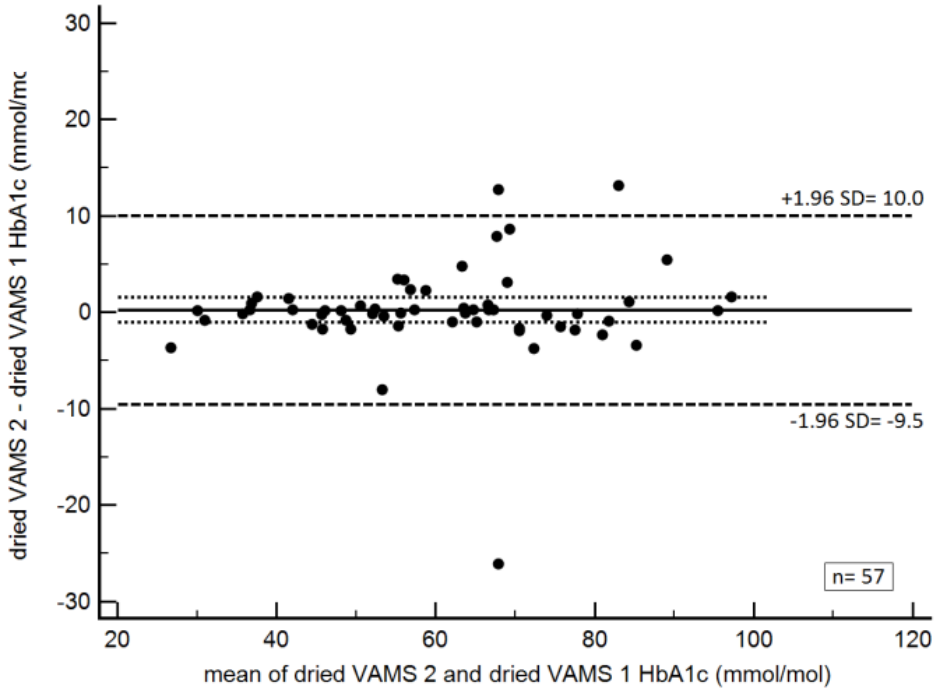
Proteins in VAMS: HbA1c

Deviating results in dried VAMS are not owing to sampling or measurement variation *in se*

Passing & Bablok regression curve and Bland-Altman plot of **duplicate HbA1c measurements in dried VAMS**





Solid line: average difference, with its 95% CI indicated as dotted lines
Dashed lines: lower and upper limit of agreement (±1.96 SD)

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Proteins in VAMS: HbA1c

Result of questionnaire

	Demonstration leaflet for sample collection				
	Very clear	Fairly clear	No opinion	Rather confusing	Confusing
Adults	72%	24%	2%	2%	/
Children	72%	19%	2%	7%	/
All	72%	21%	2%	5%	/
	DBS sampling				
	Very convenient	Fairly convenient	No opinion	Rather cumbersome	Cumbersome
Adults	53%	39%	3%	5%	/
Children	46%	44%	/	10%	/
All	50%	42%	1%	7%	/
	VAMS sampling				
	Very convenient	Fairly convenient	No opinion	Rather cumbersome	Cumbersome
Adults	56%	36%	/	8%	/
Children	79%	17%	/	4%	/
All	69%	25%	/	6%	/
	Preferred sampling technique				
	Traditional blood sampling	DBS	VAMS	DBS and VAMS	No opinion
Adults	21%	15%	44%	10%	10%
Children	12%	14%	64%	10%	/
All	16%	14%	56%	10%	4%

Proteins in VAMS: HbA1c

Conclusions

- The majority of patients considered microsampling (either DBS sampling or VAMS) fairly convenient to very convenient
- VAMS was the preferred sampling technique in the majority of patients
- Immediate (<1h) processing of VAMS yielded HbA1c results meeting the strict clinical criteria
  → **Potential to replace capillary microsampling by VAMS in a hospital context**
- Drying of blood is associated with changes in the Hb profile that the HbA1c analyzer cannot cope with
  → **Results obtained from dried VAMS do not meet the clinical acceptance criteria**
- Does this mean that HbA1c cannot be measured in dried microsamples?
  NO → **(Use another technique)**
  → **Use a stabilizing approach**

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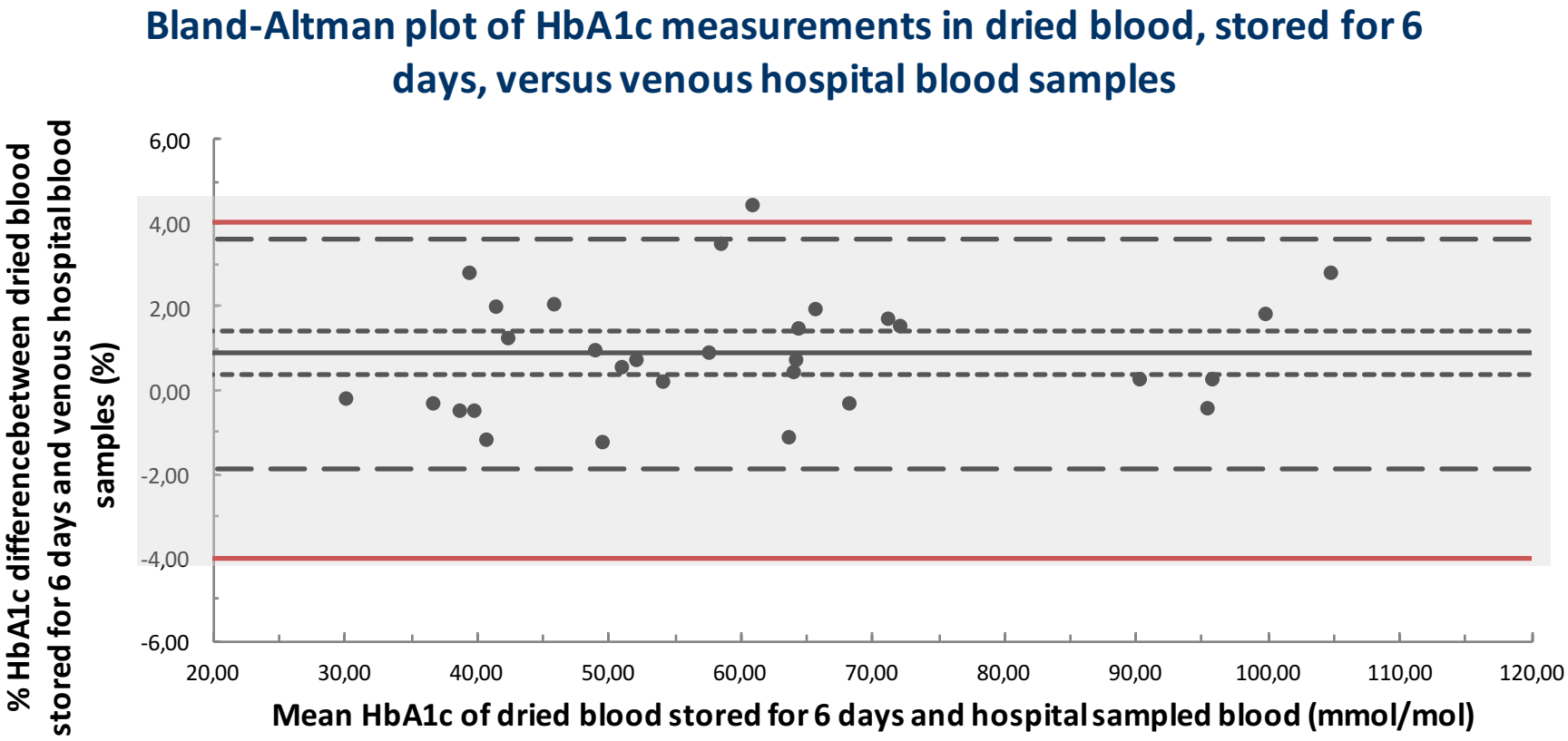
Proteins in VAMS: HbA1c



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Unpublished data

VAMS: GENERAL CONCLUSIONS

- VAMS has been used with success in a wide variety of (clinical) applications
- The number of VAMS applications is rapidly increasing
- VAMS has been confirmed to be Hct-independent in terms of sampling
- Hct is still an important parameter when considering optimization of extraction
- VAMS is relatively easy to use and preferred over DBS by patients
- VAMS is (likely to be) used (more) for routine clinical applications

Acknowledgments

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Addictive days and Toxic nights

TIAFT 26-30th August 2018