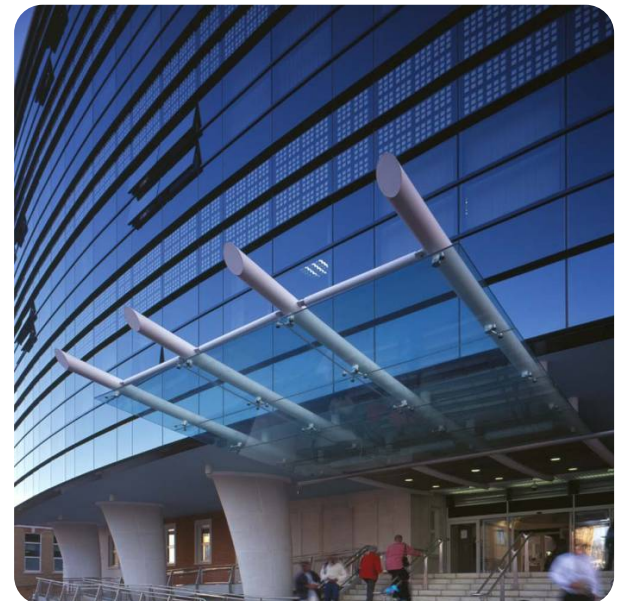


Evaluation of a Volumetric Absorptive Microsampling Device for Tacrolimus Measurement in Routine Drug Monitoring

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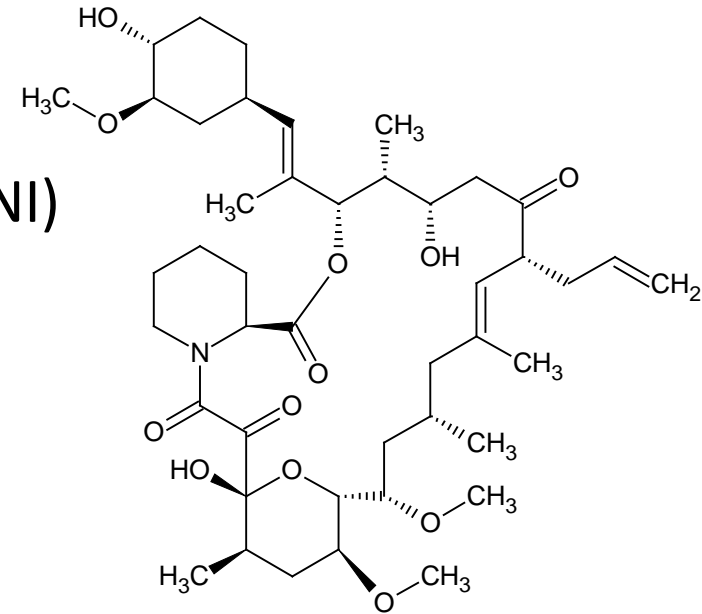
VAMS for Tacrolimus

- Aim: Test the volumetric absorptive microsampling (VAMS) device for the measurement of tacrolimus

VAMS for Tacrolimus

- Tacrolimus

- Widely used calcineurin inhibitor (CNI) immunosuppressant drug
- High pharmacokinetic variability
- Serious side effects
- Narrow therapeutic index
- Concentration requirement changes with time



Requires regular monitoring to ensure optimal survival

- Tacrolimus
 - Current protocol for monitoring
 - Call patient to clinic
 - Patient undergoes venepuncture
 - Trained phlebotomist, exposed sharps
 - Suitable facility
 - Patient goes home
 - Sample sent to lab
 - Biohazard
 - If sample is not suitable:



- Alternatives
 - Dried blood spot (DBS)
 - Small volume sample from finger-prick
 - Patient can sample at home
 - No biohazard risk and drug is stable – sample can be posted
 - Result is available before clinic attendance
 - Methods have been validated and are in use for tacrolimus

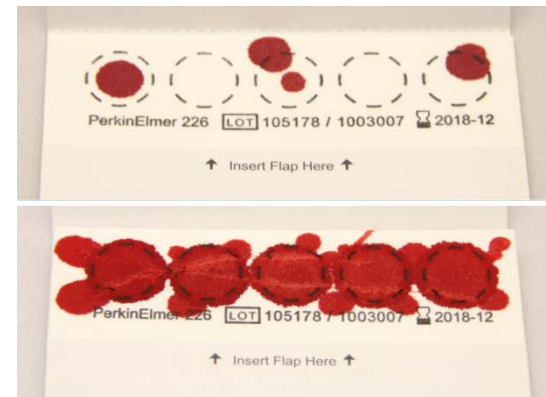
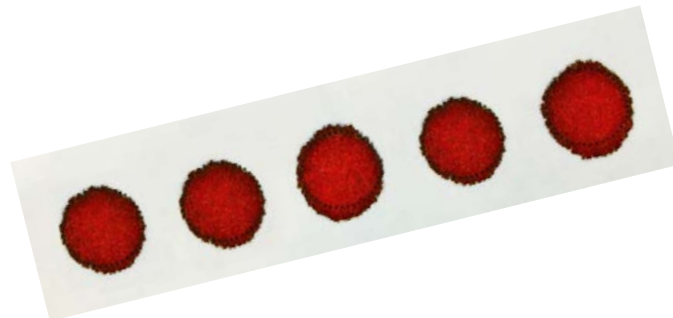


VAMS for Tacrolimus

- Alternatives

- Limitations to DBS

- Sample volume is (usually) variable
 - There can be haematocrit bias
 - Chromatographic effects within the paper matrix
 - Inconsistent paper matrix properties
 - How to sample the spot?
 - Analytical process can be difficult



VAMS for Tacrolimus

- Alternatives
 - Volumetric absorptive micro sampler (VAMS™)
 - Advantages of DBS, plus
 - Fixed sample volume – no waste
 - Quantitative processing of sample (i.e. whole tip)
 - Lacks haematocrit bias
 - Reproducible properties



VAMS for Tacrolimus

- Routine patient samples for tacrolimus were also sampled onto VAMS tips
- Results compared with PPT method
- Assay validation included
 - Accuracy and precision
 - LLOQ
 - Haematocrit effects
 - Stability of analyte on the tip
 - Comparison with proficiency testing samples

VAMS for Tacrolimus

- VAMS evaluated for tacrolimus measurement by comparison with established method

| Routine method | VAMS method |
|---|---|
| Sample 10 μ L | Sample 10 μ L tip |
| | Dry for 24 h |
| | Vortex mix tip in water (50 μ L, 5 min) |
| Add ZnSO ₄ (0.1 mol/L, 40 μ L) | |
| Add internal standard (13CD ₂ -Tacrolimus, 12 μ g/L in acetonitrile, 100 μ L) | |
| Vortex mix (2 min) | |
| Centrifuge (16,060 g, 10 min) | |
| LC: Waters Acquity I-Class. C18 cartridge, 0.6 mL/min, 1.8 min Detector: Waters Xevo TQS micro | |

- Results

- Within-day

- Inaccuracy -3.5 to 2.6 %
- Imprecision 2.5 to 6.0 %

- Between-day

- Inaccuracy -0.1 to 4.9 %
- Imprecision 2.0 to 9.0 %

- LLOQ

- 0.5 µg/L (10 µL tip, CV 18.3 %)

- Haematocrit

- Tested at 0.192, 0.276, 0.355, 0.463 and 0.552
- No evidence of bias

- Stability

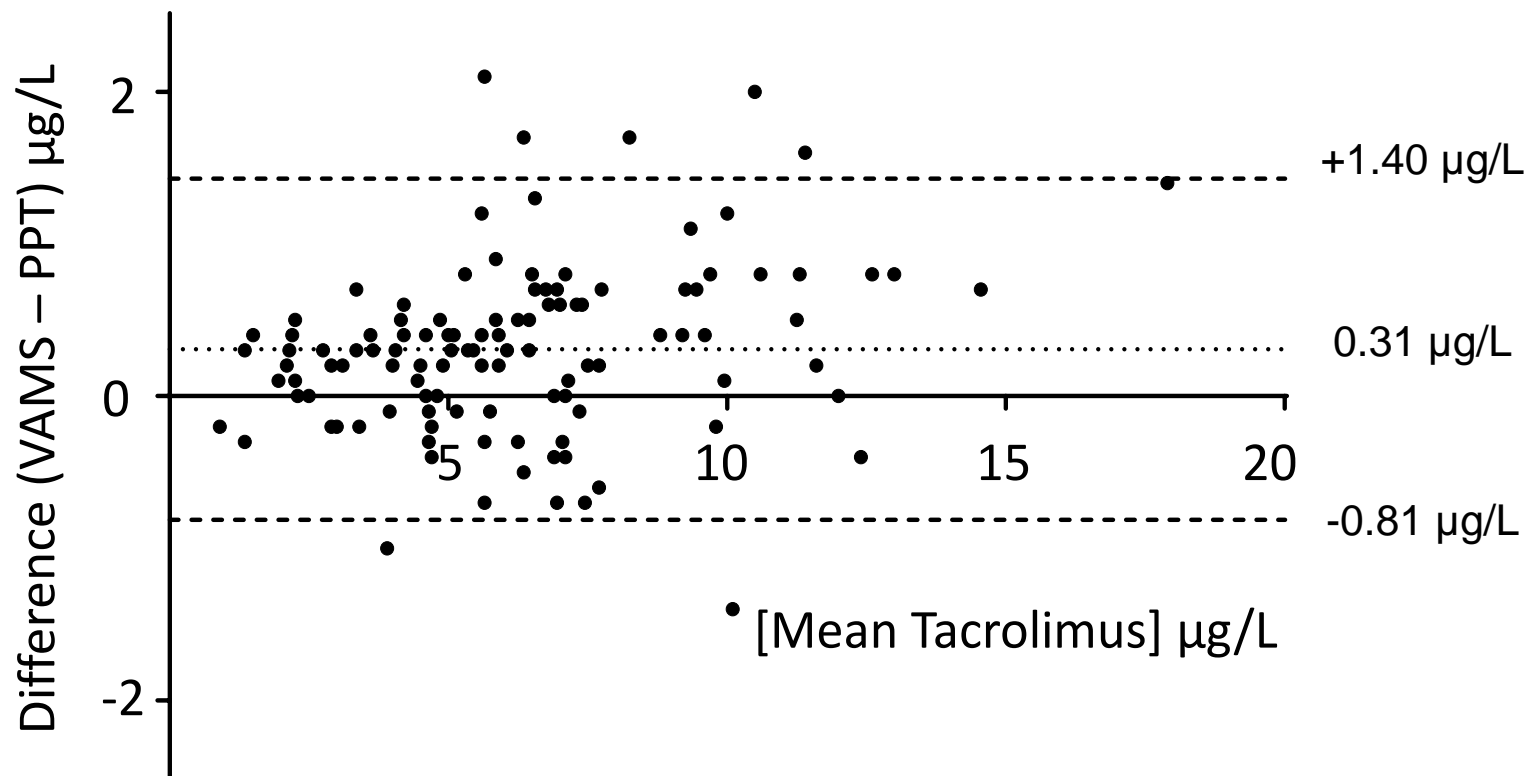
- After 4 days less than 13 % difference
- After 29 days less than 12 % difference

- Interference

- No evidence of contamination leaching from tips

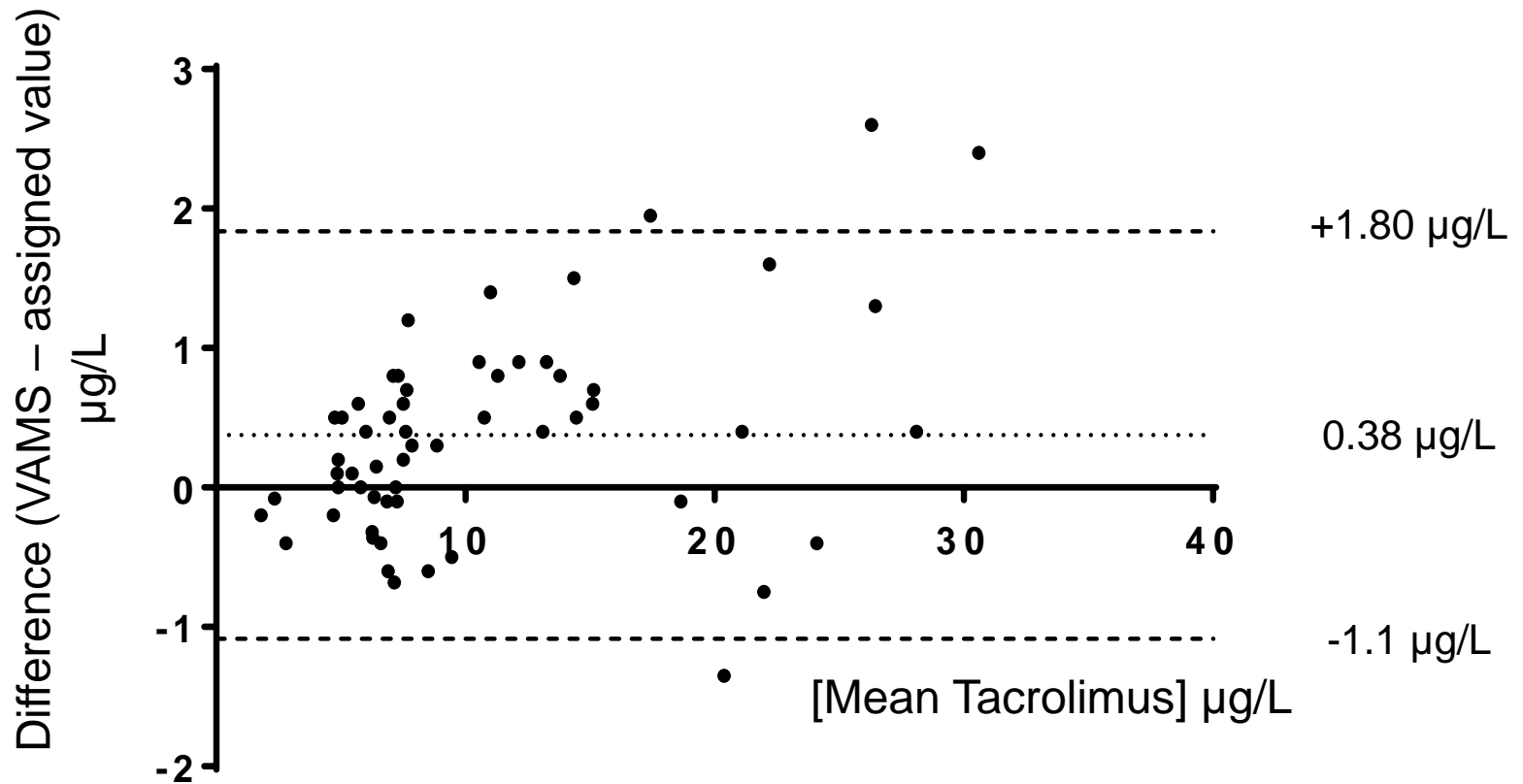
VAMS for Tacrolimus

- Patient samples (n = 114)



VAMS for Tacrolimus

- Proficiency testing samples (n = 59)



- Summary
 - Straightforward to measure tacrolimus from VAMS
 - Simple, precise, accurate, fast
 - Results are reproducible
 - No haematocrit effect, no interference, no batch variability
 - Tacrolimus is stable on VAMS tip
 - Limitation: equivalence between capillary VAMS sample and venous blood for tacrolimus measurement to be demonstrated
 - Potential to improve patient care?

- Acknowledgements

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