Volumetric Absorptive Microsampling (VAMS) as an alternative tool for tacrolimus and mycophenolic acid TDM

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INTRODUCTION

Therapeutic drug monitoring (TDM) of immunosuppressants (IMS) is crucial to prevent rejection or toxicity after solid organ transplantation[1]. **Volumetric absorptive microsampling (VAMS) could be a good alternative to conventional venous sampling** for IMS' TDM[1]. It enables the collection of precise and accurate blood volumes, **overcoming the volumetric** hematocrit **(Hct) effect related to dried blood spots, while offering the same benefits**[1]. However, a **clinical validation** study must be established **before the application** of a new VAMS methodology **to routine care for TDM purposes**[2]

AIM

To **evaluate the performance of Mitra™ VAMS devices as an alternative to venous whole blood** (WB) **for monitoring tacrolimus** (TAC) **and mycophenolic acid** (MPA) **by comparing capillary VAMS** (c-VAMS), **venous VAMS** (v-VAMS) **and WB concentrations** for both analytes

METHODOLOGY

Specimens' collection:

c-VAMS and WB collected from hepatic transplant patients ➡ **63 for TAC, 26 for MPA**

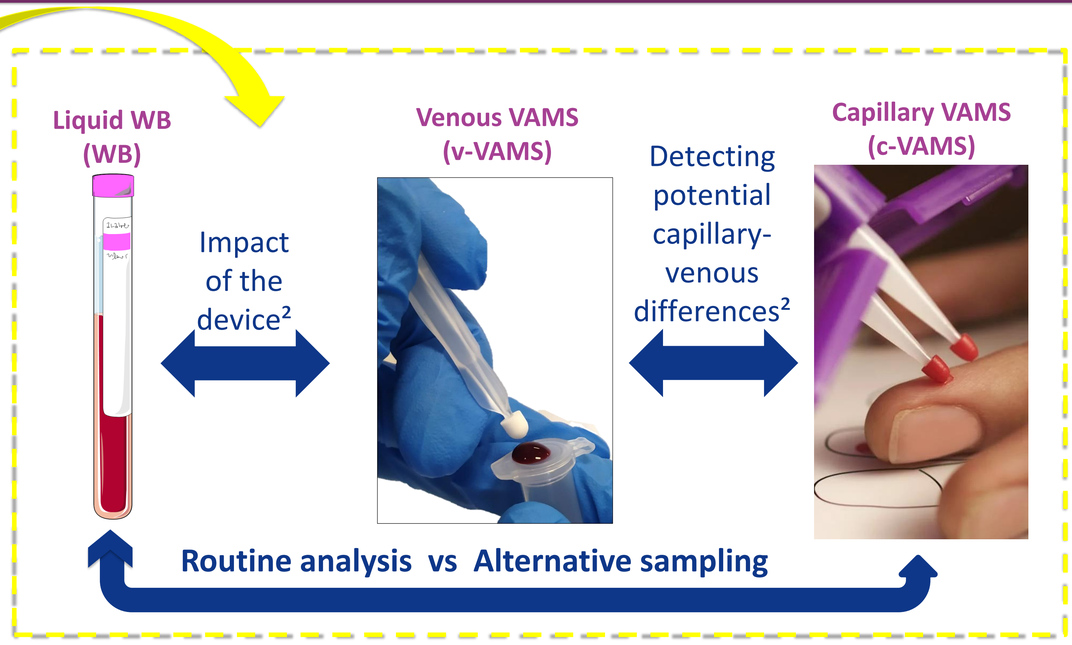
*To initially study the impact of the device in the results, **v-VAMS** were also prepared from each liquid WB sample*

Specimens' analysis:

Following a method previously fully and satisfactorily validated [3], showing no impact of the Hct on the recovery (range 0.2 to 0.62 L/L). LLOQs were 0.5 ng/mL for TAC and 75 ng/mL for MPA

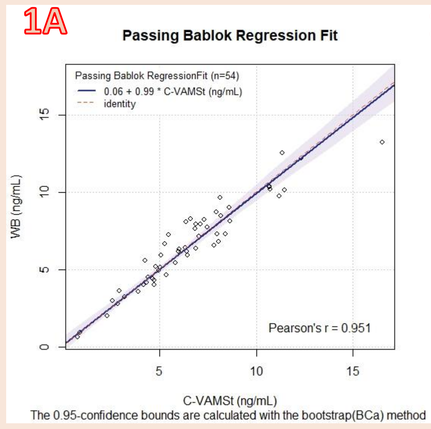
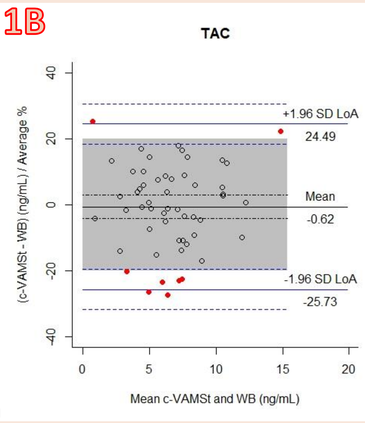
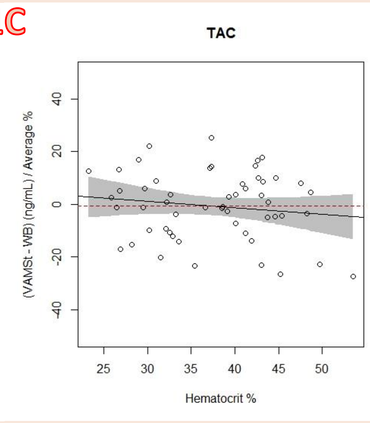
Statistical analysis:

◊ *Method comparison* ➡ **Passing-Bablok (PB) regression**
◊ *To assess the predictive performance of the conversion equation:*
  for the bias ➡ **Median Percentage Predictive Error (MPPE)**
  for the imprecision ➡ **Median Absolute Percentage Error (MAPE)**
◊ *To evaluate the correlation* ➡ **Intraclass Correlation Index (ICC)**
◊ *Method agreement* ➡ **Bland-Altman plot**
◊ *Hct impact* ➡ **Linear Regression** (%concentration difference vs Hct)

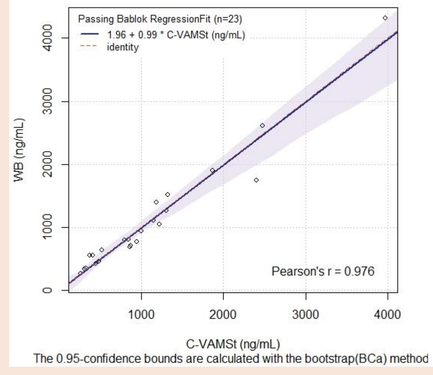
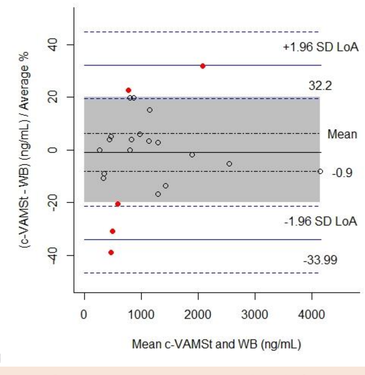
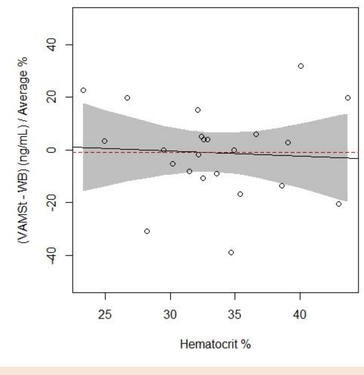


RESULTS

TAC

WB vs v-VAMS [3]	WB vs c-VAMS	v-VAMS vs c-VAMS
N=60 ◊ Passing-Bablok regression → **transformation** (v-VAMSt = -0.06+1.29*v-VAMS) ◊ MPPE: 0.02% ; MAPE: 6.71% → both <15 %, **converse equation acceptable** ◊ ICC: 0.931 → **excellent correlation** ◊ Bland-Atman plot → **no pattern found; 90% of the samples within ±20% bias** ◊ Hct linear regression → **no Hct impact**	1A  1B  1C  ◊ Passing-Bablok regression → **transformation needed** (c-VAMSt = 0.08+1.48*c-VAMS) **(Fig. 1A)** ◊ MPPE: 0.53% ; MAPE: 9.61% → both <15 %, the **converse equation given by PB regression can be considered acceptable** ◊ ICC: 0.95 (95%CI: 0.916, 0.971) → **excellent correlation between both methods** ◊ Bland-Atman plot **(Fig. 1B)** → **no pattern found; 85.2% of the samples within ±20% bias** ◊ Hct linear regression **(Fig. 1C)** [slope= -0.25 (95%CI: -0.74, 0.24)] → **no Hct impact**	**N=51** ◊ Passing-Bablok regression → **transformation** (v-VAMSt = 0.14+1.13*v-VAMS) ◊ MPPE: 0.25% ; MAPE: 10.42% → both <15 %, **converse equation acceptable** ◊ ICC: 0.933 → **excellent correlation** ◊ Bland-Atman plot → **no pattern found; 84.3% of the samples within ±20% bias** ◊ Hct linear regression → **no Hct impact**

MPA

WB vs v-VAMS [3]	WB vs c-VAMS	v-VAMS vs c-VAMS
N=23 ◊ Passing-Bablok regression → **NO transform.** (WB = 34.63+0.97*v-VAMS) ◊ MPPE: 0.26% ; MAPE: 5.97% → both <15 %, **acceptable, no transformation needed** ◊ ICC: 0.997 → **excellent correlation** ◊ Bland-Atman plot → **no pattern found; 91.3% of the samples within ±20% bias** ◊ Hct linear regression → **no Hct impact**	2A  2B  2C  ◊ Passing-Bablok regression → **transformation needed** (c-VAMSt = -63.81+1.3*c-VAMS) **(Fig. 2A)** ◊ MPPE: 1.2% ; MAPE: 11.04% → both <15 %, the **converse equation given by PB regression can be considered acceptable** ◊ ICC: 0.977 (95%CI: 0.947, 0.99) → **excellent correlation between both methods** ◊ Bland-Atman plot **(Fig. 2B)** → **no pattern found; 78.3% of the samples within ±20% bias** ◊ Hct linear regression **(Fig. 2C)** [slope= -0.2 (95%CI: -1.66, 1.27)] → **no Hct impact**	**N=21** ◊ Passing-Bablok regression → **transformation** (v-VAMSt = -21.33+1.2*v-VAMS) ◊ MPPE: 0.87% ; MAPE: 11.74% → both <15 %, **converse equation acceptable** ◊ ICC: 0.977 → **excellent correlation** ◊ Bland-Atman plot → **no pattern found; 90.5% of the samples within ±20% bias** ◊ Hct linear regression → **no Hct impact**

CONCLUSION

In this ongoing study, VAMS seems a promising tool for the TDM of both TAC and MPA, although more studies are needed in order to have enough data. The future perspectives are to optimize the clinical validation with a bigger set of specimens for both analytes to achieve more relevant clinical conclusions

References

[1] H. Veenhof et al, Clin Chem Lab Med (2020) (doi: 10.1515/cclm-2019-1260)
[2] S. Capiau et al, Ther Drug Monit (2019) (doi: 10.1097/FTD.0000000000000643)
[3] L. Paniagua-Gonzalez et al, J Pharm Biomed Anal (2020) (doi: 10.1016/j.jpba.2020.113422)

v-VAMS publication

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