

# Application of non-contact hematocrit prediction technologies to overcome hematocrit effects on immunosuppressant quantification from dried blood spots

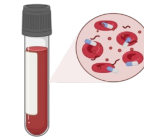
Sigrid Deprez, [Liesl Heughebaert](#), Laura Boffel, Christophe Stove // 9<sup>th</sup> Young Scientist Symposium // 12-05-2023

## Immunosuppressant drug therapy: key in transplant patient care

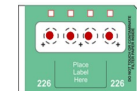
**Tacrolimus** most commonly prescribed



Follow-up of trough levels via **TDM (therapeutic drug monitoring)**

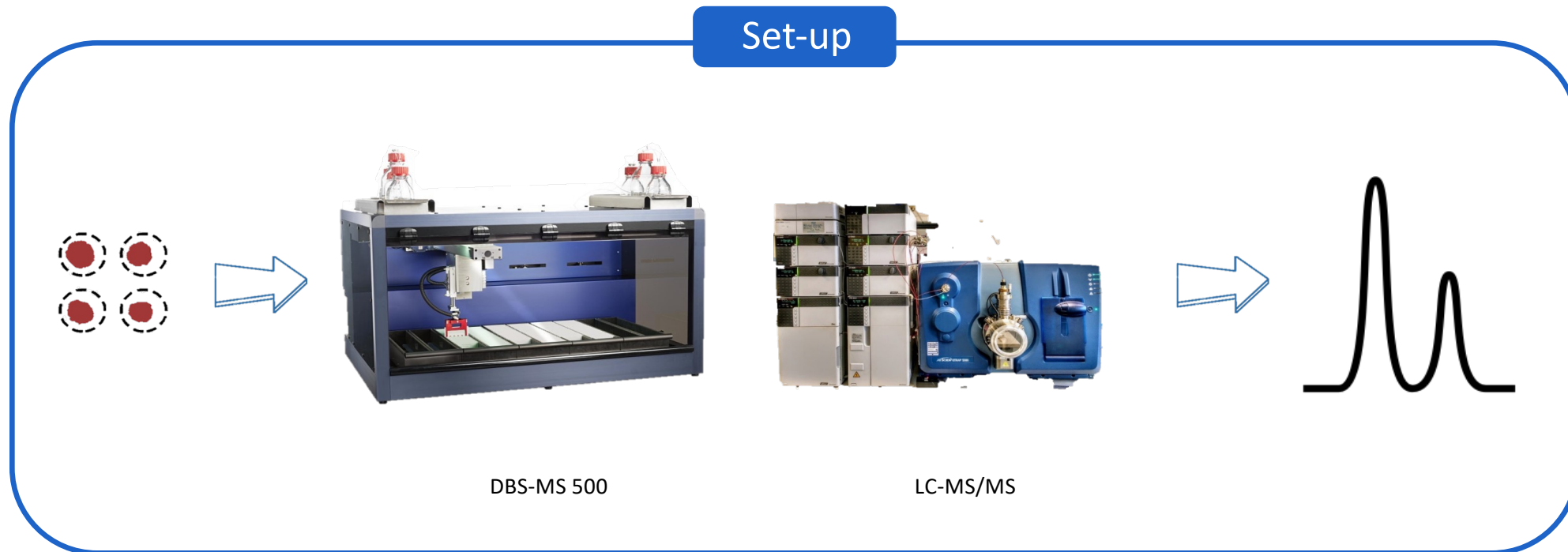


Follow-up via **DBS (dried blood spots)** to increase the patients' quality of life



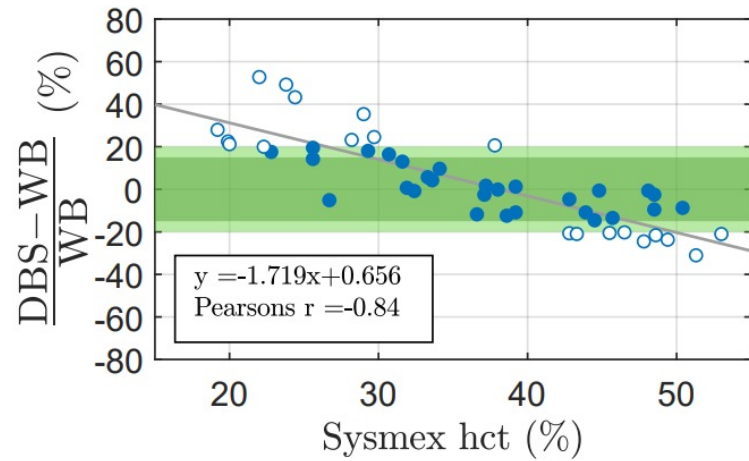
# PREVIOUSLY

Validation and application of an **LC-MS/MS** method, utilizing a fully automated extraction module (CAMAG **DBS-MS-500**), for TDM of four **immunosuppressants**.\*



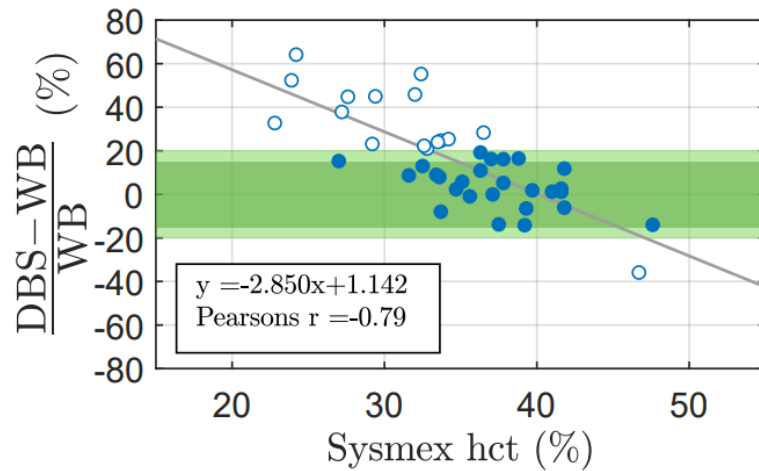
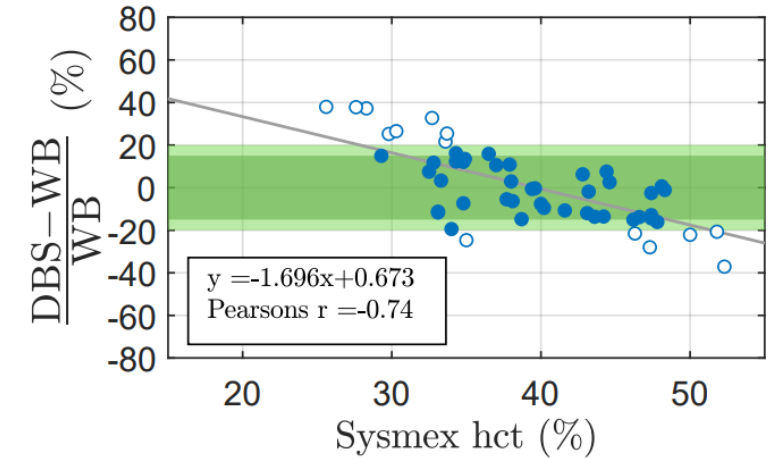
# HOWEVER...

# ...A hct dependent trend was observed



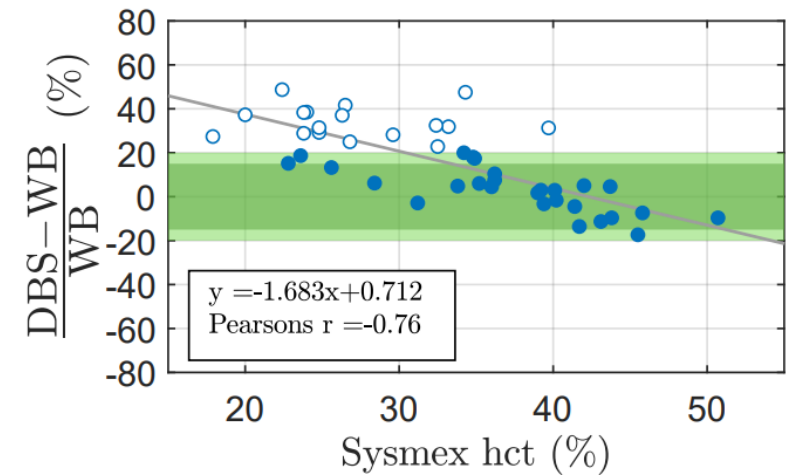
TACROLIMUS

EVEROLIMUS



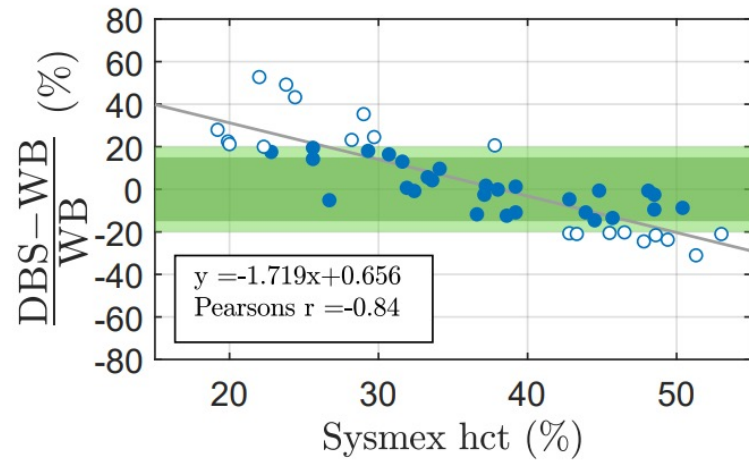
SIROLIMUS

CYCLOSPORIN A



# HOWEVER...

# ...A hct dependent trend was observed



TACROLIMUS



HEMATOCRIT EFFECT

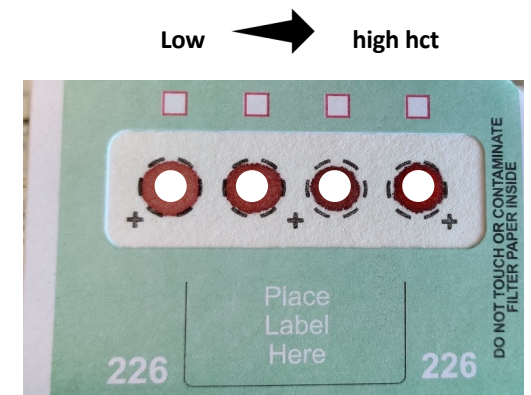
overestimation

underestimation

1. Area bias

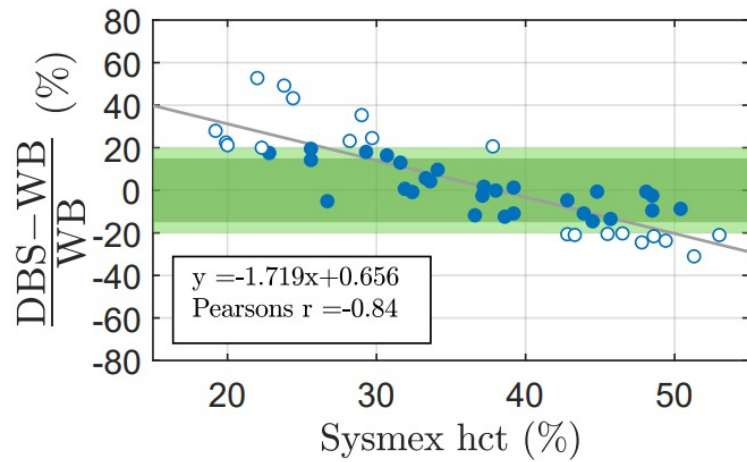


25  $\mu$ L



# HOWEVER...

# ...A hct dependent trend was observed



TACROLIMUS



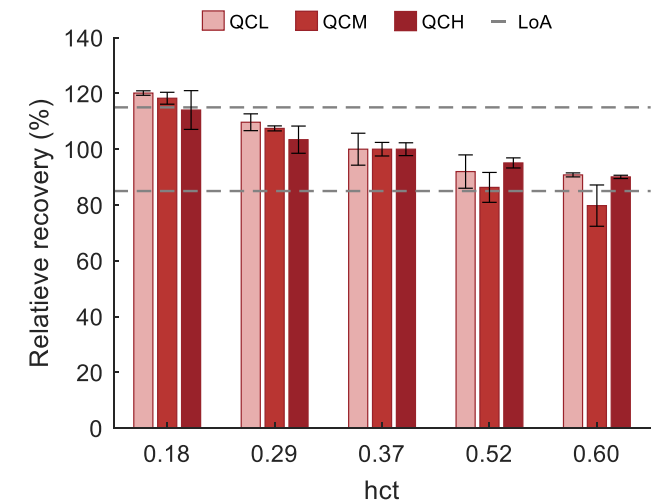
HEMATOCRIT EFFECT

overestimation

underestimation

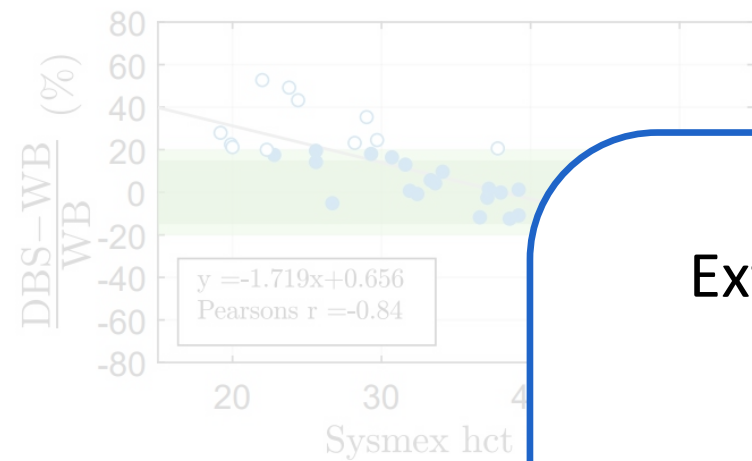
1. Area bias

2. Recovery bias



HOWEVER...

...A hct dependent trend was observed

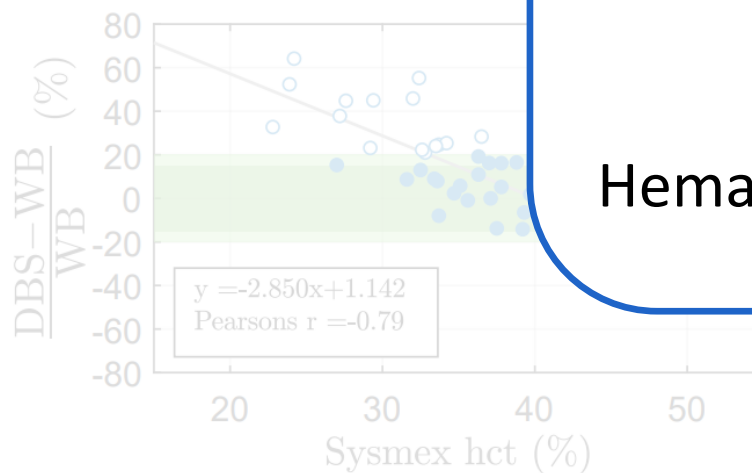


TACROLIMUS

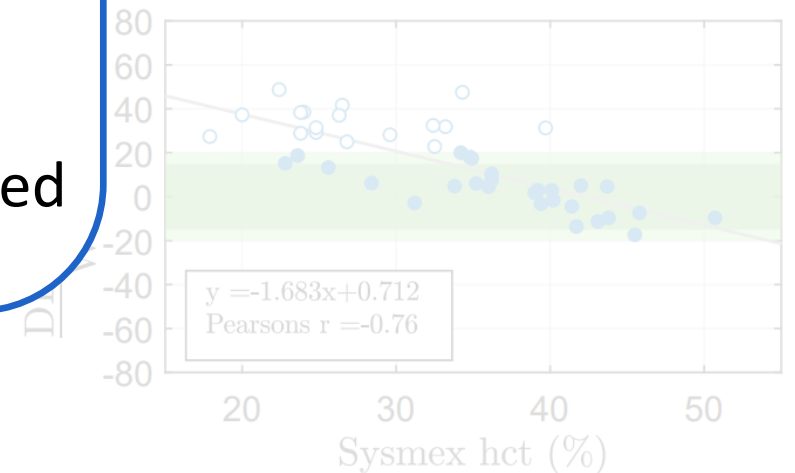
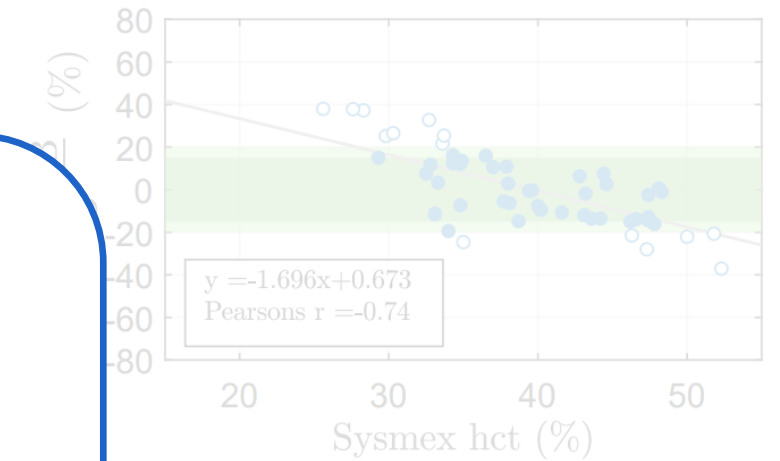
Extraction recovery is affected  
by the hematocrit



Hematocrit correction model needed



CYCLOSPORIN A

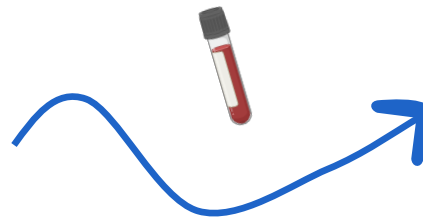
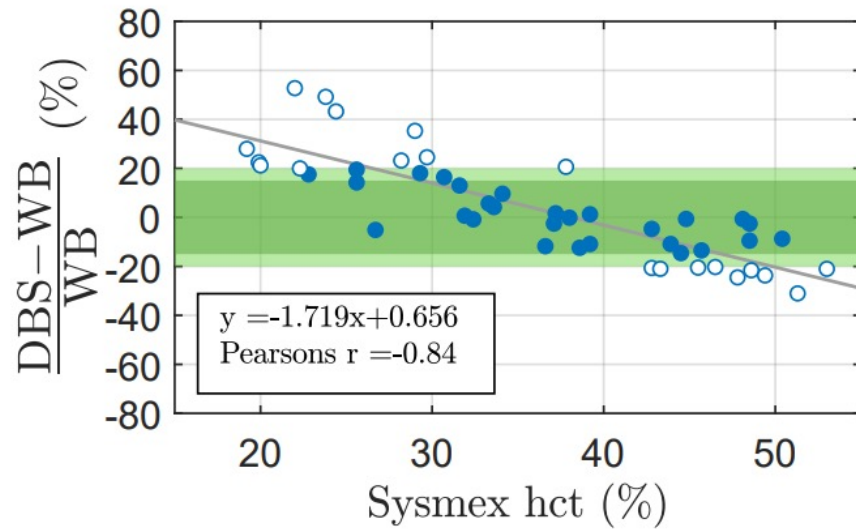


# HEMATOCRIT CORRECTION MODEL

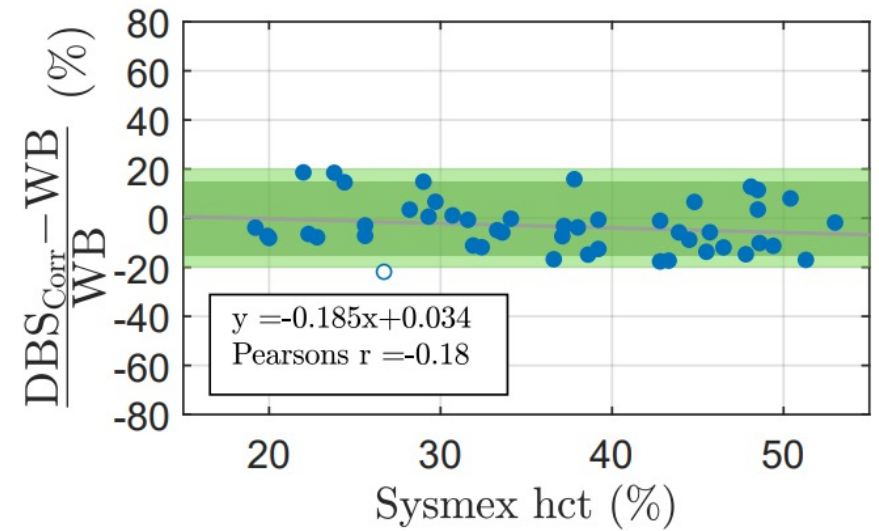
Extraction recovery is affected  
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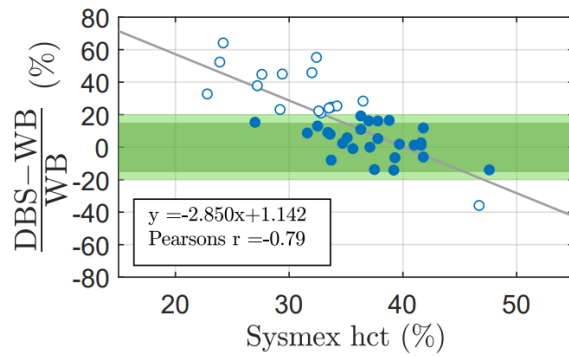
SYSMEX HEMATOLOGY ANALYZER



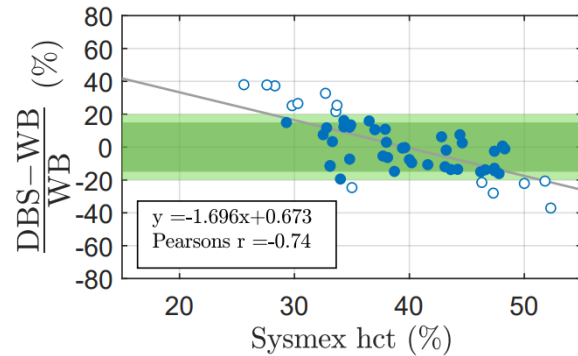


# HEMATOCRIT CORRECTION MODEL

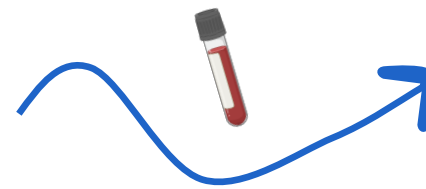
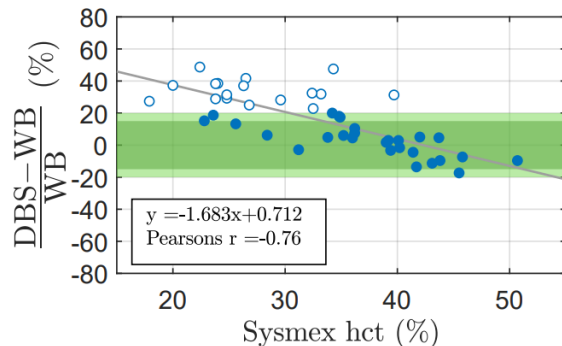
SIROLIMUS



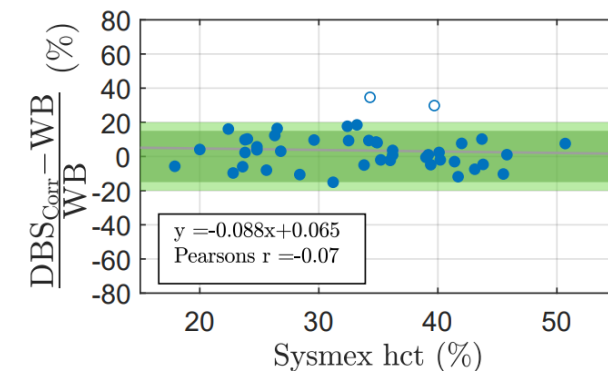
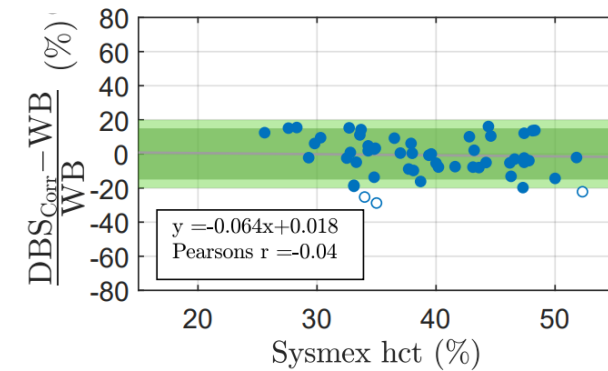
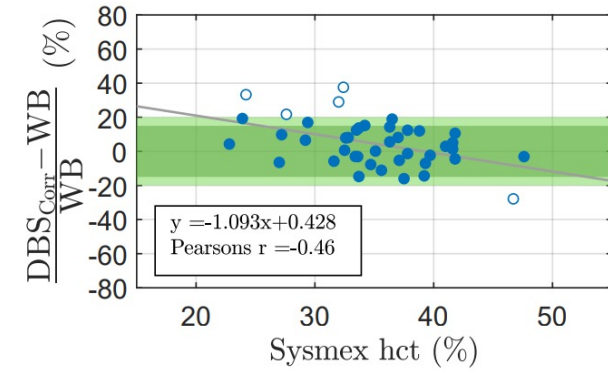
EVEROLIMUS



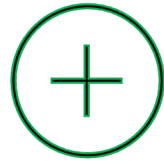
CYCLOSPORIN A



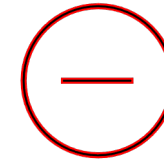
SYSMEX HEMATOLOGY ANALYZER



# HEMATOCRIT CORRECTION MODEL



- A good agreement between DBS and whole blood was obtained
- Similar results for all four immunosuppressants



- Hematocrit determination is based on whole blood
- In a home-sampling context, only DBS are available



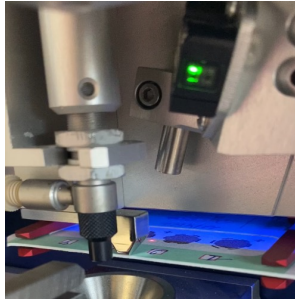
Set-up of correction model based on  
the **DBS-derived hematocrit**

# STUDY OBJECTIVES

Application of **non-contact hematocrit prediction technologies** to overcome hematocrit effects on **immunosuppressant** quantification from dried blood spots

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UV-Vis-based spectroscopy

- ⇒ Single wavelength (at 589 nm)
- ⇒ Fully automated
- ⇒ Generation of raw data



NIR-based spectroscopy

- ⇒ Spectrum (1000 to 2300 nm)
- ⇒ Manual
- ⇒ In-built calibration model

# METHODS

- N = 48, 47, 58 and 48 venous whole blood samples from patients on tacrolimus, sirolimus, everolimus and cyclosporin A therapy, respectively



Evaluation of non-contact hct prediction technologies to correct for the observed hematocrit effect

# RESULTS (UV/Vis)

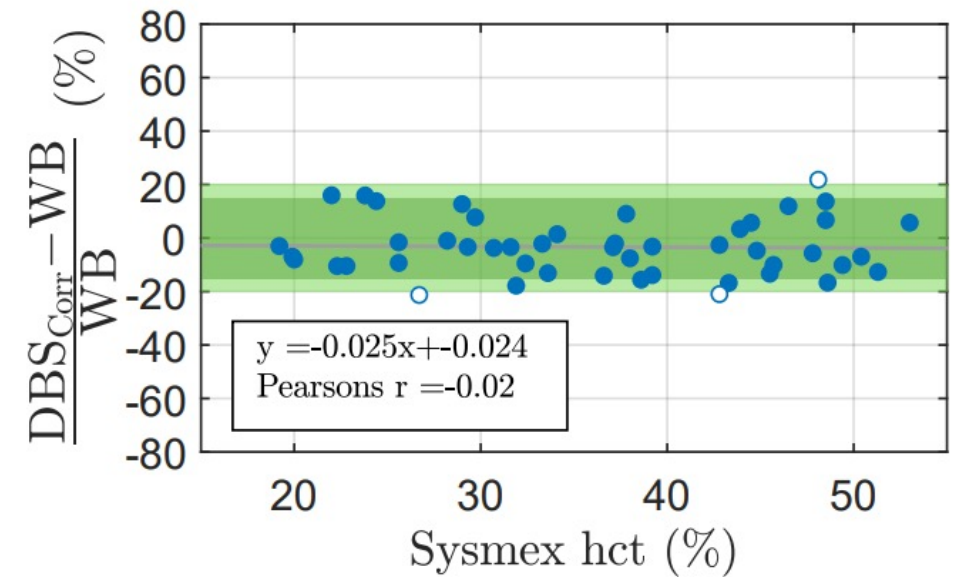
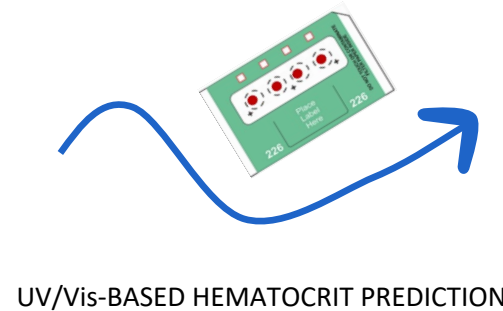
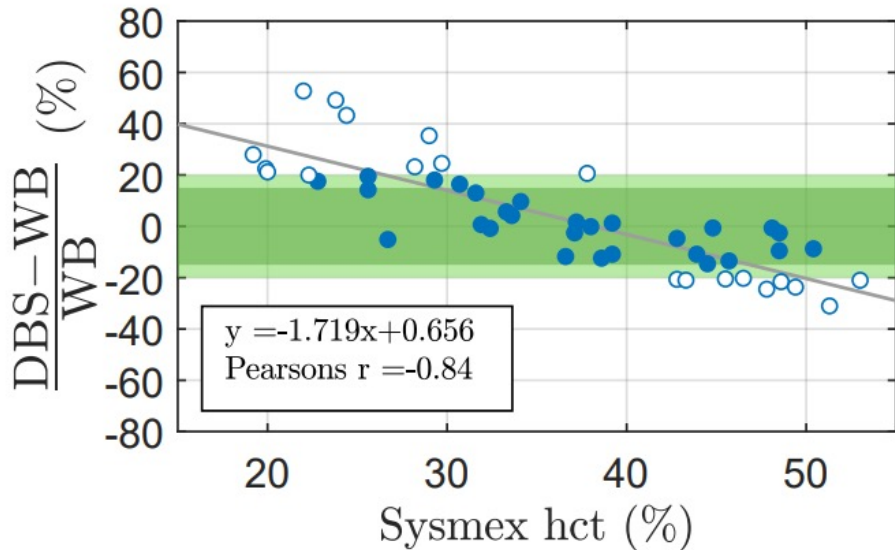
Set-up



Clinical acceptance limit

=

≥80% within 20% difference compared to whole blood

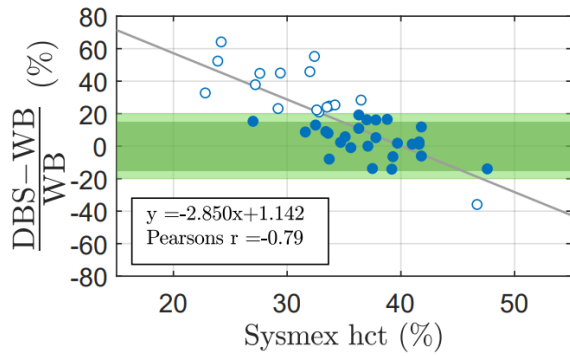


TACROLIMUS

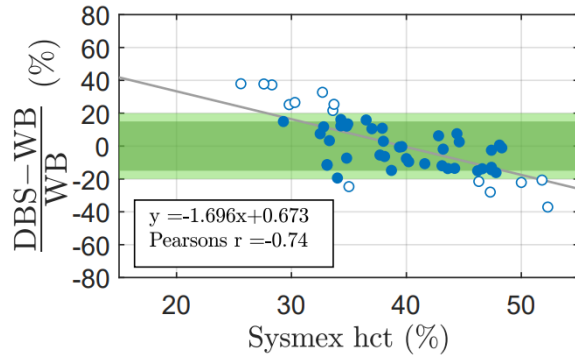
93.8%

# RESULTS (UV/Vis)

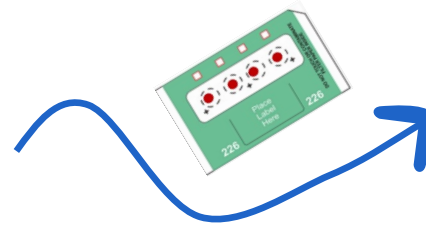
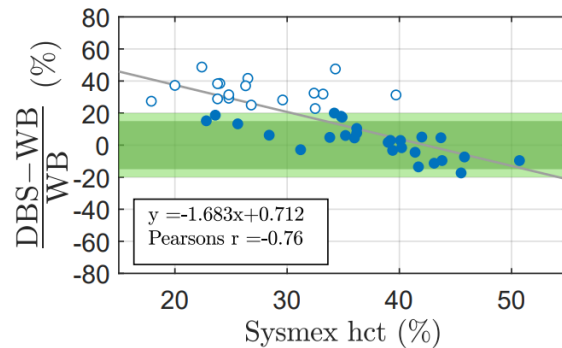
SIROLIMUS



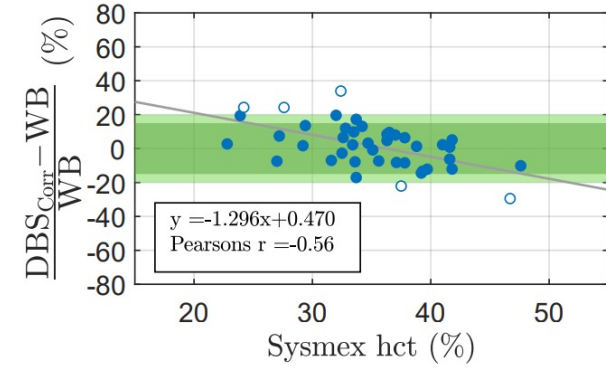
EVEROLIMUS



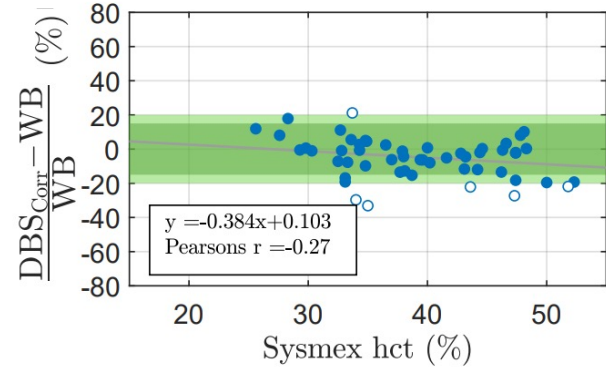
CYCLOSPORIN A



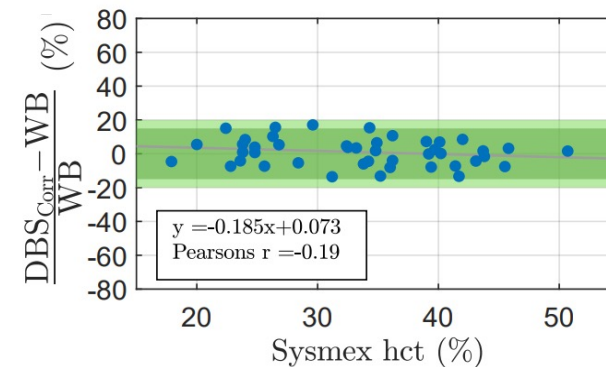
UV/Vis-BASED HEMATOCRIT PREDICTION



88.1%



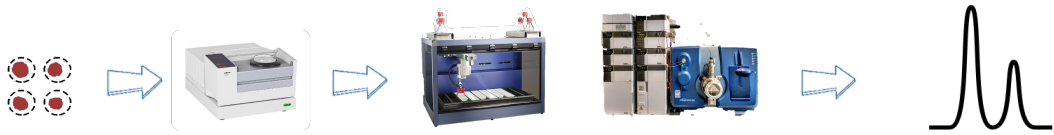
89.3%



100%

# RESULTS (NIR)

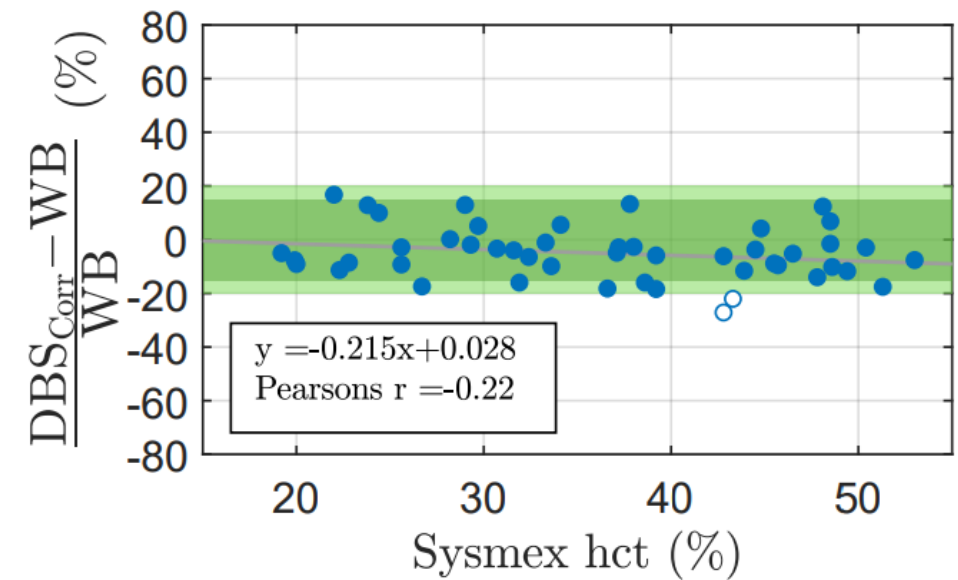
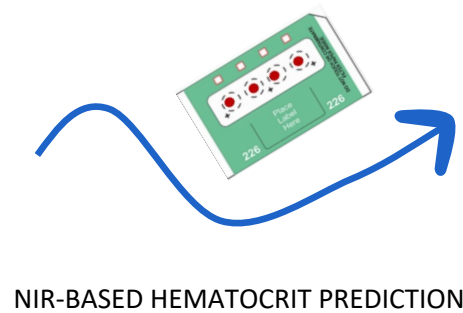
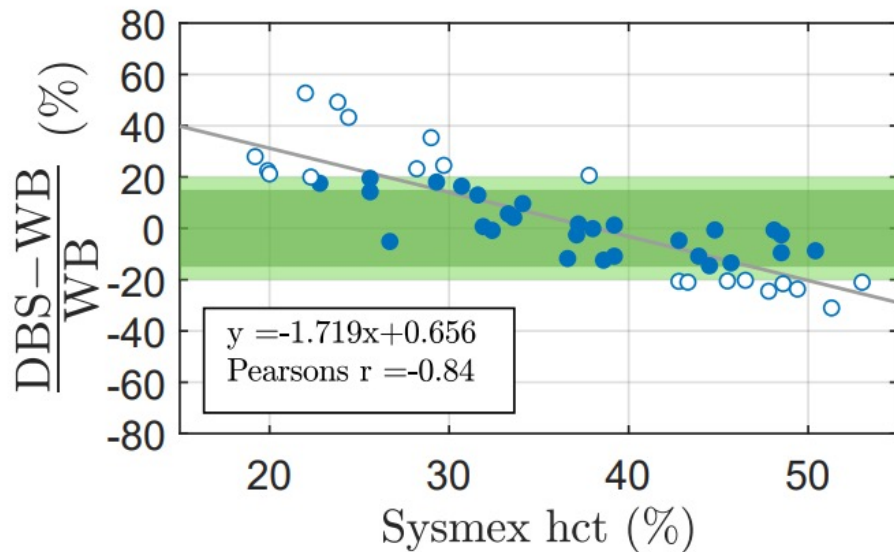
Set-up



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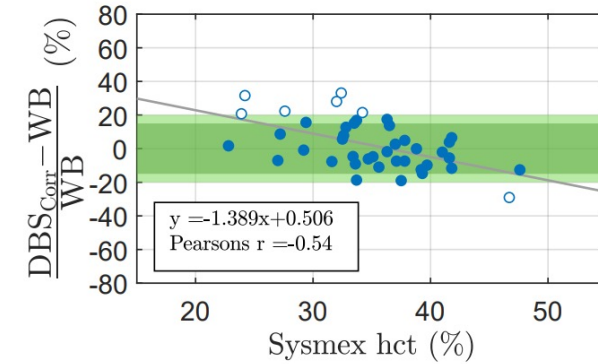
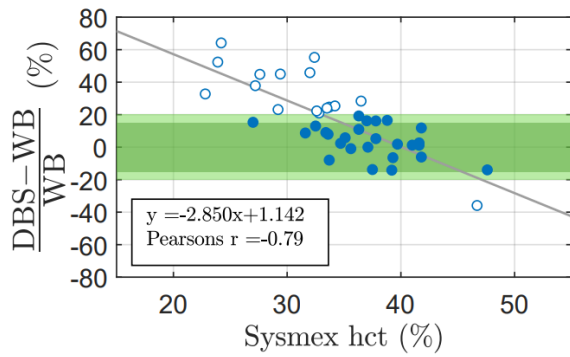
TACROLIMUS

95.8%



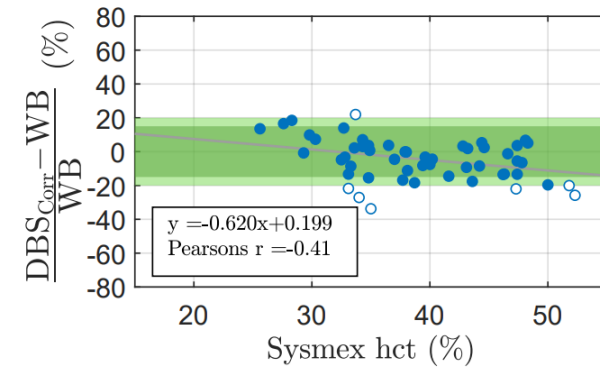
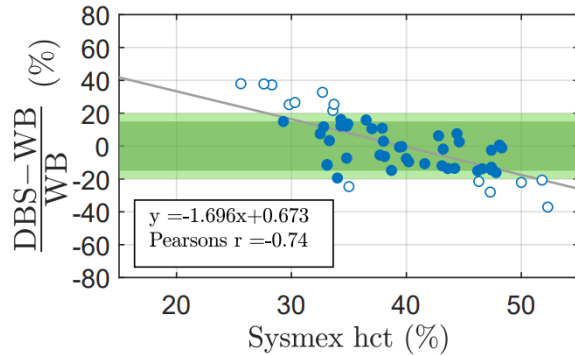
# RESULTS (NIR)

SIROLIMUS



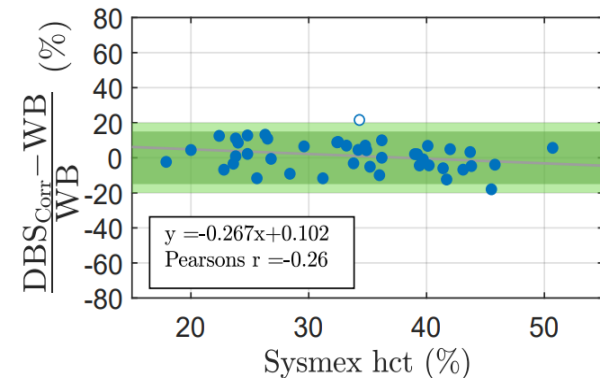
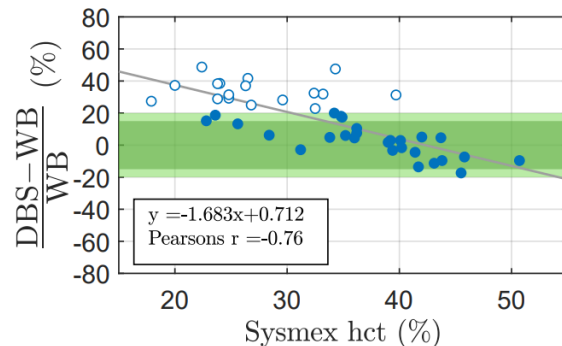
83.3%

EVEROLIMUS

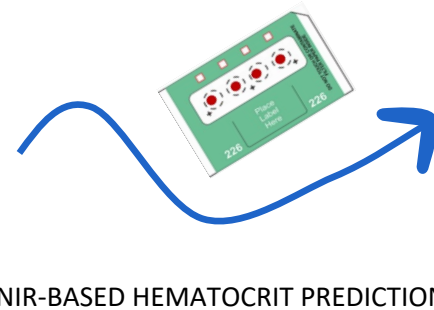


87.5%

CYCLOSPORIN A



97.7%



- For all four immunosuppressants, **clinical acceptance limits were met** using either of both hematocrit prediction strategies.
- **In the future, application** of the complete methodology **for capillary samples** (obtained after finger prick) will need to demonstrate the feasibility of this approach for upcoming home-sampling studies.

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