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ISyPeM2 RTD 2013

FNSNF

Point-of-Care analytical platform for Therapeutic Drug Monitoring

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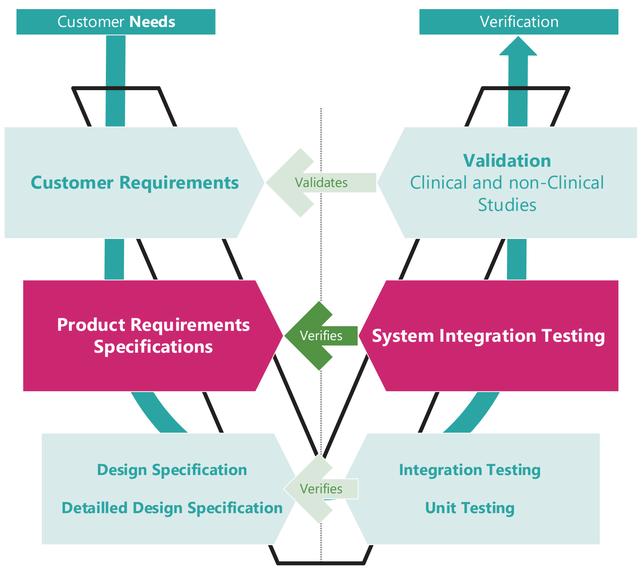
ISyPeM2 Demonstrator *Platform for TDM*

Therapeutic Drug Monitoring for personalized dosage during therapeutic treatments is often mandatory for modern potent drugs against e.g. cancer, HIV or in organ transplantation cases[1]. We aim at developing a minimally invasive Point-of-Care (POC) device that allows quantification of small drug molecules in blood with fast turnaround, based on fluorescence polarization immunoassays.

Device requirements

To answer needs it is critical to have an instrument matching clinical expectations. The table below describes requirements for Tobramycin and Tacrolimus and the V-model applied during the project to evaluate demonstrators and support further development.

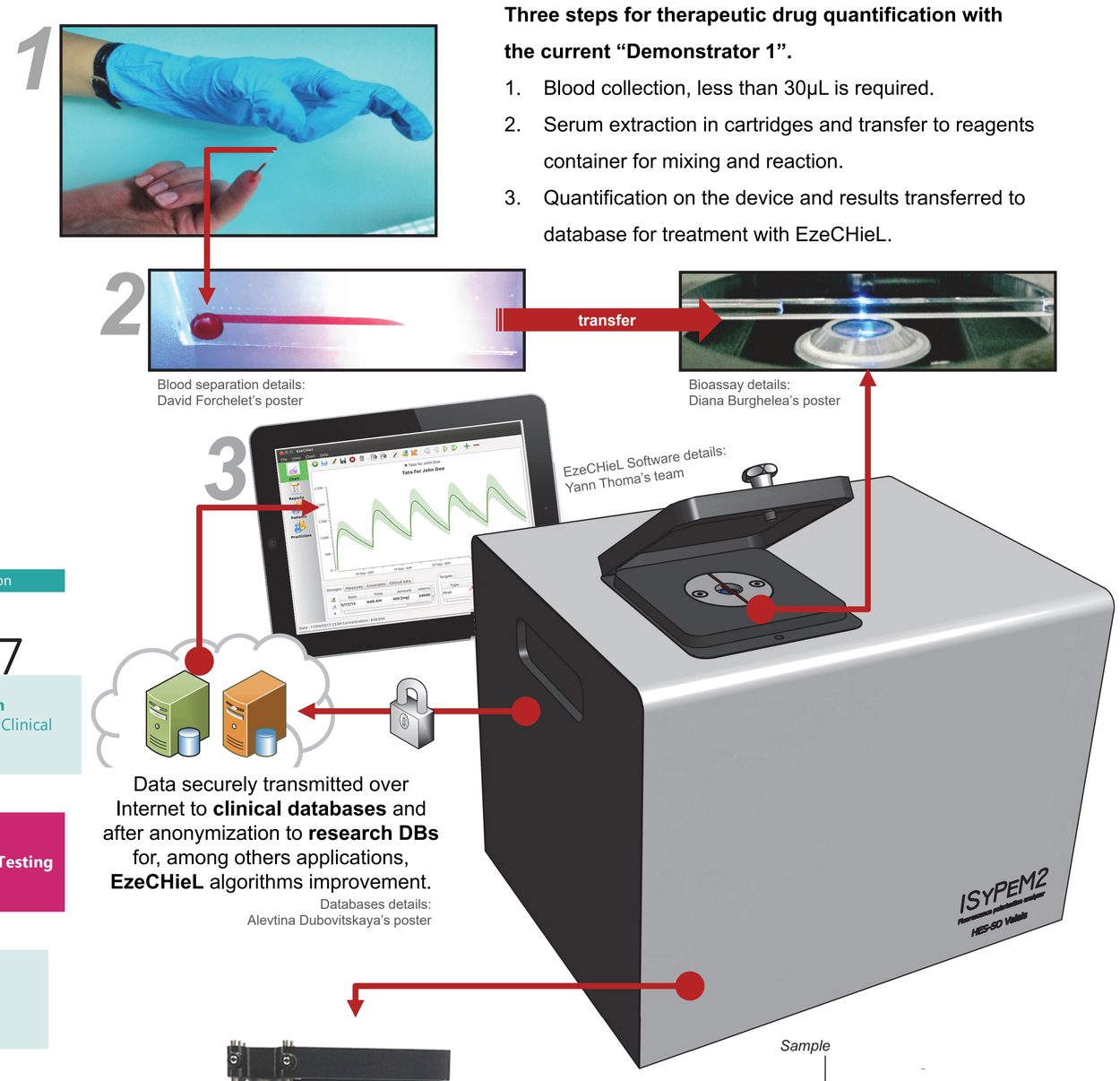
Parameters	Tobramycin	Tacrolimus
Design	Table-top instrument	
Databases	Clinical database and anonymized research database with bridge to EzeCHieL	
Time to results	< 10 min	
Sample preparation	Single use integrated plasma extraction cartridges with reagents mixing and reading cell	Single use integrated whole blood drug extraction with reagents mixing and reading cell
Range	0.1mg/L to 30mg/L	1µg/L to 20µg/L
Reproducibility	CV <20%	
Accuracy	80 ~ 120%	
Sample	20µL	
Reagents	<200µL	
Measurement	<20µL	



ISyPeM2 consortium, together around an instrument

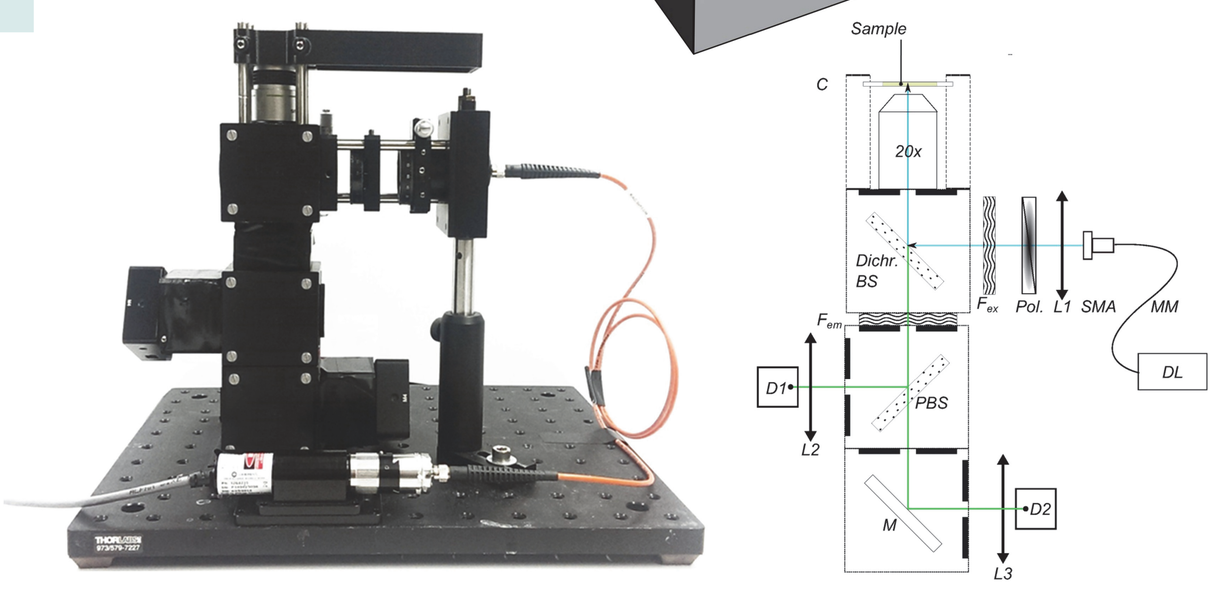
Three demonstrators with increasing integration are planned up to the end of the Nano-Tera in 2017. The final demonstrator will include a sample preparation cartridge to process whole blood and mix reagents required to quantify drugs by fluorescence polarization immunoassays (FPIA). The instrument it-self is composed of an optic module, an embedded computer to process measured values and data transmission to research and clinical databases. The following table indicate the level of integration and development for the three expected demonstrators (2015, 2016 and 2017) and the CTI prototype.

	NT 2016 meeting	Nov. 2016	End of NT Project	CTI
Features	**Demonstrator 1**	**Demonstrator 2**	**Demonstrator 3**	**Prototype**
Blood collection	Finger prick and capillary	Finger prick and capillary	Finger prick and capillary	Blood collection kit
Sample preparation for drug as "Tobramycin"	External module	Preliminary integration in one cartridge	Integrated in one cartridge	Integration in one cost effective cartridge
Sample preparation for dug as "Tacrolimus"	-	External module	Preliminary integration in one cartridge	Integration in one cost effective cartridge
Bioassay for "Tobramycin"	Implemented but not integrated in cartridge	Implemented in preliminary cartridge	Cartridge for bioassay coupled with sample preparation	Integration in one cost effective cartridge
Bioassay for "Tacrolimus"	-	External module	Implemented in preliminary cartridge	Integration in one cost effective cartridge
Reading cell	Independent capillary	Integrated in one cartridge	Integrated in one cartridge	Integration in one cost effective cartridge
Optic module	Breadboard system	Partially integrated and simplified	Further integration and simplification	Low cost sensitive module
Data acquisition and software	Proprietary, NI LabView based	Proprietary, NI LabView based	Embedded solution established	Integration in a embedded PC
Databases & EzeCHieL	Preliminary data transfer link established	Data transmitted to dedicated database EzeCHieL analysis	Data transmitted to dedicated database EzeCHieL analysis	Centralized in clinical database and on demand process on EzeCHieL



Three steps for therapeutic drug quantification with the current "Demonstrator 1".

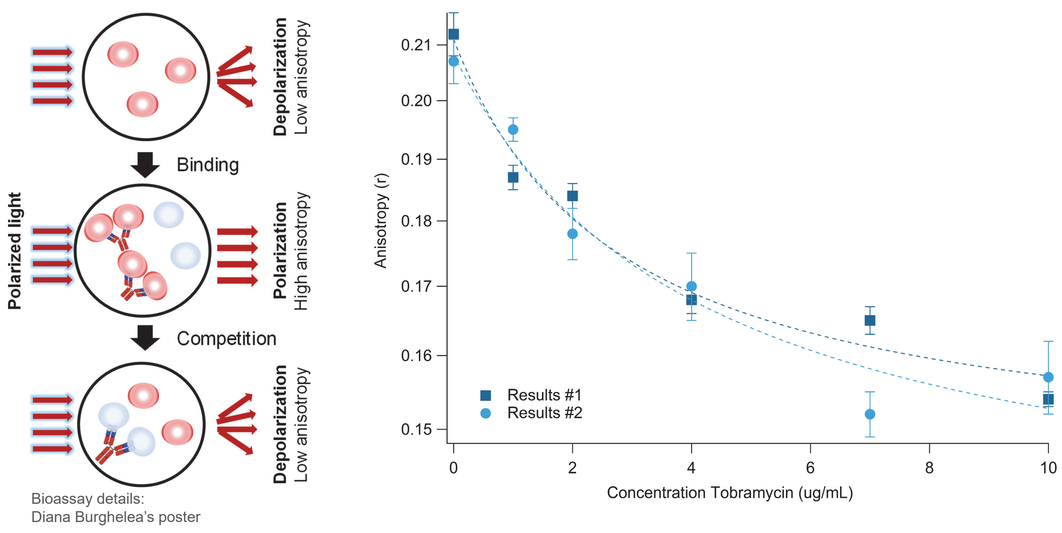
1. Blood collection, less than 30µL is required.
2. Serum extraction in cartridges and transfer to reagents container for mixing and reaction.
3. Quantification on the device and results transferred to database for treatment with EzeCHieL.



Compact FP Optic module for capillary FPIA measurement.

Results

Results obtained on the "Demonstrator 1" are promising as it is possible to quantify Tobramycin in whole blood samples with ISyPeM2 developed technologies. However some issues were spotted during the "System Performance Verification" and are under investigation. Solutions will be implemented in the "Demonstrator 2".



On the left, principle of FPIA quantitative measure. On the right, results for Tobramycin on the "Demonstrator 1".

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[1] Dasgupta, A., Wahed, A., 2014. Chapter 14 - Therapeutic Drug Monitoring, in: Wahed, A.D. (Ed.), Clinical Chemistry, Immunology and Laboratory Quality Control. Elsevier, San Diego, pp. 249–273.