SHIMADZU

WP-137

NeoSickle and NeoHemog MALDI-MS platforms for sickle cell disease screening and hemoglobinopathy detection

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1. Introduction

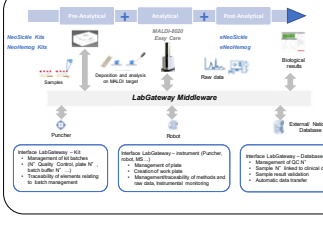
Hemoglobinopathies, including sickle cell disease (SCD), represent a major global public health burden and require reliable and scalable screening strategies. Neonatal screening programs commonly rely on dried blood spot (DBS) samples combined with separation techniques such as high-performance liquid chromatography (HPLC). While effective, these approaches can present limitations in throughput, standardization, and detection of certain variants.

MALDI-MS has emerged as a robust alternative for protein analysis in clinical laboratories, offering rapid acquisition, high reproducibility, and suitability for high-throughput workflows. In this context, two complementary solutions are presented by Shimadzu Chemistry & Diagnostics (France): NeoSickle, an IVDR-compliant platform dedicated to SCD screening based on intact hemoglobin chain detection, and NeoHemog solution under development using peptide-based analysis to extend the detection of hemoglobin variants.

These approaches aim to support standardized, scalable, and comprehensive workflows for neonatal screening, diagnosis, and epidemiological applications.

2. Methods

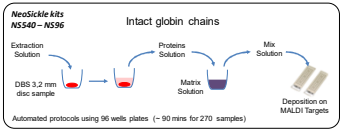
2-1. NeoSickle & NeoHemog workflow



2-2. NeoSickle Pretreatment processing

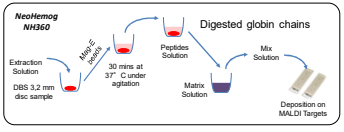
Newborn Screening was carried out with a dry blood spot sample obtained at 3 day of life. Samples were prepared for MS measurements following the instructions of the NeoSickle kit using an automate.

3.2-mm diameter sample disc was eluted by shaking in extraction solution and then mixed with the matrix solution. The "sample matrix" mixture was loaded on the MALDI plate and dried, ready for MALDI analysis.



2-3. NeoHemog Pretreatment processing

3.2-mm diameter sample disc was eluted by shaking in extraction solution followed by digestion step and then mixed with the matrix solution. The "digest sample matrix" mixture was loaded on the MALDI plate and dried, ready for MALDI analysis



3. Results

3-1. NeoSickle

On 787 samples, the results were compared to the sample classification obtained with the Variant NBS HPLC (Bio-Rad) technique used for SCD neonatal screening in the laboratory (3 HPLC systems were used).

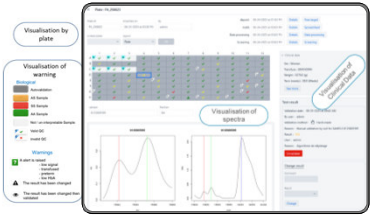
The classification of the patterns and correlation between the MALDI-8020 EasyCare and NBS-HPLC were studied and summarized in the following tables:

NeoSickle MALDI-8020 classification	NBS-HPLC Classification		
	FA	FAS	FS
FA	649	0	0
FAS	1	95	0
FS	0	0	42

FA : HbF and HbA
FAS: HbF, HbA and HbS
FS : HbF and HbS

For the detection of samples from individuals carrying HbS, i.e., expressing at least one HbS hemoglobin chain, the sensitivity is 100 % and the specificity is 99.85 %. The positive predictive value is 0.99 and the negative predictive value is 1.
For the detection of Sickle cell disease samples, the sensitivity is 100 % and the specificity is 100 %. The positive predictive value is 1 and the negative predictive value is 1.

Example of result visualization after treatment of raw data through the middleware and eNeoSickle software :



3-2. NeoHemog

NeoHemog preliminary performance was evaluated on multiple cohorts from adult and newborn samples. For common hemoglobin variants such as HbS, HbC and HbE sensitivity and specificity exceeded 93–100 % depending on the target.

	Adults samples = Age > 5 days			Newborn samples = Age < 5 days		
	~ 1000 samples			~ 300 samples		
Hemoglobin variants	number of carrier samples	Sensitivity (%)	Specificity (%)	number of carrier samples	Sensitivity (%)	Specificity (%)
HbS	297	100	100	134	97	100
HbS/HbC	25	93	100	5	100	100
HbS/HbS	74	100	100	8	100	100
HbC	46	100	99	67	100	97
HbC/HbC	6	93	100	19	100	86
HbE	22	96	99	31	97	100

Moreover, thirteen rare hemoglobin variants were detected through peptide-specific alerts, with target peptide scores consistently higher than in non-carrier samples, supporting the feasibility of extended hemoglobinopathy screening.

3. Conclusions & Perspectives

- **NeoSickle demonstrates excellent clinical performance for detecting sickle cell disease and carriers, with full concordance to standard methods and robust large-scale routine use. Implemented in France for seven years across multiple MALDI-MS systems from different manufacturers, it has enabled the analysis of over 1.5 million samples. Now deployed in four neonatal screening centers, it achieves a combined throughput of up to 35,000 samples per month.**
- **NeoHemog enables broader detection of hemoglobin variants, including rare forms.**
- **Future developments include expansion toward comprehensive variant detection, increased automation of workflows, and wider implementation in neonatal screening programs.**