BioMedomics
TESTS FOR LIFE

HEMATOLOGY

Sickle SCAN®

“*Sickle SCAN* **could revolutionize the survival prospects for children** born with sickle cell disease in resource-limited areas.”

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Background on Sickle Cell Disease

Sickle cell disease (SCD) is a painful and life threatening hereditary hematological disorder affecting approximately 400,000 newborns annually worldwide.[1]

50 - 90% of children with SCD will die if their condition is undetected. Early diagnosis is crucial to initiating life-saving therapies.[2]

Knowledge of sickle cell carrier status is also an important part of parental planning for at-risk populations.

All current diagnostic methods for SCD rely on advanced laboratory systems and are often prohibitively expensive and time-consuming in developing countries. Sickle SCAN was designed to meet this need by producing accurate diagnostic results for SCD and carrier status at the point of care without the need for electricity or any additional equipment.

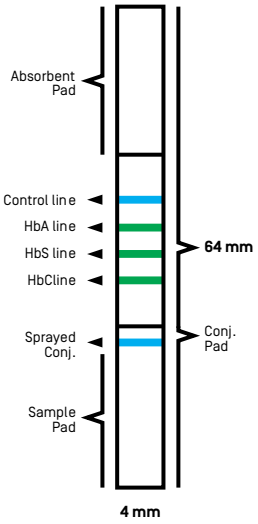

Figure 1 - Schematic illustration of the design of Sickle SCAN strip

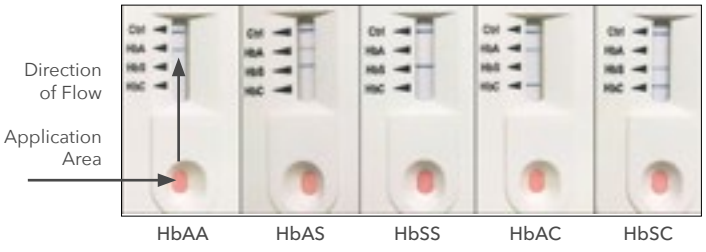

Figure 2 - POC device and possible results for common hemoglobin patterns. The 4 possible combinations of HbA, HbS, and HbC are illustrated.

Design of the Testing Device

The Sickle SCAN device is a lateral flow qualitative immunoassay for the rapid determination of the presence or absence of HbA, HbS, and HbC. The testing cartridge has 4 detection bands, including a distal control band that appears when the sample has flowed through the end of the testing strip. The presence of normal (HbA) or variant (HbS or HbC) hemoglobins are indicated by a dark blue line in the specific region indicated on the device.

The test requires 5 µL of blood added to a provided buffer-loaded module designed to release hemoglobin by lysing erythrocytes. The resulting hemolyzed solution is dispensed into the sample well of the Sickle SCAN cartridge. A total of 6 combinations of HbA, HbS, and HbC are possible, but the 4 most commonly encountered conditions are: Normal (HbAA), SCD (HbSS), Carrier (HbAS), and HbSC Disease.

Testing Procedures

The Sickle SCAN assay is a rapid and point-of-care device performed easily in several minutes. First, 5 µL of blood (either from the finger as depicted in Fig. 3, or pipetted from a previously collected sample) is added to 1.0 mL of buffer solution.

The tube containing the sample is dipensed into the buffer solution and mixed well by inverting 3 times. Then 5 drops of the lysate are added to the sample well in the Sickle SCAN cartridge. The test result is often visible within 1 minute, but the final result is scored after 5 minutes with a blue band indicating the presence of corresponding hemoglobin. The speed of the test allows for real-time communication of results between the clinician and the patient. Moreover, the test requires no electricity and should avoid the cost and added complexity of sample transport and the feedback of results.

Figure 3 - Sickle SCAN testing procedures

Test Reliability

The innovative design for Sickle SCAN described above provides: 1) high specificity to identify HbS, HbC, and HbA, even in the the presence of up to 30% HbF (as in patients on hydroxyurea) or HbA2; 2) high sensitivity to simultaneously detect HbS, HbC, HbA, even in anemic patients; and 3) an unprecedented capacity to differentiate SCD (homozygous HbSS, heterozygous HbSC, and HbSb-thalassemia) from sickle cell trait (heterozygous HbAS) and normal adult hemoglobin (HbAA)[3].

Comparison With Other Methods

A number of different methods can be used to diagnose SCD, of which the most common are hemoglobin electrophoresis, high performance liquid chromatography (HPLC), isometric focusing and molecular approaches such as PCR. However, all require a well-trained staff working with well-maintained equipment in climate-controlled laboratory facilities with a reliable supply of power and systems for the delivery and storage of reagents, the commercial costs of which can typically be $12 to $25 per test. Moreover, lab rotary-based approaches require functional systems for sample transport and the return of results.

Solubility testing is a common rapid and cheaper alternative to expensive lab tests, but the test has low sensitivity, is cumbersome, and only detects patients with SS. Confirmatory lab tests are still needed for accurate results.

Sickle SCAN has successfully combined the high sensitivity, specificity, and versatility of lab tests with the simplicity and affordability of point-of-care tests.

	Diagnosis Time	Sample Prep	Carrier Detection	Low Cost	Predictive Value
Sickle SCAN	**5 Minutes**	**NO**	**YES**	**YES**	**>99%[3]**
Solubility Testing	38 Minutes	YES	NO	YES	33.3%[4]
HPLC	2-7 Days	YES	YES	NO	>99%
IEF	2-7 Days	YES	YES	NO	>99%
Electrophoresis	2-7 Days	YES	YES	NO	>99%

Table 1 - Comparison with other sickle cell testing methods

Limit of Detection

The Sickle SCAN™ limit of detection for hemoglobins A, S, and C is determined to be <10%, <10%, and <10%, respectively.

	Limit of Detection
Hemoglobin A	<10%
Hemoglobin S	<10%
Hemoglobin C	<10%

Table 2 - Sickle SCAN Limit of Detection for HbA, HbS, and HbC

Sensitivity and Specificity

Sickle SCAN was compared to High Performance Liquid Chromatography (HPLC) using guidelines outlined in CLSI document EP15-A2-IR. Patient samples (n=290) were collected and measured in duplicate on both systems.

	SS	AS	SC	AC	AA	Total
Clinical SS	95	0	0	0	0	**95**
Clinical AS	0	89	0	0	0	**89**
Clinical SC	0	0	53	0	0	**53**
Clinical AC	0	0	0	8	0	**8**
Clinical AA	0	0	0	0	45	**45**
Total	95	89	53	8	45	**290**
Specifity	>99%	>99%	>99%	>99%	>99%	>99%
Sensitivity	>99%	>99%	>99%	>99%	>99%	>99%

Table 3 - Sickle SCAN performance compared to genotypes identified by HPLC

Interfering Factors

Sickle SCAN demonstrates ≤ 10% interference with the following substances at the concentrations indicated: Protein (Albumin) 50 mg/mL, Bilirubin 2.5 µg/mL, Triglycerides 2.5 mg/mL, Hydroxyurea 75 µg/mL, and Penicillin 500 µg/mL.

References

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(2) Williams, T.N. (2015). An accurate and affordable test for the rapid diagnosis of sickle cell disease could revolutionize the outlook for affected children born in resource-limited settings. BMC Medicine, 13(1), 238.

(3) Kanter, J., Telen, M.J., Hoppe, C., Roberts, C.L., Kim, J.S., & Yang, X. (2015). Validation of a novel point-of-care testing device for sickle cell disease . BMC Medicine, 13(1), 225.

(4) Okwi, A.L., Byarugaba, W., Parkes, A., & Ocaido, M. (2010). The reliability of sickling and solubility tests and peripheral blood film method for sickle cell disease screening at district health centers in Uganda. Clinics in Mother and Child Health, 7(1)