Hemex Health

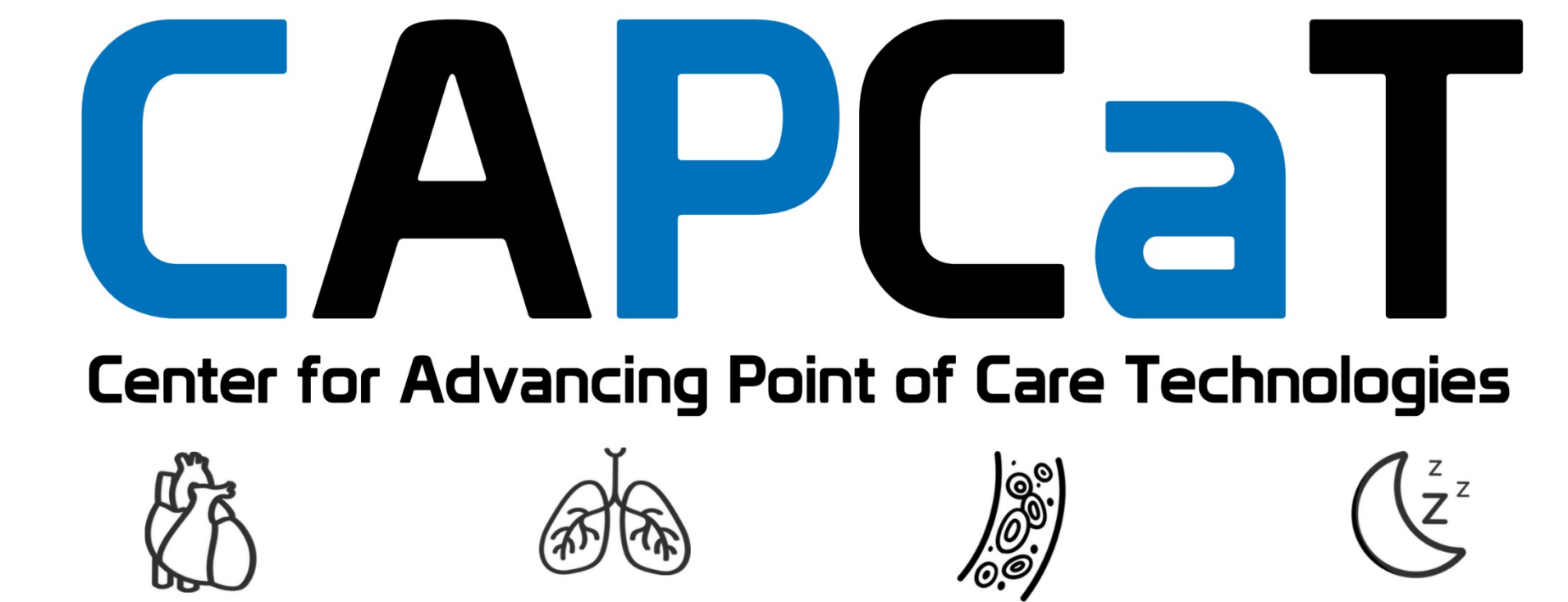# Gazelle: Integrated Anemia and Hemoglobin Variant Test

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CASE SCHOOL OF ENGINEERING — Case Western Reserve University

LOWELL · WORCESTER — M2D2 — Advancing Med Device & Biotech Innovations

CAPCaT — Center for Advancing Point of Care Technologies

UNMET NEED

- Anemia affects more than 2 billion people worldwide (~25% of world population)
- Nearly 7% of the world's population carry significant hemoglobin (Hb) variants, the large majority of affected births occurring in low-income countries
- Hemoglobinopathies, including Sickle Cell Disease (SCD) and Thalassemia, are the 3rd most prevalent causes for anemia
- Timely and proper management of anemia benefits from understanding of the exact cause
- Timely and proper management of SCD benefits from understanding of patient anemia status
- The unmet need for affordable, portable, accurate point-of-care tests to facilitate decentralized hemoglobin testing in resource-constrained countries is well-recognized
- We present the first POC diagnostic integrated test for anemia and SCD, Gazelle-Multispectral, is an 8-minute point-of-care microchip electrophoresis test for determining both hemoglobin level and hemoglobin variant level, in one single test.
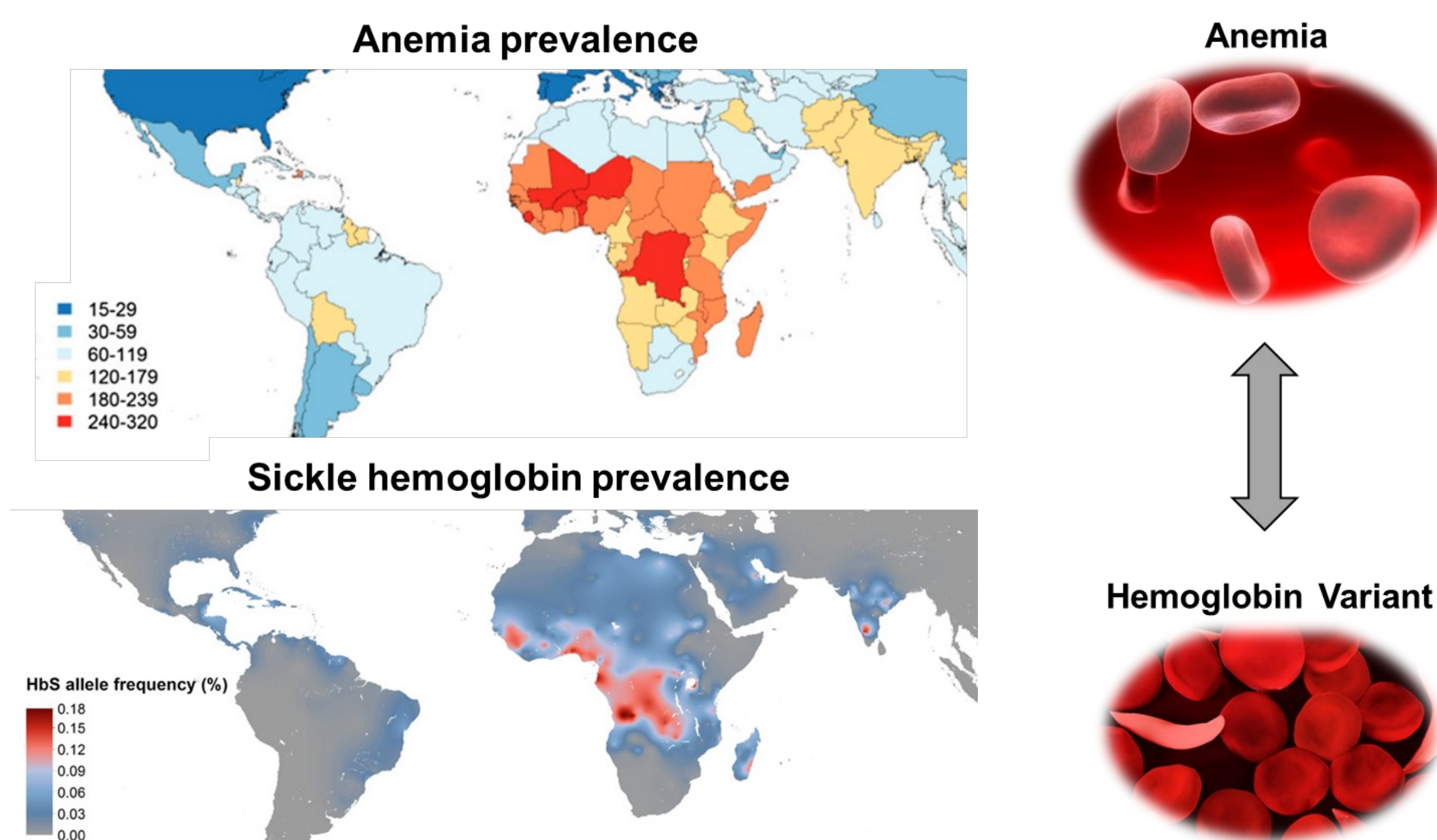
Anemia prevalence

Sickle hemoglobin prevalence

Anemia

Hemoglobin Variant

Figure 1: Prevalence of anemia and sickle hemoglobin variant overlap in geographical distribution and are pathologically associated

MATERIALS & METHODS

- Institutional Review Board approvals were obtained at each study site, and blood samples were collected as part of the standard clinical care.
- Clinical studies presented here were performed with a fully functional, portable Gazelle-Multispectral machine based on technology initially invented at Case Western Reserve University. The commercial product, based on this technology, was developed by Hemex Health Inc. (**Fig. 2B**).
- Blood samples were tested with both Gazelle and the standard reference methods, complete blood count (CBC) and high performance liquid chromatography (HPLC). Reference test results were not available to the Gazelle users. Similarly, Gazelle test results were not available to the users of the standard reference tests.
- Microchip Electrophoresis operation has three stages – (i) Sample preparation, (ii) cartridge preparation, (iii) Hemoglobin separation, and image analysis.

POINT-OF-CARE MICROCHIP ELECTROPHORESIS TECHNOLOGY
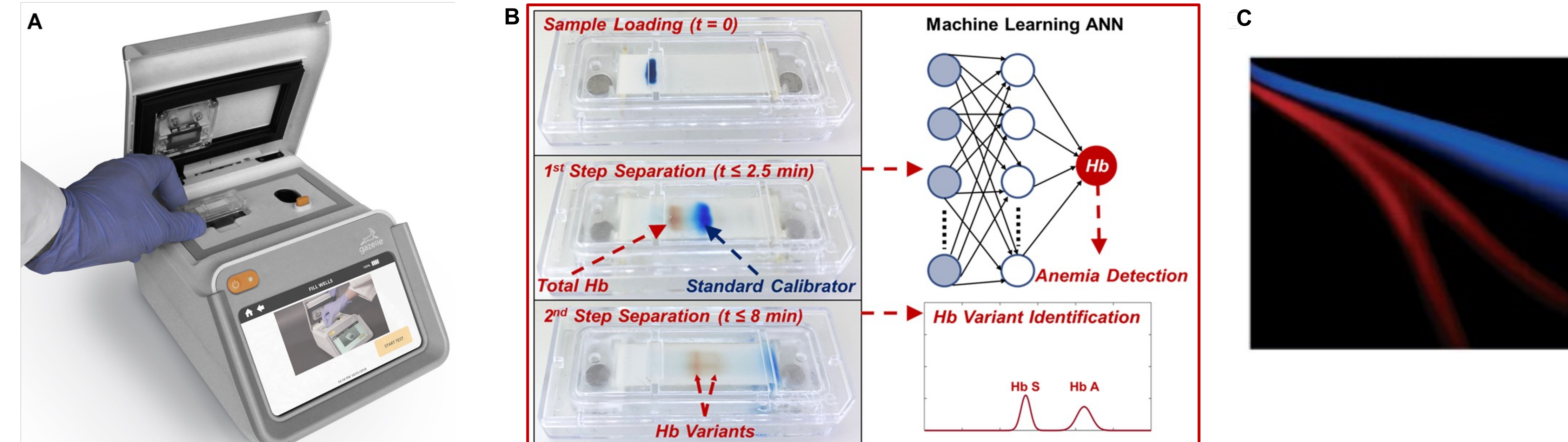
Gazelle provides the first POC solution for β-thalassemia test. (A) The Gazelle perform real time imaging and data analysis tracking the Hb electrophoresis process. **(B)** Gazelle test overview. First, a drop of blood (red) was mixed with standard calibrator and applied on the CA paper (t = 0). Within the first 2.5 minutes (t ≤ 2.5 min), the total Hb (red) and standard calibrator (blue) were electrophoretically separated, at which time blood Hb level (g dL−1) and anemia status was determined by the algorithm. Next, Hb variant separation occurred (t ≤ 8 min), which is then analyzed to determine the presence of major hemoglobin variants and types in the blood sample. The entire electrophoresis process was tracked in real-time and the captured data was analyzed by the machine learning artificial neural network (ANN) algorithm for integrated blood Hb level determination, anemia detection, and Hb variant identification in a single test.. **(C)** Space-time plots generated by capturing the entire electrophoresis process.

- The reader includes a rechargeable battery, storage and operation to 45 degrees C, Wi-Fi, Bluetooth , GPS and touchscreen operation.
- The reader guides the user through the test procedure via on-screen instructions, uses real- time imaging, automated data analysis, result storage, and on screen analysis including interpretation.
- Gazelle can store up to 2400 test results.
- Has GPS geo-location capability, test reports can be printed wirelessly, transmitted in PDF format or transmitted directly to the cloud.

RESULTS AND DISCUSSION
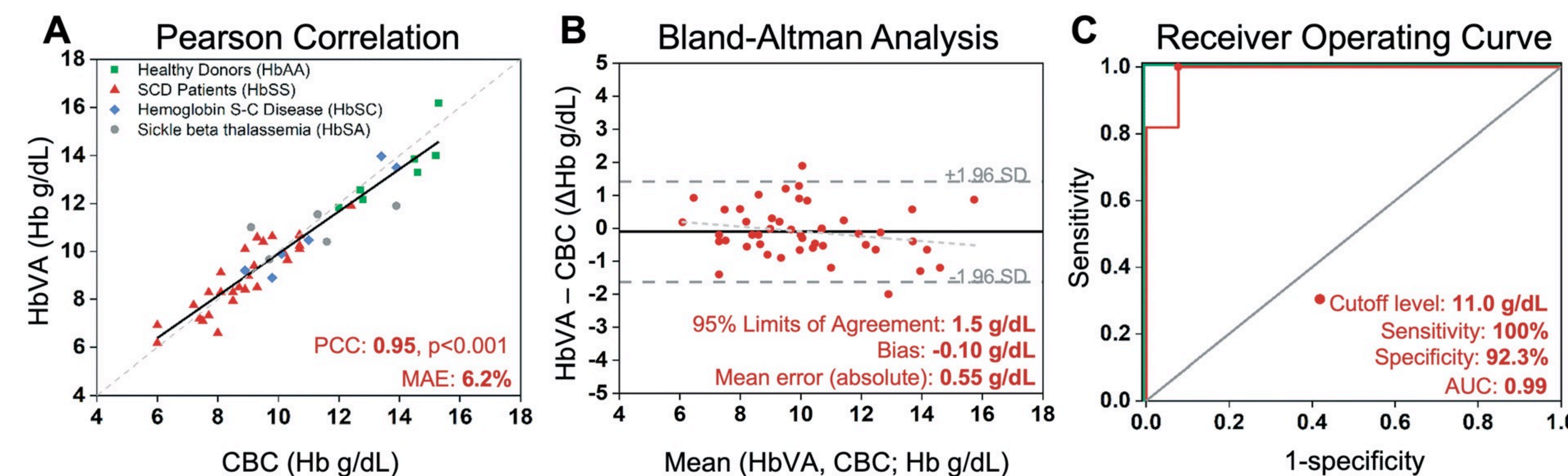
Gazelle artificial neural network (ANN) based machine learning algorithm accurately determines Hb levels and anemia status. (A) Gazelle measures blood Hb levels were strongly associated with CBC measured results (PCC=0.95, p<0.001). The dashed line represents the ideal result where Gazelle Hb level is equal to the CBC Hb level whereas solid line represents the actual data fit. **(B)** Bland-Altman analysis revealed Gazelle determines blood Hb levels to within ±0.55 of the Hb level (absolute mean error) with minimal experimental bias with -0.1 g/dL, indicating that Hb determination has very small bias. The dashed light grey line indicated the relationship between the residual and the average Hb level measurements obtained from the CBC and Gazelle (r = -0.07). The dashed dark grey line represented 95% limits of agreement (±1.5 g/dL). **(C)** The receiver-operating characteristic (ROC) analysis graphically illustrates Gazelle performance against a random chance diagnosis (grey line), with an area under the curve of 0.99, and a perfect diagnostic (green lines), with an area under the curve of 1. The area under the curve of 0.99 suggested Gazelle's viable diagnostic performance. n=46

Table 1. Sensitivity and specificity of Hb Variant/Anemia on determining anemia severity

	Anemia vs. Non-Anemia (Cut-off: 11.0 g/dL)
True Positive, TP	33
True Negative, TN	12
False Positive, FP	1*
False Negative, FN	0
Sensitivity, TP/(TP+FN)	100%
Specificity, TN/(TN+FP)	92.30%

Table 2. Sensitivity and specificity of Hb Variant/Anemia on Hb variant identification

	Hb SS vs. others	Hb SC vs. others	Hb AA vs. others
True Positive, TP	9	6	7
True Negative, TN	37	40	39
False Positive, FP	0	0	0
False Negative, FN	0	0	0
Sensitivity, TP/(TP+FN)	100%	100%	100%
Specificity, TN/(TN+FP)	100%	100%	100%

CONCLUSION

- Gazelle is a versatile point-of-care system that enables affordable, accurate, decentralized hemoglobin testing in resource-limited settings.
- Gazelle provides quantitative and integrated point-of-care allowing testing for anemia and hemoglobin variant within 8 minutes in single test
- The overall simplicity of the Gazelle-Multispectral enables users to quickly and accurately screen for anemia and hemoglobin disorders. The ability to securely store and transfer digital test results has utility for clinicians, patients, public health and treatment providers.

ACKNOWLEDGEMENTS

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