HbA\textsubscript{2} is a widely used biomarker for the management of diabetes mellitus because it provides valuable information for long-term glycemic control and assessment of the patient’s risk for chronic complication. Recently, the test has been recommended for use in diagnosing diabetes [1]. Therefore, accurate and precise measurement of HbA\textsubscript{2} is extremely important. The measurement of HbA\textsubscript{2} values can be affected by hemoglobin disorders such as hemoglobinopathies and thalassemia. Recent studies showed that \( \beta \)-thalassemia could directly affect the measurement of HbA\textsubscript{2} values, similar to other known analytical interferences (e.g., carbamylated hemoglobin, fetal hemoglobin, and acetylated hemoglobin) [2]. The assays which are incapable of identifying thalassemia would report misleading HbA\textsubscript{2} values for thalassemia patients whose red blood cell life span is decreased [3]. The thalassemia is quite prevalent, especially in the southern region of the country. In the Guangdong province, 12.03%, 3.80% and 0.63% of individuals are carriers of \( \alpha \)-thalassemia, \( \beta \)-thalassemia and combined \( \alpha \)/\( \beta \)-thalassemia respectively. The genotype of 51.7% of all \( \alpha \)-thalassemia is \( ^{s s}/\alpha \alpha \). [4]

### Material and Methods

The measurement of HbA\textsubscript{2} is used for thalassemia screening usually based on the accurate determination by using long separation programs on IEX-HPLC or CE instruments. Recently, the HbA\textsubscript{2} assay on the Capillary2 Flex Piercing (C2FP) system has been shown to separate and quantify the HbA\textsubscript{2} fraction as well as the HbA1c detection and providing both HbA\textsubscript{2} values and HbA\textsubscript{1c} values at the same time, thus allowing for the incidental detection of \( \beta \)-thalassemia [5]. In this study, we evaluated the application of C2FP HbA\textsubscript{2} system for screening thalassemia.

This study was approved by the Ethics Committee of Peking University Shenzhen Hospital. Whole blood samples from 258 healthy adult patients without hemoglobin disorders, 80 \( \alpha \)-thalassemia adult patients with \( ^{s s}/\alpha \alpha \) genotype, and 225 adult patients with minor \( \beta \)-thalassemia were collected in ethylene diamine tetraacetic acid (EDTA)-containing tubes. The samples with iron deficiency were excluded. All samples were measured using C2FP HbA\textsubscript{2} system (Sebia, Lisses, France) and Capillary2 hemoglobin system (Sebia, Lisses, France).

All statistical analyses were carried out using SPSS software version 19.0. The correlation between the HbA\textsubscript{2} values determined by two systems was assessed using Pearson’s correlation. Receiver operating characteristic curve (ROC) were performed to determine the cut-off values of HbA\textsubscript{2} for screening \( \alpha \) and \( \beta \) thalassemia.

ROC analysis of HbA\textsubscript{2} were performed using 258 healthy adult patients and 80 \( \alpha \)-thalassemia adult patients with \( ^{s s}/\alpha \alpha \) genotype and 225 adult patients with \( \beta \)-thalassemia with 10 common genotypes. For screening samples with a thalassemia, the optimal HbA\textsubscript{2} cut-off values of the C2FP HbA\textsubscript{2} System is 2.35% with the area under curve (AUC) 0.969, sensitivity 88.1% and specificity 92.5%, and the optimal HbA\textsubscript{1c} cut-off value of the Capillary2 hemoglobin system is 2.55% with AUC 0.951, sensitivity 90.99% and specificity 88.6%. Fig 1 (A and B) shows the details.

### Results

For screening samples with \( \beta \) thalassemia, the optimal HbA\textsubscript{2}, cut-off value of the C2FP HbA\textsubscript{2} system is 3.38% with the AUC 0.994, sensitivity 100% and specificity 98.2%, and the optimal HbA\textsubscript{1c} cut-off value of the Capillary2 hemoglobin system is 3.75% with AUC 0.993, sensitivity 98.2% and specificity 100%. Fig 1 (C and D) shows the details.

Many scientific publications have already demonstrated that the Capillary 2 Flex Piercing is a robust and reliable system for the measurement of HbA1c in presence of hemoglobin variants. Thanks to its high resolution power with a clear separation and accurate quantification of the HbA2 fraction, it can also provide valuable information to clinicians for potential \( \alpha \) and \( \beta \)-thalassemia contexts in diabetic patients while measuring HbA\textsubscript{2}. The HbA\textsubscript{2} values of the C2FP HbA\textsubscript{2} system can be used to screen doubtfull thalassemia samples without other prescription.

### References


3) Shin H, Rachmilewitz EA. Differences in the pathophysiology of hemolysis of \( \alpha \) and \( \beta \)-thalassemic red blood cells(J). J Am Acad Sci 1995;6:112-126.


### CONCLUSION

The CAPILLARYS 2 FLEX PIERCING HbA1c system can separate and accurately measure HbA2 values for screening thalassemia besides reporting accurate HbA1c value, which provides valuable information to clinicians for the interpretation of the HbA1c result in patients with thalassemia trait.