DISSERTATION ABSTRACT

Sickle cell disease (SCD) is a common inherited blood disorder which gives rise to life-long health problems. Technologies capable of sensitive and specific early diagnosis of SCD as well as accurate quantification of HbS exist, but are expensive, complex, slow, laborious, and also require stable electricity, specialized equipment, and well trained technicians. Additionally, tools for quantifying stored RBC quality and selecting well-preserved RBC units for transfusion to vulnerable patients (e.g., chronically transfused individuals with SCD) are currently lacking. These limitations have largely prevented implementation of universal newborn screening programs in low-income, developing regions (e.g., sub-Saharan Africa) and have made it difficult for clinicians to personalize care for individuals with SCD even in high-income, developed countries.

In this dissertation, we engineered and validated several novel microfluidic and paper-based devices which address the limitations of existing technologies and thereby increase access to quality SCD care while enabling further understanding and optimization of transfusion medicine practices. First, we created a simple, rapid and equipment-free paper-based newborn SCD screening test capable of sensitive and specific detection of sickle hemoglobin (HbS) and SCD. Next, we made a rapid, low-cost paper-based assay for quantifying HbS in blood samples based on the color intensities of bloodstain patterns in paper, which showed high correlation and agreement with 'gold-standard' quantification methods. Then, we engineered a simple microfluidic device and associated image analysis algorithm capable of high throughput, automated analysis of stored RBC morphology – a potential metric for assessing the quality of stored blood and selecting well-preserved units for vulnerable patients. Finally, we used these novel devices, in combination with commercially available technologies and previously developed microfluidic devices, to quantify the impact of two novel RBC storage and rejuvenation techniques on stored RBC quality, as well as to quantify the effect of several physiologically relevant processes – i.e., RBC morphology, osmolality, aggregation and hematocrit – on overall blood rheology.

If adopted, these novel tools for diagnosis, monitoring and treatment optimization could drastically increase the quality and accessibility of SCD care for millions of affected individuals worldwide, in both high-income, developed countries and resource-limited, developing regions.