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PRBC MEMBRANE FRAGILITY AS A POTENTIAL STORAGE-TIME-INDEPENDENT QUALITY METRIC

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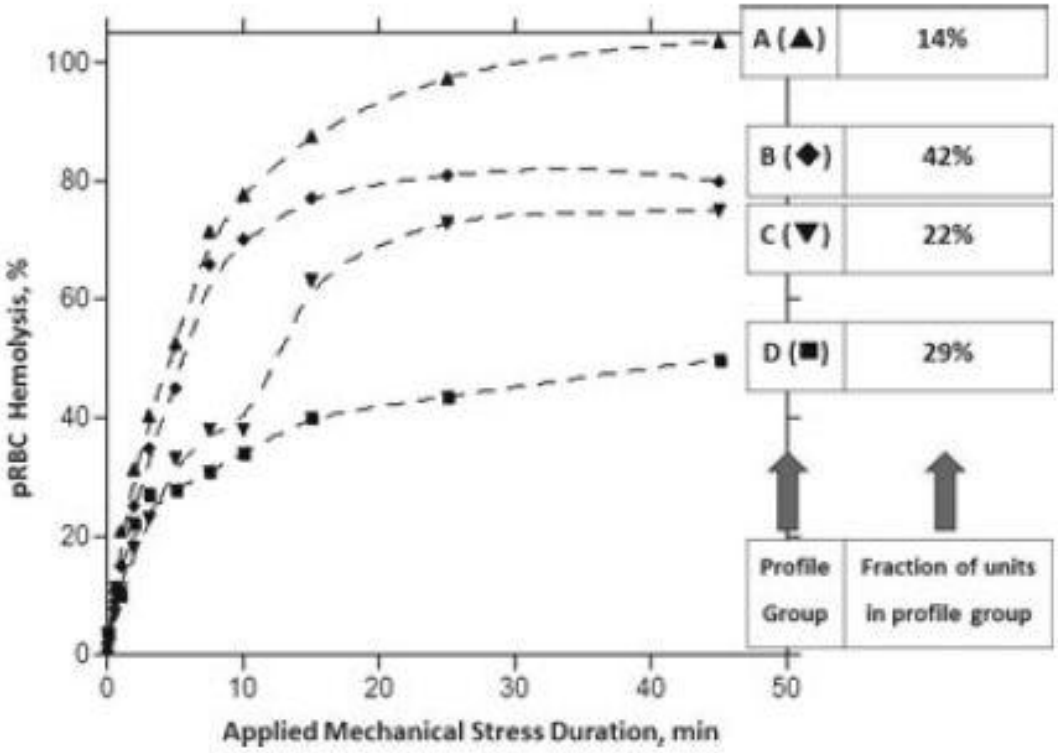
Background: The effect red blood cell (RBC) storage and 'storage lesion' ('new' vs 'old' blood) has on transfusion efficacy and outcomes remains the subject of a considerable debate. However, focusing on storage time as the sole metric for RBC viability loss ignores the variability in properties of RBC even of the same age. Units in storage can potentially differ due to donor-specific differences as well as due to differences in pRBC manufacturing and storage protocols. While the clinical relevance of any in-vitro metrics remains to be shown, it is important to assess age-independence and inter-unit variability of candidate metrics. RBC membrane mechanical fragility has been proposed as a metric of storage lesion potentially relevant to cells' performance in-vivo.
Aims: To evaluate variability and storage-time dependence of RBC membrane mechanical fragility, and its dependence on several donor-specific and manufacturing variables.
Methods: Fiffty-nine pRBC samples, all leukoreduced and irradiated, were collected (sample combined from four test segments identical in content to the units) and characterized by storage time (AGE), total hemoglobin (HBT), auto hemolysis (AH), blood type, and donor demographics. To obtain variable-parameter fragility profiles, mechanical stress was applied using a bead mill with the oscillation frequency held at 50 Hz while durations were varied between 0.5 and 45 min. Fragility profiles were described in terms of hemolysis levels at particular durations (H), the inverse thereof (S), and the slope of the fragility profile curve (K).
Results: pRBC units exhibited complex and varied mechanical fragility (MF) profiles with many profiles indicative of the existence of intra-unit sub-populations with significantly different MF properties. Samples from different units varied significantly in their MF properties, varying by up to 100-fold for some fragility parameters. Overall, AGE was not a significant predictor of pRBC fragility parameters, accounting for a maximum of 13%of their observed variability. No statistically significant correlation was observed between the MF parameters and donor-specific variables including donor age, hemoglobin at donation, gender and race. Auto-hemolysis was weakly correlated

with both MF parameters and with AGE, indicating that its variability in due predominantly to other, age-independent factors. Method of pRBC manufacturing (whole blood vs apheresis) was an independent predictor of pRBC MF and was responsible for up to 20% variability for some fragility parameters.

Figure 1: Examples of pRBC mechanical fragility profiles



Conclusions: High variability and complexity of pRBC mechanical fragility profiles and parameters, including their suggestion of distinct sub-populations, demonstrates the potential of MF to characterize RBC quality. MF properties, though highly variable, were only weakly correlated to storage time. Certain manufacturing methods were found to be a potentially stronger predictor of pRBC membranes' ability to withstand mechanical stress. Remaining variability in MF fragility was likely due to the impact of other manufacturing variables and donor-to-donor differences.

Disclosures: This work was supported in part by Blaze Medical Devices of Ann Arbor, MI.