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Packed Red Blood Cells Accumulate Oxidative Stress with Increased Storage Duration

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Dear Sir

The red blood cell (RBC) storage lesion is the term used to describe the collective metabolic, chemical and structural changes occurring in RBCs during processing and storage, and preparation for transfusion, including thawing after cryopreservation [1, 2]. Multiple mechanisms of the RBC storage lesion have been described that produce functional consequences in stored RBCs, ultimately leading to systemic inflammation, end-organ damage, and coagulopathy [3]. These changes have been associated with increased storage time, and data suggest that transfusion of aged RBCs as opposed to fresher RBCs may influence clinical outcomes [1–4].

One major mechanism of the RBC storage lesion is the accumulation of oxidative stress [1]. Oxidative stress in trauma patients has been correlated with severity of injury, adverse effects and increased morbidity and mortality [4–6]. Oxidative stress can be measured as the oxidation-reduction potential (ORP) of plasma, a single measurement indicating the balance of total reductive and oxidative species in a system [5, 6]. Contributions to this oxidative stress from any source, including RBC transfusion, could be detrimental to critically-ill patients. No standard and reproducible method for measuring oxidative stress clinically or in research currently exists.

A novel platform, the RedoxSys Analyzer (Aytu Biosciences, Englewood, CO), was used to test the effects of storage on total ORP in aged RBCs. Aliquoted samples of leukocyte-

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reduced RBC units were collected from our institution's blood bank, at approximately 7 days ("young") and 42 days ("old") of storage. Samples were centrifuged at 1000 g for 10 min at 4°C to separate RBCs from the supernatant. Supernatant ORP (mV) was measured on the RedoxSys Analyzer by applying 30 μL to the electrode sensor. Statistical analysis was performed using unpaired Student's t-tests for difference in means; normality was confirmed by D'Agostino-Pearson omnibus test for the use of parametric statistical analysis (Graphpad Prism, Graphpad Software, La Jolla, CA).

Samples were stored for a mean of 9.7 ± 0.6 days for young samples (n=11) and 40.6 ± 0.4 days for old samples (n=13). Mean ORP differed between young and old samples by 12.58 mV (p=0.016, 95% CI [2.625–22.54]) (Figure 1). Old RBC units had significantly increased ORP values over young RBC units. Thus, RBCs accumulate ORP during storage, which may contribute to the RBC storage lesion and poor clinical outcome of patients. This is consistent with reports of ORP measurements in aged samples from previous studies [5].

Further exploration of this platform's utility for measuring ORP in blood banked products is necessary. Studies should be performed to determine whether RBCs consistently increase their ORP as they age, or whether certain units increase ORP drastically over time with others remaining relatively the same. Future clinical trials could test whether increased ORP in transfused blood products will correlate with increased oxidative stress in patients.

Samples stored for longer times have an increased amount of oxidative stress in their supernatant, detectable by the RedoxSys platform. These results are consistent with using ORP as a point-of-care measurement of oxidative stress in stored RBCs, which may guide treatment options in future.

With regards,

The Authors

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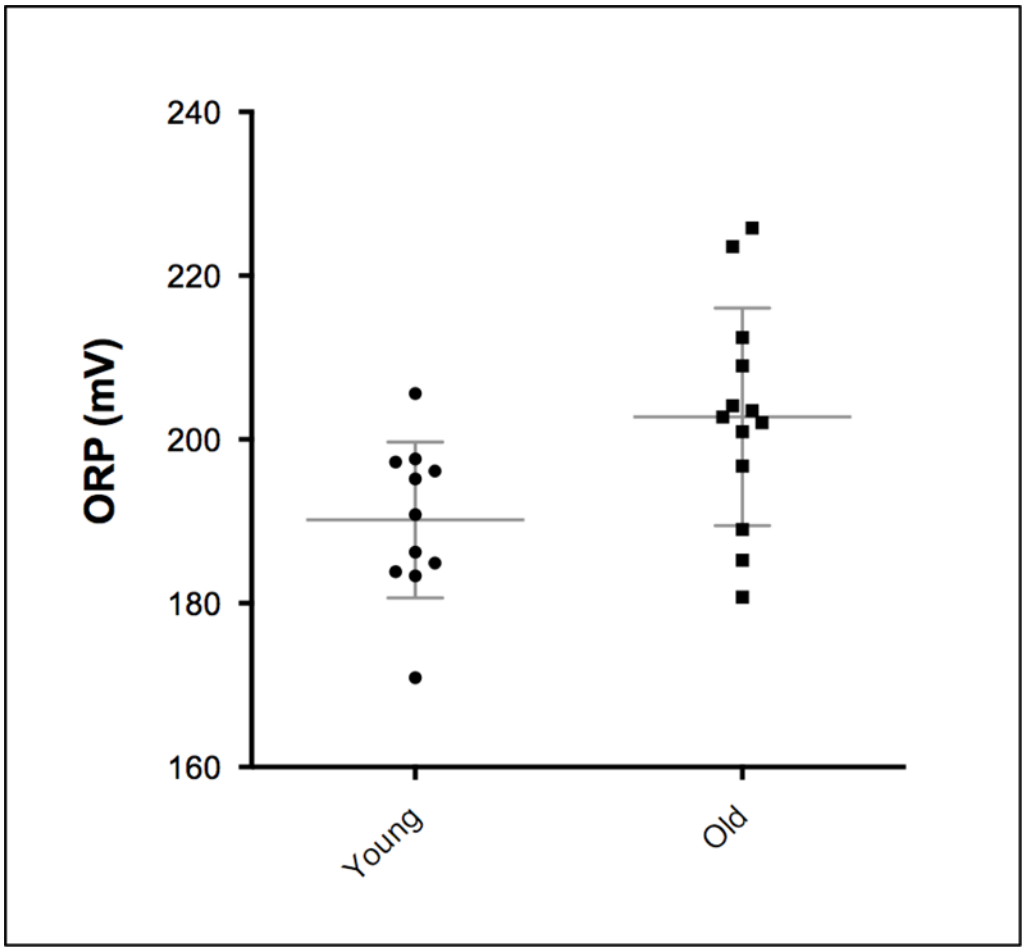

Figure 1. Comparison of ORP of Young vs. Old PRBC samples

Individual data points are displayed, with grey lines representing mean ± SD. Mean ORP for young samples was 190.2 mV ± 2.9. Mean ORP for old samples was 202.8 mV ± 3.7. Difference in means was 12.6 mV (p=0.016, 95% CI [2.625–22.54]).