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SUPPLEMENT ARTICLE

TRANSFUSION

In vitro characteristics and in vivo platelet quality of whole blood treated with riboflavin and UVA/UVB light and stored for 24 hours at room temperature

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Abstract

Background: There is a global increase in whole blood usage and at the same time, emerging pathogens give cause for pathogen reduction technology (PRT). The Mirasol PRT has shown promising results for plasma and platelet concentrate products. Treatment of whole blood with subsequent platelet survival and recovery analysis would be of global value.

Study Design and Methods: A two-arm, open-label laboratory study was performed with 40 whole blood collections in four groups: non-leukoreduced non-PRT-treated, non-leukoreduced PRT-treated, leukoreduced non-PRT-treated, and leukoreduced PRT-treated.

Leukoreduction and/or PRT-treatment was performed on the day of collection, then all WB units were stored at room temperature for 24 h. Sampling was performed after hold-time and after 24-h storage in RT. If PRT-treatment or leukoreduction, samples were also taken subsequently after treatment.

Thirteen healthy volunteer blood donors completed the in vivo study per protocol. All WB units were non-leukoreduced and PRT-treated. Radioactive labeling of platelets from RT-stored, PRT-treated whole blood, sampling of subjects, recovery, and survival calculations were performed according to the Biomedical Excellence for Safer Transfusion Collaborative protocol.

Results: In vitro characteristics show that PRT-treatment leads to increased levels of hemolysis, potassium, and lactate, while there are decreased levels of glucose, FVIII, and fibrinogen after 24 h of storage. All values are within requirements for WB.

In vivo recovery and survival of platelets were 85.4% and 81.3% of untreated fresh control, respectively.

Conclusions: PRT-treatment moderately reduces whole blood quality but is well within the limits of international guidelines. Recovery and survival of platelets are satisfactory after Mirasol treatment.

KEYWORDS
in vivo recovery and survival, leukoreduction, pathogen reduction, platelets, radiolabeling, riboflavin, UVA/UVB light, whole blood

1 | INTRODUCTION

In developed countries, whole blood has been used nearly exclusively as a source for blood component production for many years. However, with the focus on early blood transfusion with balanced component therapy as a very important issue in damage control resuscitation, there is a new focus: Reintroduction of the idea that whole blood (WB) may be the optimal component in the initial phase of massive transfusion therapy.[1]

United States military experience has been a driving force in this development and programs have been developed to make whole blood available.[2-4] At the same time, there is universal agreement that optimal transfusion safety not only involves accessibility, but also the quality of the components.

From each year between 1940 and 2004, an estimated average of 5.3 viruses have emerged, 60%–70% of which are human pathogens.[5] In addition to donor selection, the risk of transfusion-transmitted infection may be reduced by donor screening and blood testing; however, such testing is not available for every pathogen and emergency transfusion may be needed in areas without testing facilities. Also, tests can only detect pathogens above a certain threshold.[6-8]

Blood products also transfer white blood cells (WBCs) that can elicit harmful immune responses. Although the vast majority of WBCs in blood products can be removed by leukoreduction, residual levels of WBCs remain and may cause complications such as transfusion-associated graft-versus-host disease (TA-GvHD).[9,10] Gamma irradiation is currently used in many parts of the world for inactivation of WBCs in blood products that will be transfused to individuals identified as being at risk for TA-GvHD. Clear disadvantages to this approach include difficulty in maintaining radiation sources as well as public health and safety risks associated with the use of cesium (^{137}Cs) or cobalt (^{60}Co).[11] For this reason, many centers have now changed to conventional X-ray technology.[12] X-ray technology is however not active against contaminating agents, opposed to pathogen reduction technologies, which both prevent WBC-induced complications and protect against transmission of infection.

These challenges highlight the need for a safe and convenient method for pathogen inactivation of whole blood. Worldwide, many blood donors are exposed to various pathogens that may be transmitted through transfusion—and the epidemiological situation makes deferral impossible (e.g., blood donors in high-endemic malaria regions may not be excluded).

The Mirasol pathogen reduction technology (PRT) System for WB (Terumo BCT, Lakewood, CO) uses ultraviolet (UV) light energy and addition of riboflavin (vitamin B_2) to the blood products to reduce the pathogen load and inactivate WBCs.[13] This combination treatment results in more robust cell damage than UV light alone, since riboflavin associates with nucleic acids and mediates an oxygen-independent electron transfer process, leading to the irreversible modification of nucleic acids and resultant inhibition of deoxyribonucleic acid and ribonucleic acid replication.[13] Compared with gamma irradiation, Mirasol has also shown better performance in terms of T-cell activation and inhibition of cytokine production in WBCs.[14]

This PRT system is currently used for treatment of platelets and plasma products. With an adjustment to the energy dose, it can also be used for the treatment of whole blood. Pathogen reduction of whole blood may provide an important safety step in areas where transmission of infectious agents is common and the testing abilities are limited. This includes military missions in locations without access to a regular blood bank service. Under such circumstances, on demand blood donation followed by immediate transfusion may be the only available possibility. Therefore, we conducted a study to investigate if Mirasol-treated whole blood could preserve sufficient quality after 24 h storage at room temperature. The study consists of two in vitro arms providing information on the essential parameters for storage and an in vivo study focusing on platelet recovery and survival.

2 | MATERIALS AND METHODS

2.1 | Study design

An in vitro study and an in vivo study were performed. Initially, a two-arm, open-label, randomized study was conducted to characterize the in vitro parameters of leukoreduced and non-leukoreduced whole blood (i.e., plasma, platelets, and RBCs), either treated with the Mirasol PRT System or not treated and stored for 24 h at room temperature (22°C ± 2°C). Treatment was allocated in a 1:1 ratio by assigning the first 20 evaluable WB units to Arm 1 (no leukoreduction) and the next 20 evaluable WB units to Arm 2 (leukoreduction with an Imuflex WB-SP filter [Terumo BCT, Lakewood, CO]) before in vitro testing. Within each arm, we randomized WB units such that one-half of the WB units in each arm

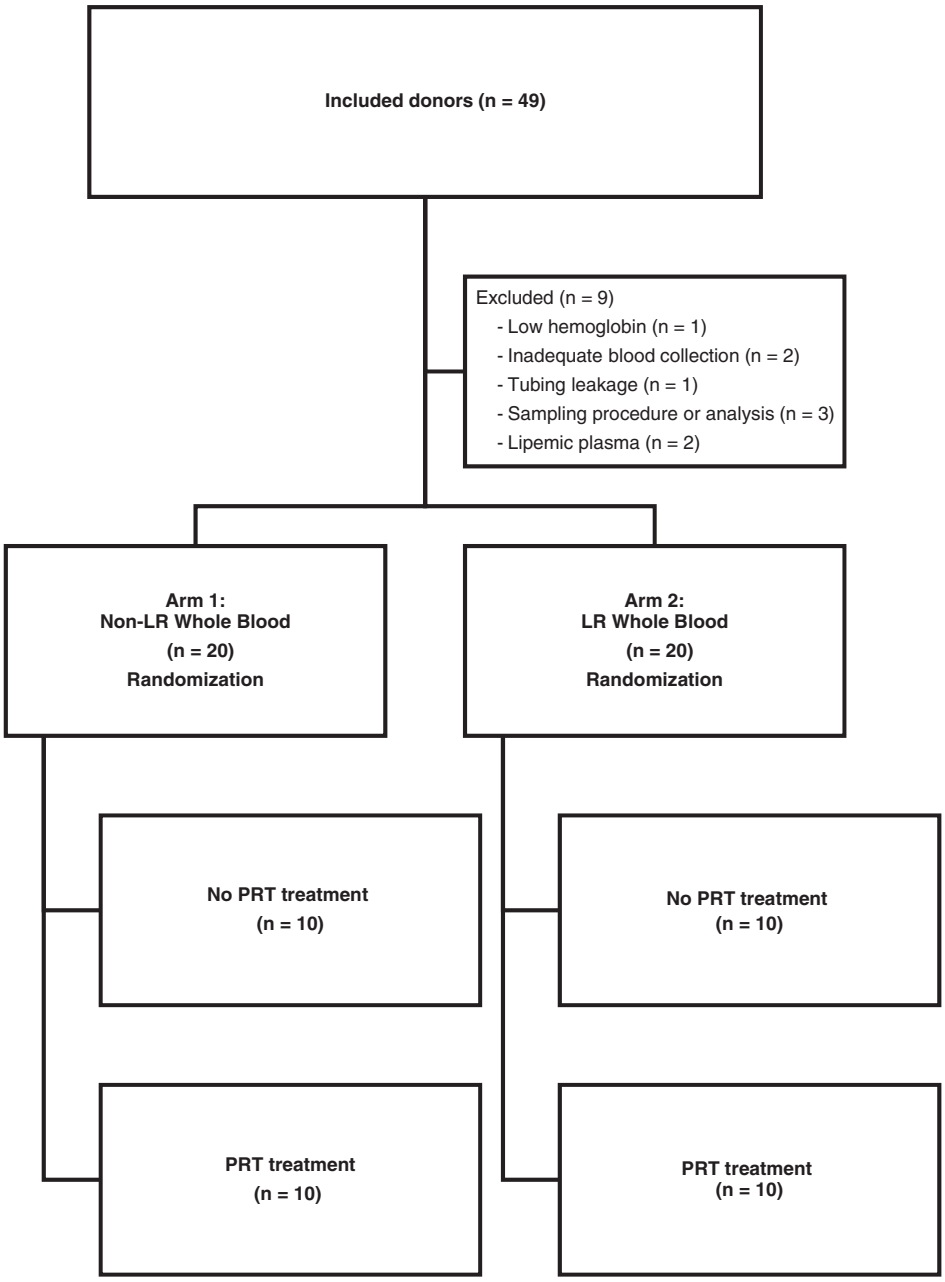

FIGURE 1 Diagram over the in vitro study

were treated with the Mirasol PRT System and one-half were untreated (Figure 1).

When the initial study was evaluated and the results were considered to be satisfactory, a second part of the study was performed (Figure 2).

Subjects provided written informed consent prior to initiating study procedures. A regional ethics committee approved the study protocols.

2.2 | Selection of participants

Eligible subjects were aged ≥18 years, met the criteria for WB donation as defined by institutional blood center standards, and had adequate venous access. Subjects were not eligible if they were pregnant or using medications that interfered with platelet function within 5 days of WB donation. In the in vivo study, subjects were also ineligible for participation in another investigational study within 12 months that may have interfered with data analysis.

2.3 | Collection, storage, and sampling of whole blood

Eligible subjects in the in vitro study donated 1 unit of WB (450–500 ml) using collection sets containing 63 ml of the

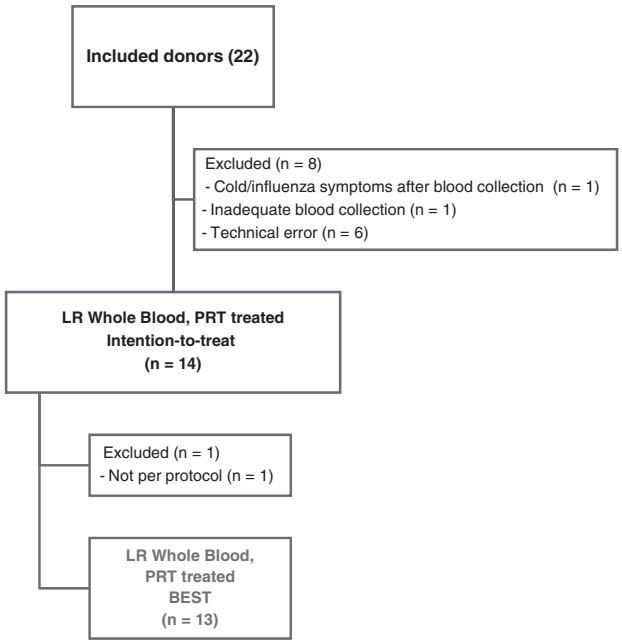

FIGURE 2 Diagram over the in vivo study

anticoagulant citrate phosphate dextrose (CPD). Arm 1 used OptiPure CPD quadruple collection sets (Fenwal Inc., Bad Homburg v.d.H., Germany), and Arm 2 used Imuflex WB-SP quadrouple collection sets (Terumo BCT).

Blood samples for in vitro testing were collected from Mirasol-treated WB units on Day 1 (post collection, i.e., before addition of riboflavin and following leukoreduction in Arm 2), Day 1 (after treatment), and Day 2 (24 h after treatment). Blood samples for in vitro testing were collected from control WB units on Day 1 (after collection, i.e., following leukoreduction in Arm 2) and Day 2 (24 h). We used 150 ml Teruflex sampling bags (Terumo BCT) and sterile welding (TSCD-II, Terumo BCT).

2.4 | Recovery and survival of platelets

Following completion of the in vitro study, an independent, non-randomized, open-label in vivo study was performed using intra-subject controls to investigate the quality of platelets (i.e., in vivo recovery and survival) derived from Mirasol-treated WB following room temperature storage (22°C ± 2°C) for 24 ± 1 h compared with platelets derived from untreated, freshly collected WB.

On Day 0, subjects in the in vivo study donated 450 ± 45 ml of WB into collection sets containing 63 ml of CPD (Imuflex WB-SP, Terumo BCT). The WB unit was tested for in vitro parameters, treated with the Mirasol PRT System, and stored for 24 ± 1 h at room temperature. On Day 1, one 20 ml aliquot and one 50 ml aliquot of WB were removed from the Mirasol-treated, stored unit for additional in vitro testing and platelet radiolabeling, respectively. Also on Day 1, subjects first returned to the investigational site and donated a second sample of fresh WB (43 ± 2 ml into a 50 ml syringe containing 9 ml of sterile CPD-A). We isolated platelets from both the untreated, fresh aliquots of WB and the Mirasol-treated, stored aliquots of WB, and radiolabeled with either 111Indium (15 μCi) or 51Chromium (20 μCi) in accordance with the Biomedical Excellence for Safer Transfusion (BEST) Collaborative protocol. The two radiolabeled platelet aliquots were then autologously reinfused at the same time on Day 1. Serial venous blood samples were collected and analyzed in a gamma counter (Wizard2, 2480 1-Detector, Perkin Elmer, Waltham, MA) for radiolabeled platelet recovery and survival analyses per protocol on Day 1 (pre-infusion, 1.5 ± 0.5 h post-infusion), Days 2, 3, 4, 6, 7 and 10.

2.5 | Study endpoints

The primary endpoint of the in vitro study was characterization of the in vitro parameters of WB units that had been either leukoreduced or not and either treated with the Mirasol PRT System or not and stored for 24 h at 22°C ± 2°C. The main criteria were hematology parameters, plasma free hemoglobin, blood gas parameters, bacteriological testing, blood chemistry, and percent hemolysis. The primary endpoints of the in vivo study were relative recovery and survival of radiolabeled platelets derived from Mirasol-treated WB units compared with radiolabeled platelets derived from freshly collected WB. Secondary endpoints were identical to the primary endpoints of the in vitro study. Safety was evaluated with adverse event (AE) monitoring from Day 0 through the end of study, and treatment emergent adverse events (TEAEs) would be graded using the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.

2.6 | Pathogen reduction procedure

Following WB collection, WB units were transferred to the Illumination Bag. The Riboflavin Solution was mixed with the WB and the Illumination Bag was placed in the Illuminator, which delivered UV light (80 J/ml RBC) while agitating in a horizontal motion for approximately 1 h.

2.7 | Hematology and biochemical analysis

Hemoglobin, hematocrit, platelet count, and WBC were analyzed on a Cell-Dyn Sapphire analyzer (Abbot

Diagnostics, Abbot Park, IL). The Leucocount kit from BD (BD Biosciences, San Jose, CA) was used for residual WBC analysis, with a BD FACSCanto II cytometer.

Plasma hemoglobin was analyzed with the HemoCue Plasma/Low Hb photometer (HemoCue AB, Angelholm, Sweden) to calculate hemolysis.

Lactate and blood gas analysis was performed on whole blood samples with an ABL 800 FLEX (Radiometer Medical ApS, Brøndshøj, Denmark).

Glucose, potassium, and Factor VIII were analyzed with the Cobas 8000 ISE module (Roche Diagnostics GmbH, Rotkreuz, Switzerland). FVIII and fibrinogen levels were analyzed with the STA-R Evolution/STA-R Max platform (Stago S.A.S., Asnieres-sur-Seine, Paris, France).

All plasma samples were prepared by centrifugation at 1850 G for 10 min in RT.

2.8 | Statistical analyses

No formal hypothesis testing was performed. Sample sizes of 40 evaluable WB units in the in vitro study and 12 evaluable subjects in the in vivo study were prespecified without consideration of statistical power.

In the in vitro study (Figure 1), the differences between test and control in vitro characteristics were calculated using a standard *t*-test. In vitro analyses were performed on all evaluable WB units (i.e., those that met specified weight and volume criteria). Graphic data presentations were generated using GraphPad Prism 6.04 software (GraphPad Software, San Diego, CA). Safety analyses were performed using the entire study population.

In the in vivo study, relative recovery and survival were analyzed with a one-sample *t*-test, and the lower one-sided 95% confidence limit was provided to compare against the US Food and Drug Administration (FDA) criteria for in vivo platelet recovery and survival of ≥66% and ≥58%, respectively.[15] Analyses were conducted using SAS (v.9.3, SAS Institute, Cary, NC).

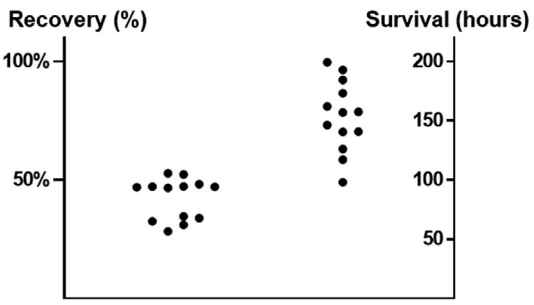

FIGURE 3 In vivo recovery and survival of Mirasol-treated platelets stored for 24 h at room temperature

The in vivo population comprised all enrolled subjects with valid data, as described in Figure 3. The BEST-population, whose platelets were treated according to the BEST Collaborative procedure for radiolabeled platelet studies,[16] comprised the subjects who had one blood sample collected on Day 1; five to seven samples from Days 2 through 8; and one sample from Days 10 through 12 for a comparison of sampling time points.

3 | RESULTS

3.1 | Subject disposition and demographics

3.1.1 | In vitro study

Forty-nine healthy volunteer blood donors participated in the in vitro study between September and December 2014. Forty WB units were evaluable for inclusion in the in vitro analyses, with 20 units in Arm 1 and 20 units in Arm 2 (10 Mirasol-treated and 10 untreated per arm).

Nine WB units were ineligible for in vitro analyses for incomplete WB donation due to inadequate blood flow ($n = 2$), tubing leakage ($n = 1$), low hemoglobin level ($n = 1$); incorrect sample process for adenosine triphosphate ($n = 2$) or clinical laboratory ($n = 1$) analysis; lipemic blood samples ($n = 2$).

Limited demographic information was collected. All female subjects were either not of child-bearing potential (95.9%) or of child-bearing potential with negative pregnancy tests (4.1%).

3.1.2 | In vivo study

Twenty-two healthy volunteer blood donors participated in the in vivo study between April and July 2015. Twenty subjects (90.9%) completed study procedures, including autologous reinfusion of radiolabeled untreated fresh and Mirasol-treated stored platelets. Two subjects (9.1%) discontinued prematurely for an AE of cold/influenza ($n = 1$) and for an incomplete WB donation ($n = 1$).

Data from the first eight subjects were irreparably confounded due to a calibration error of the gamma counter, resulting in overlapping of ^{111}Indium and ^{51}Chromium signals. The data were not evaluable for recovery and survival endpoints as it was impossible to reanalyze the samples. These subjects were only included in the Safety Population ($N = 22$).

Subject demographics are presented in Table 1. A majority of subjects were female (71.4%) and all were Caucasian. The mean age was 40.4 years, the mean

TABLE 1 Summary of in vitro characteristics in whole blood (in vitro study)

	Post-collection (mean ± SD)	Post-treatment (mean ± SD)	24 h (end of storage) (mean ± SD)
PLTi count ($\times 10^9$ cells/L)			
PRT-treated (Arm 1)	153 ± 43	105 ± 24	127 ± 29
PRT-untreated (Arm 1)	160 ± 37	NA	187 ± 48
PRT-treated (Arm 2)	138 ± 57	118 ± 53	134 ± 71
PRT-untreated (Arm 2)	126 ± 36	NA	165 ± 30
RBC hemolysis (%)			
PRT-treated (Arm 1)	0.07 ± 0.03	0.08 ± 0.04	0.11 ± 0.03
PRT-untreated (Arm 1)	0.05 ± 0.03	NA	0.06 ± 0.03
PRT-treated (Arm 2)	0.05 ± 0.03	0.07 ± 0.02	0.10 ± 0.03
PRT-untreated (Arm 2)	0.03 ± 0.03	NA	0.08 ± 0.03
WBC count ($\times 10^9$ cells/L)			
PRT-treated (Arm 1)	5.0 ± 1.5	4.6 ± 1.3	4.3 ± 1.1
PRT-untreated (Arm 1)	4.3 ± 0.9	NA	4.2 ± 1.0
PRT-treated (Arm 2)	<0.2[a]	<0.4 ± 0.3	<0.2
PRT-untreated (Arm 2)	<0.3 ± 0.2	NA	<0.2
Glucose (mmol/L)			
PRT-treated (Arm 1)	21.1 ± 1.4	19.1 ± 1.3	15.4 ± 1.1
PRT-untreated (Arm 1)	21.3 ± 1.0	NA	17.3 ± 0.7
PRT-treated (Arm 2)	19.8 ± 0.9	17.9 ± 1.0	14.6 ± 1.1
PRT-untreated (Arm 2)	20.3 ± 1.0	NA	16.5 ± 1.0
Potassium (mmol/L)			
PRT-treated (Arm 1)	3.2 ± 0.2	3.2 ± 0.2	6.3 ± 0.7
PRT-untreated (Arm 1)	3.3 ± 0.2	NA	4.5 ± 0.3
PRT-treated (Arm 2)	3.1 ± 0.2	3.1 ± 0.1	5.8 ± 0.7
PRT-untreated (Arm 2)	3.3 ± 0.2	NA	4.5 ± 0.4
pH			
PRT-treated (Arm 1)	7.008 ± 0.021	7.015 ± 0.022	6.806 ± 0.030
PRT-untreated (Arm 1)	7.002 ± 0.019	NA	6.810 ± 0.028
PRT-treated (Arm 2)	7.062 ± 0.022	7.062 ± 0.020	6.849 ± 0.030
PRT-untreated (Arm 2)	7.041 ± 0.025	NA	6.850 ± 0.023
Lactate (mmol/L)			
PRT-treated (Arm 1)	2.0 ± 0.6	2.6 ± 0.5	9.1 ± 1.0
PRT-untreated (Arm 1)	2.4 ± 0.5	NA	9.7 ± 1.2
PRT-treated (Arm 2)	2.1 ± 0.5	2.5 ± 0.5	8.6 ± 0.9
PRT-untreated (Arm 2)	2.7 ± 0.6	NA	9.5 ± 1.1
Fibrinogen (g/L)			
PRT-treated (Arm 1)	3.2 ± 0.9	2.0 ± 0.5	2.3 ± 0.6
PRT-untreated (Arm 1)	3.0 ± 0.6	NA	3.0 ± 0.5
PRT-treated (Arm 2)	2.9 ± 0.6	2.3 ± 0.5	2.2 ± 0.4
PRT-untreated (Arm 2)	3.1 ± 1.0	NA	3.1 ± 0.9
FVIII (%)			
PRT-treated (Arm 1)	106.7 ± 13.6	73.6 ± 25.7	48.5 ± 20.5
PRT-untreated (Arm 1)	124.1 ± 16.7	NA	97.1 ± 23.6

TABLE 1 (Continued)

	Post-collection (mean ± SD)	Post-treatment (mean ± SD)	24 h (end of storage) (mean ± SD)
PRT-treated (Arm 2)	98.4 ± 31.0	63.0 ± 23.0	40.2 ± 13.9
PRT-untreated (Arm 2)	112.0 ± 16.1	NA	101.2 ± 27.9

Abbreviations: L, liter(s); PLTi, Platelet (impedance measurement); PRT, pathogen reduction technology; RBC, red blood cell; SD, standard deviation; WBC, white blood cell.

[a]All units for which a value <0.2 was reported were mathematically averaged as 0.2, and the mean value is reported as < the reported number.

height was 172.6 cm, and the mean weight was 78.7 kg. Blood types were A (42.9%), B (7.1%), and O (50.0%); all subjects were Rh+.

3.2 | Pathogen reduction procedure

No Mirasol PRT System device malfunctions were reported in either study, and no samples tested positive for bacterial contamination.

3.2.1 | In vitro study

The mean weight of blood collected from completed donations was just above the protocol-specified range for Arm 1 (mean weight 495.0 ± 3.7 g; target range 488–494 g) and within the range for Arm 2 (mean weight 527.2 ± 2.9 g; target range 523–530 g); excess volume was diverted to post-collection samples and was not illuminated/stored. The mean time between collection and transfer to the illumination bag was 2.4 h in Arm 1 and 1.8 h in Arm 2.

The addition of riboflavin diluted the Mirasol-treated WB units, resulting in slight decreases in hematocrit, WBC count, RBC count, platelet count, and fibrinogen between post-collection and post-illumination. While many of these values increased between post-illumination and end of storage (24 h), most mean values in the Mirasol-treated units remained slightly lower than untreated units at 24 h in both arms.

The results for samples of platelets, plasma, and RBCs from Mirasol-treated WB units are presented in Table 1.

As Arm 2 employed leukoreduction, WBC counts in Arm 2 were lower for both untreated and Mirasol-treated units compared with Arm 1. No effects of leukoreduction in Arm 2 were observed for hemoglobin, potassium, RBC count, RBC mean cell volume, metabolic platelet function, or fibrinogen compared with Arm 1 for either Mirasol-treated or untreated units, as 24-h values were similar between both sets of untreated units and both sets of Mirasol-treated units. The volume lost during filtration is almost 50 ml and should be taken into account when choosing collection sets. The mean platelet yield for all units was above FDA recommendation ($\geq 3.0 \times 10^{11}$).

Levels of RBC hemolysis were well below published guidelines for the Council of Europe (<0.8%) and AABB (1%) for both untreated and Mirasol-treated units across both study arms.

Plasma potassium levels increased in all units, with Mirasol-treated units demonstrating greater increase in both arms (Table 1). Plasma levels of glucose decreased and lactate increased over the storage period. Corresponding to increased lactate, the pH of both Mirasol-treated and untreated units decreased during storage but remained above the FDA recommendation for platelets (pH ≥ 6.3).

3.2.2 | In vivo study

No device deficiencies were reported and all Mirasol treatments were considered successful. The mean mass of the Mirasol-treated WB units post-collection was 492.2 ± 2.3 g, the mean mass of the Illumination Bag following addition of riboflavin was 636.4 ± 2.8 g, and mean hematocrit prior to illumination was 35.2% ± 2.01%. The mean time between collection and illumination was 1.92 ± 0.158 h, the mean time between illumination and placement in storage was 13.2 ± 4.4 min, the mean illumination time was 46.2 ± 3.4 min, and the mean storage time was 23.37 ± 0.264 h (range 23.0–23.9 h).

The addition of riboflavin to the WB units prior to illumination resulted in sample dilution and subsequent decreases in mean hematocrit, hemoglobin, WBC count, and platelet count from post-collection to post-illumination, but many of these mean values returned to the normal range following 24-h storage.

For the platelet recovery study, Mirasol-treated stored mean platelet recovery (42.19% ± 8.68%) was 85.4% of the untreated fresh control (one-sided 95% lower confidence limit 74.91%). Mean platelet survival (153.4.1 ± 41.9 h [approximately 6.5 days]) was 82% of the untreated fresh control (one-sided 95% lower confidence limit 77.3).

3.3 | Safety

Ten subjects (45.5%) reported 13 TEAEs on study, all of which were mild in severity. Events reported for >1 subject were hematoma (22.7%) and anxiety (9.1%). No TEAEs were considered related to the device. Ten TEAEs reported for eight subjects were considered related to the procedure. One subject discontinued the study early for an AE of cold/influenza. Nine TEAEs resolved without sequelae, with four TEAEs ongoing at the end of the study (three hematomas and one blister on both feet). No SAEs, deaths, or UADEs were reported, and no clinically significant changes or trends in vital sign measurements were observed before, during, or for 30 min after reinfusion. No clinically relevant abnormalities or trends in clinical laboratory parameters were observed at Day 0 or Day 1.

4 | DISCUSSION

The in vitro characteristics of PRT-treated WB units during and following 24 h of storage at room temperature were consistent between the in vitro and in vivo studies and aligned with previously reported results from WB that had been similarly treated and stored. As shown in Table 1, the PRT treatment resulted in several biochemical and metabolic changes. The potassium leakage increased significantly but the hemolysis remained nearly constant throughout the storage period—and the hemolysis was below the required limit[17,18] with solid margins. The mean glucose concentrations decreased and mean lactate concentrations increased attributed to upregulation of platelet metabolism following Mirasol treatment, in accordance with observations from other studies. Likely related to the increased lactate, pH decreased during storage while pO_2 decreased and pCO_2 correspondingly increased. These results are completely in line with published results from testing of both Mirasol-treated platelet concentrates and treated whole blood.[7,19-23]

In connection with PRT, the need for additional WBC removal by filtration has been debated. The laboratory testing performed in this study (Table 1) indicates that there is no substantial effect of WBC reduction on the platelet parameters tested. The clinical relevance is however linked to prevention of human leukocyte antigen (HLA)-alloimmunization and TA-GvHD. There is evidence that Mirasol PRT is very effective to prevent TA-GvHD,[13,24] and promising concerning prevention of HLA-immunization.[25-28]

The critical question is if the in vitro negative effects significantly affect function—and if the benefits of PRT outweigh these disadvantages. Our results show that the survival and recovery of platelets stored at room temperature for 24 h after Mirasol treatment are fulfilling the international requirements[15,16,29] and the platelet recovery and survival is also comparable to reports from other studies, not using PRT-platelets.[30-32]

This study is designed for short-time whole blood storage under suboptimal conditions, as this will be the reality when there is an urgent need for transfusion in settings without access to blood bank facilities. For general civilian purposes, long-term cold WB storage is the preferred alternative[1,33-35] and studies must be undertaken to elaborate if this is possible.

The benefits of PRT are maximal under constrained circumstances with high infection rate in the donor population without access to advanced testing for infectious diseases. Both clinical and in vitro studies indicate good and consistent effects after use of the Mirasol PRT.[36-48]

In conclusion, in vitro testing of Mirasol-treated whole blood stored for 24 h at room temperature—both with and without WBC filtration—document that the quality of the whole blood unit is suitable for transfusion. Recovery and survival studies of platelets isolated from these whole blood units prove well-preserved platelet quality.

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CONFLICT OF INTEREST

LH was employed at Terumo BCT (Sponsor) during the time when the studies were designed and executed. Sponsor was awarded the funding from U.S. Department of Defense; award number W81XWH-12-2-0135. All other authors have disclosed no conflicts of interest.

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