

Pathogen Inactivation and Function of Platelets and Red Cells

Dr. Dana Devine

Professor of Pathology & Laboratory Medicine

UBC Centre for Blood Research

Chief Medical and Scientific Officer, Canadian Blood Services



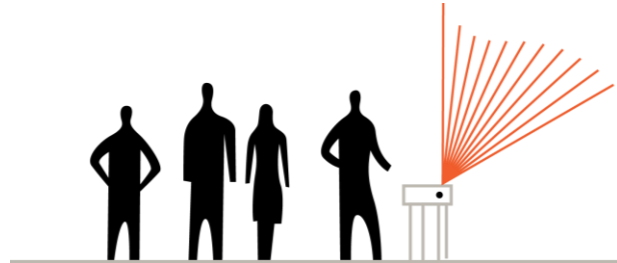
Disclosures

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Member of the medical advisory committee of Fresenius Kabi Deutschland GmbH

Overview

- Laboratory investigations of the effect of PI on platelet and RBC function
- Clinical assessment of platelet and RBC function after PI
- Where do we go from here?



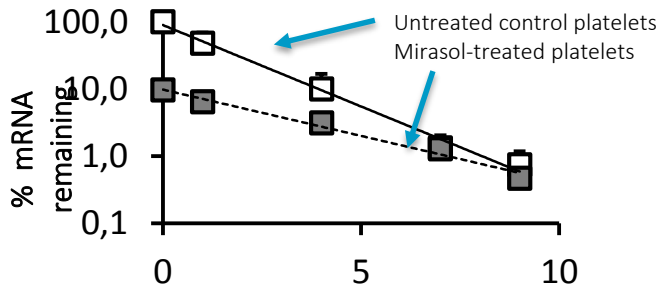
PI technologies



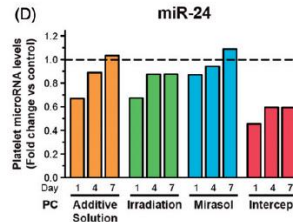
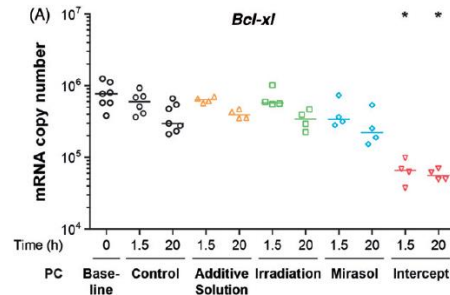
- Effective against most transfusion transmissible agents
- Dose must balance killing pathogens with killing the transfusion cells
- Risk mitigation must consider both infectious risks and risks to product efficacy

Laboratory Assessment of Platelet and RBC Function

Abundant laboratory data indicate that all PI treatments damage platelets



Klein-Bosgoed C et al. *Transfusion*, 2016;56:2286-95.



Osman A et al. *Platelets* 2015; 26:154-63

Function of Platelets After PI

Numerous studies have demonstrated increased activation with Intercept treatment

Vox Sanguinis

Labile Blood Components and Blood Donation

Vox Sang 2000;79:206-214

Received: July 6, 1999
Revised manuscript received: May 17, 2000
Accepted: May 23, 2000

Functional Characteristics of S-59 Photochemically Treated Platelet Concentrates Derived from Buffy Coats

D.J. van Rhenen^{a,b} J. Vermeij^a V. Mayaudon^c C. Hind^c L. Lin^d
L. Corash^{d,e}

^aBloodbank, Rotterdam; ^bDepartment of Haematology, University Hospital, Rotterdam, The Netherlands;

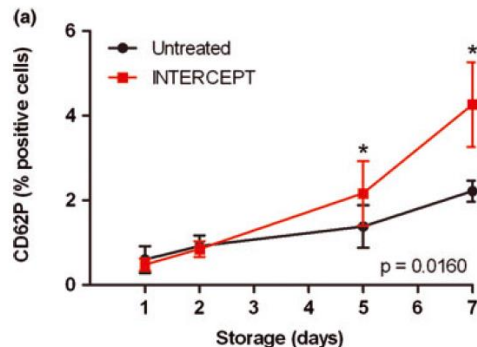
^cBaxter R and D Europe SC, Nivelles, Belgium; ^dCerus Corporation, Concord, Calif., and

^eDepartment of Laboratory Medicine, University of California, San Francisco, Calif., USA

BLOOD COMPONENTS

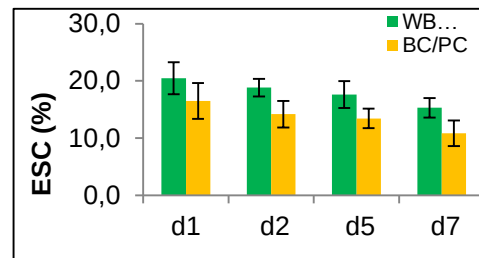
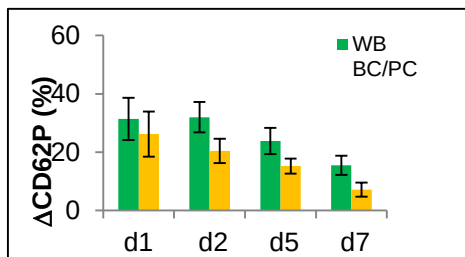
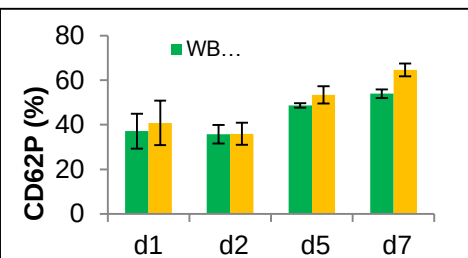
Functional characteristics of buffy-coat PLTs photochemically treated with amotosalen-HCl for pathogen inactivation

Susanne M. Picker, Relindis Speer, and Birgit S. Gathof



Johnson L et al. Transfus Med 2013; 23:121

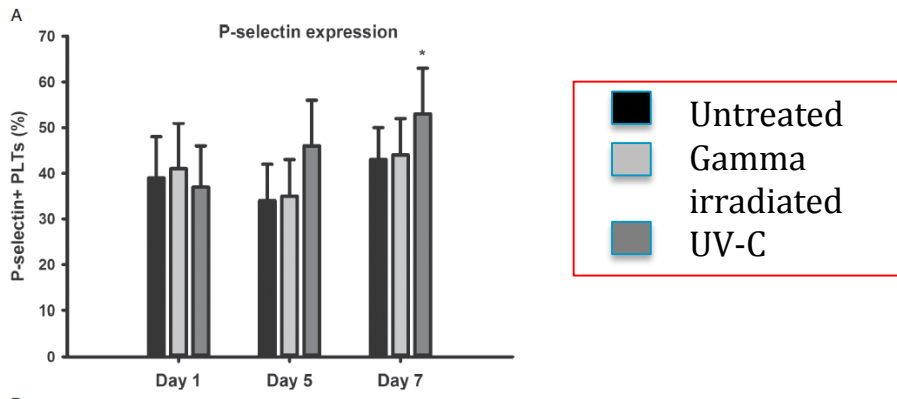
Mirasol treatment related damage to platelets can be modulated by inactivation approach



Platelet concentrates derived from Mirasol-treated whole blood had better quality parameters than Mirasol-treated platelet concentrates on day 7 of storage.

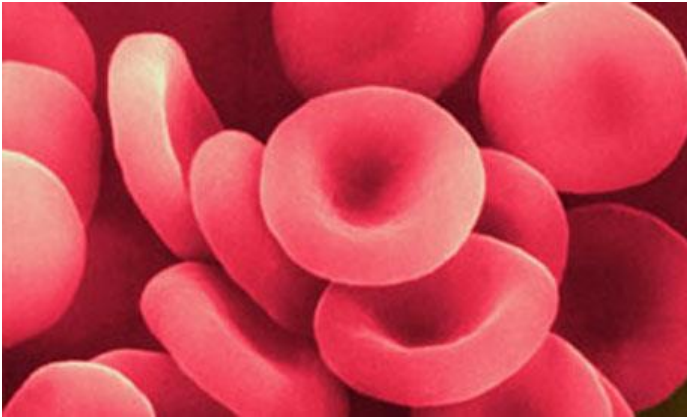
Schubert P *et al.* Transfusion 2015;55:815–823

UV-C (Theraflex) also accelerates storage lesions



Tynngard N et al. Transfusion 2015; 55:1169

Approaches to PI for RBC vary more than platelet methods



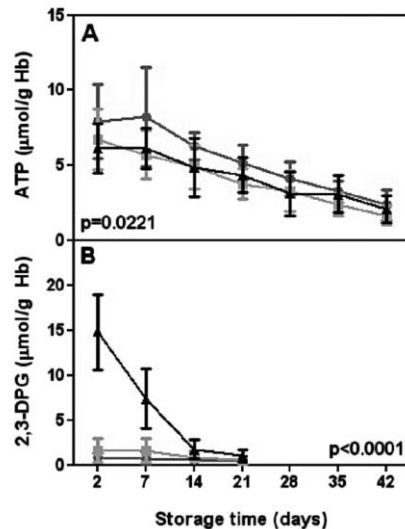
- PI treatment protocols differ for Mirasol and Intercept and this is reflected in final product.
- Due to wash step (exchange), Intercept-treated RBC have lower hemolysis and higher ATP than control RBCs. (Wiltshire M et al. Transfus Med. 2016;26:208-14)

Intercept for RBC (S-303) causes only modest changes

BLOOD COMPONENTS

Red blood cell in vitro quality and function is maintained after
S-303 pathogen inactivation treatment

Kelly M. Winter,¹ Lacey Johnson,¹ Matthew Kwok,¹ Diana Vidovic,¹ Ryan A. Hyland,¹ Nina Muftic,²
Anna Erickson,² and Denese C. Marks¹



RBC quality is negatively affected by Mirasol treatment of WB

Assay	Week 0		Week 1		Week 3		Week 6	
	RCC	RCC ^{PI-WB}	RCC	RCC ^{PI-WB}	RCC	RCC ^{PI-WB}	RCC	RCC ^{PI-WB}
Hemolysis (%)	0.04 ± 0.01	0.05 ± 0.01	0.06 ± 0.01	*	0.40 ± 0.01	0.12 ± 0.03	0.47 ± 0.06	0.27 ± 0.06
Potassium (mM)	1.1 ± 0.2	*	1.7 ± 0.5	*	27.1 ± 1.3	20.1 ± 0.9	35.4 ± 1.3	28.4 ± 1.4
ATP (μmol/g Hb)	4.25 ± 0.36	*	4.14 ± 0.31	*	4.15 ± 0.32	3.81 ± 0.29	3.23 ± 0.28	2.67 ± 0.49
MP count (× μL ⁻¹ SN)	749 ± 220		765 ± 220		838 ± 318	2227 ± 929	1759 ± 512	19900 ± 4819

Pool and split model: RCC prepared from untreated vs. Mirasol treated whole blood.

Schubert et al. Transfusion 2015; 55:815-23

Clinical Assessment of Platelet and RBC Function

Upon careful assessment, effects of PI on platelet transfusions can be seen

TABLE 3. Results of the two Phase III clinical trials: EuroSPRITE and SPRINT

	EuroSPRITE (pool PLTs)		SPRINT (apheresis PLTs)	
	Test units	Control units	Test units	Control units
Number of enrolled patients	103		645	
Observation period (days)	56		28	
Mean PLT dose ($\times 10^{11}$)	3.7*	4.0	3.9*	4.3
Total PLT dose ($\times 10^{11}$)	22.3	21.2	29.4*	24.1
Mean number of transfusions	7.5	5.6	8.4*	6.2
Transfusion interval (days)	3.0	3.4	1.9*	2.4
Mean CI ($\times 10^9/L$)				
1-hr	28†	36	12*	34
24-hr	16†	25	13*	22
Mean CCI ($\times 10^3$)				
1-hr	13.0	14.9	11.1*	16.0
24-hr	7.5*	10.6	6.4*	10.1

* $p < 0.001$.

† No longer significant after longitudinal regression.

But do these differences matter?

Experience with routine use in European centres would suggest that they do not.

Perhaps effects are masked by transfusion practice (high dosing, scheduling).

RBCs produced from Mirasol treated whole blood have a shortened shelf-life

BLOOD COMPONENTS

**Red blood cells derived from whole blood treated with
riboflavin and ultraviolet light maintain adequate
survival in vivo after 21 days of storage**

*Jose A. Cancelas,¹ Sherrill J. Slichter,^{2,3} Neeta Rugg,¹ P. Gayle Pratt,¹ Shawnagay Nestheide,¹
Jill Corson,² Esther Pellham,² Marty Huntington,⁴ and Raymond P. Goodrich⁵*

TRANSFUSION 2017;57;1218–1225

Intercept treated RBCs are not exposed to UV and have near normal storage time

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The International Journal of Transfusion Medicine

ISBT International Society
of Blood Transfusion

Vox Sanguinis (2017) 112, 210–218

ORIGINAL PAPER

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DOI: 10.1111/vox.12500

Red blood cell concentrates treated with the amustaline (S-303) pathogen reduction system and stored for 35 days retain post-transfusion viability: results of a two-centre study

J. A. Ancelas,¹ J. L. Gottschall,² N. Rugg,¹ S. Graminske,² M. A. Schott,³ A. North,³ N. Huang,³ N. Muftic,³ A. Erickson,³ S. Rico³ & L. Corash³

¹Hoxworth Blood Center, Cincinnati, OH, USA

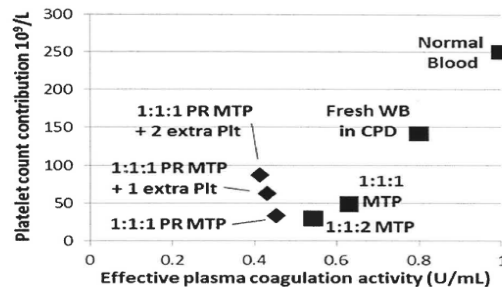
²BloodCenter of Wisconsin, Milwaukee, WI, USA

³Cerus Corporation, Concord, CA, USA

Are concerns over use of PI-products in trauma warranted?

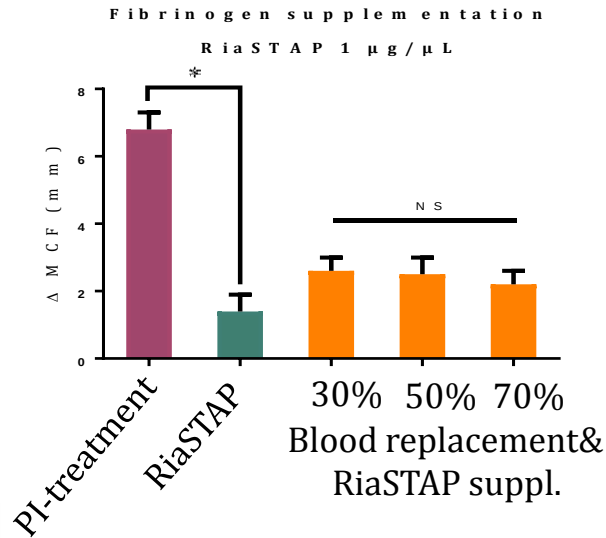
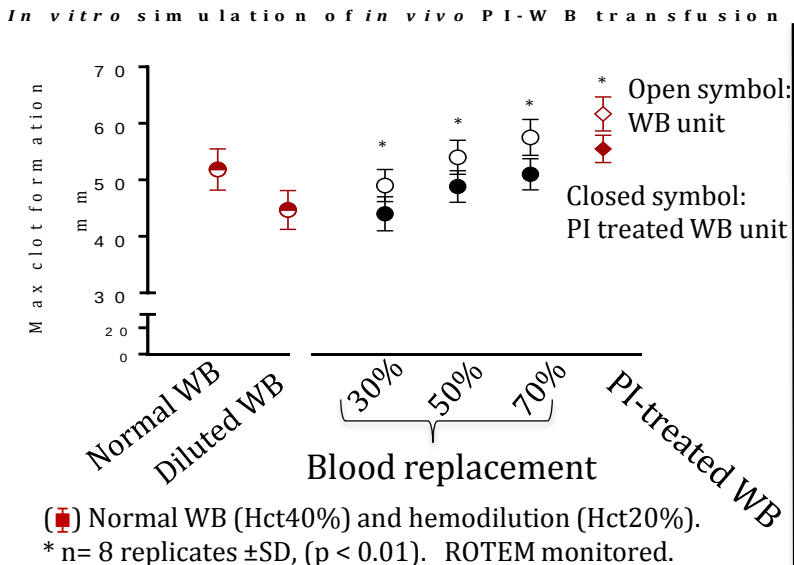
Beware of Pathogen Reduced blood products with reduced potency

Losses of clotting activity associated with the manipulation of blood products



Hess JR, et al., *Transfusion*, 2016; 56:1236-41

Pathogen Inactivation of Blood Products



Arbaeen A. et al ISBT Copenhagen 2017

Perhaps not....

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of Blood Transfusion

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DOI: 10.1111/vox.12489

Patient outcomes and amotosalen/UVA-treated platelet utilization in massively transfused patients

W. Nussbaumer,¹ M. Amato,¹ H. Schennach,¹ M. Astl,¹ C. Y. Chen,² J.-S. Lin,² L. Corash² & R. J. Benjamin²

¹Central Institute for Blood Transfusion and Immunology, Medical University Hospital Innsbruck, Innsbruck, Austria

²Cerus Corporation, Concord, CA, USA

We need to see publications of the recent clinical studies and await the results of new studies!

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ISBT International Society
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DOI: 10.1111/vox.12287

A prospective, active haemovigilance study with combined cohort analysis of 19 175 transfusions of platelet components prepared with amotosalen–UVA photochemical treatment

F. Knutson,¹ J. Osselaer,² L. Picirelli,³ M. Lozano,⁴ J. Cid,⁴ R. Tardivel,⁵ O. Garraud,⁶ T. Hervig,⁷ D. Domanovic,⁸ M. Cukjati,⁹ S. Gudmundson,⁹ I. B. Hjalmarsson,⁹ A. Castrillo,¹⁰ R. Gonzalez,¹⁰ D. Brihante,¹¹ M. Santos,¹¹ P. Schlenke,¹² A. Elliott,¹³ J.-S. Lin,¹³ D. Tappe,¹³ A. Stassinopoulos,¹³ J. Green¹³ & L. Corash¹³

Where Do We Go From Here?



Gaps to Fill Using Research Effort

- Can we develop strategies to minimize damage to platelets and RBCs?
 - Different additive solutions or storage conditions?
- Will the use of multiple types of PI-treated products in trauma really create a problem?
- How do we determine which in vitro parameters should be used for product quality assurance? DAMPS?

Thank you for your attention

