

Dried Blood Products



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Disclosures

- **CSL Behring - Consultant and grant recipient**
- **Haemonetics - Consultant and grant recipient**
- **Cellphire – Grant recipient**
- **Octapharma – Consultant**
- **Velico – Have consulted**

Introduction

- Dried plasma
- Dried platelets
- Platelet extracellular vesicles
- Dried whole blood?





ABO Titer Label
Use this label to identify the ABO titer of the donor's blood. The titer is the number of units of donor's blood that will react with the recipient's blood.

WVLT-07048784
1/1/2018
1/1/2018
1/1/2018
1/1/2018

Lyophilized Plasma



Used for resuscitation
of all Trauma and
Burn Patients

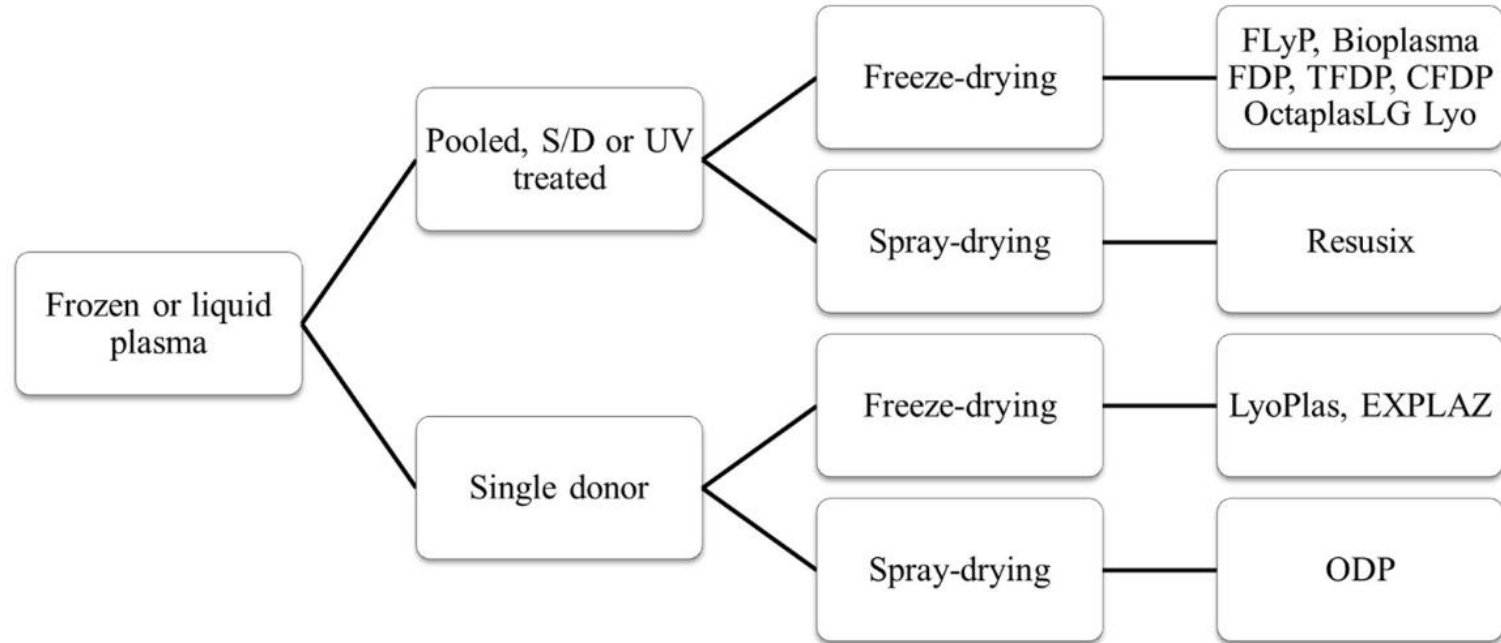


WWII

Dried Plasma

- Logistically superior and available
- Can be stored in massive quantities
- Can be single or multiple donor
- Long shelf – life
- Can be pathogen/Ag/Ab reduced

Dried Plasma Characteristics




German LyoPlas

- German LyoPlas
 - Single donor (Blood type compatibility)
 - Used in Afghanistan by German Army
 - Stored up to 15 months
 - 200,000 TFNs – 0.023% major complications similar to FFP



ORIGINAL ARTICLE

Pre-hospital freeze-dried plasma for critical bleeding after trauma: A pilot randomized controlled trial

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Marc Maegele PhD^{6,7} | Russell L. Gruen PhD⁸ | Olivia Bradley BEH⁴ | Erica M. Wood
MBBS^{2,9} | Zoe K. McQuilten PhD^{2,9} | Mark Fitzgerald MD^{10,11,12} | Toby St. Clair BEH^{3,4} |
Andrew Webb MSc¹³ | David Anderson MBChB^{3,4,5} | Michael C. Reade DPhil^{2,14,15,16}



Methods

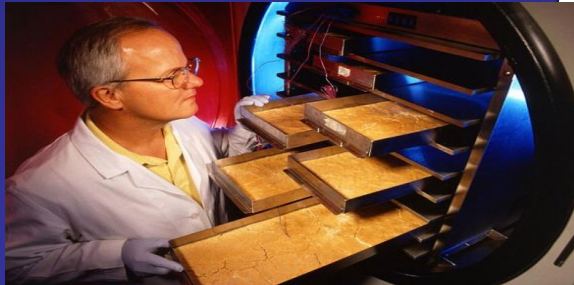
- Air transport Victoria, Australia
- Unblinded randomized trial
- After 1st unit RBCs
 - 2 units Lyoplas
 - Routine care

Results

	Freeze-dried plasma (n=9) ^a	Standard care (n=11) ^a	Relative risk or median difference (95% CI)
Mortality (censored at 24h)	1 (11.1)	5 (45.4)	0.24 (0.03 to 1.73)
Mortality (censored at hospital discharge)	3 (33.3)	5 (45.4)	0.73 (0.24 to 2.27)
ICU admission	6 (66.7)	6 (54.5)	1.2 (0.6 to 2.5)
Hemoglobin ^b (g/L)	101.5 (83 to 125)	142.5 (126 to 155)	-41.0 (-82.0 to 6.0)
Platelet count ^b (×10 ⁹ /L)	206 (148.5 to 295.5)	210.5 (156 to 296)	-4.5 (-318.1 to 300.1)
Fibrinogen ^b (g/L)	2.0 (1.8 to 2.6)	2.3 (1.9 to 2.3)	-0.3 (-2.6 to 2.4)
INR ^b	1.3 (1.2 to 1.4)	1.3 (1.2 to 1.5)	0 (-62.9 to 62.9)
≤1.3	5 (62.5)	5 (62.5)	1.0 (0.28 to 3.54)
>1.3	3 (37.5)	3 (37.5)	

French Flyp

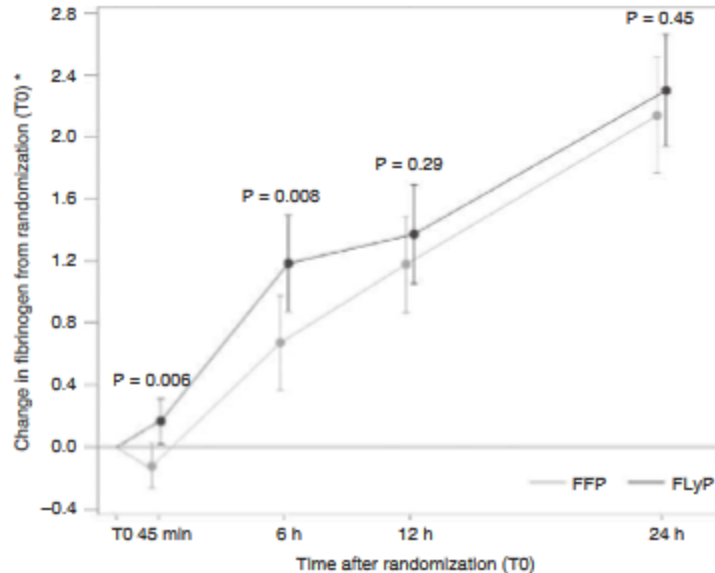
- Up to 11 donors/unit (Universal)
- Pathogen reduced
- Stored up to 24 months
- Available to US SF on IRB protocol
- 1000s TFNs with no major adverse events



Randomized Trial FLYP

- Open label randomized trial
- 48 trauma patients requiring emergent transfusion
- Exclusion criteria
 - Received blood prior to randomization
 - Moribund

Outcomes FLYP Trial



	FLyP		FFP		P-value
	No.	Median [IQR]	No.	Median [IQR]	
Fibrinogen concentrates, 1.5-g doses	23	2 [0-3]	24	3 [2-4]	0.052
Crystalloids, 500-mL doses	21	3 [2-4]	22	4 [3-5]	0.28
Colloids, 500-mL doses	22	1.5 [1-2]	23	2 [1-4]	0.12
Platelet concentrate, units	23	0 [0-1]	24	1 [0-2]	0.14
Red blood cell, units	23	6 [4-10]	24	7 [6-11.5]	0.12
Plasma, units	23	4 [4-8]	24	5.5 [4-9]	0.27

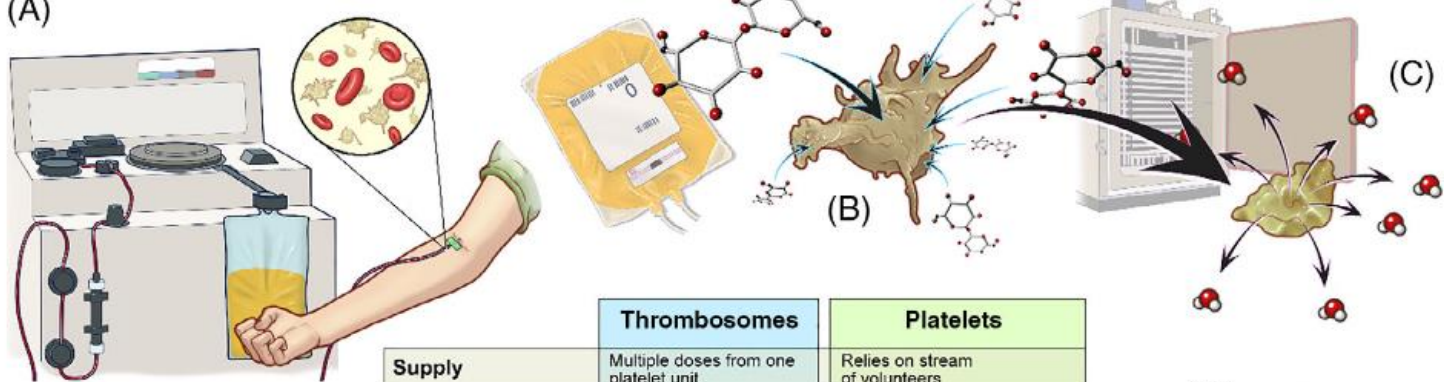
Garrigue et al *Journal of Thrombosis and Haemostasis* 2017;16:1 – 9.

S. African Bioplasma FDP

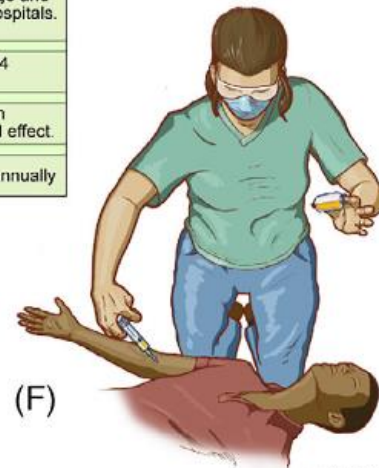
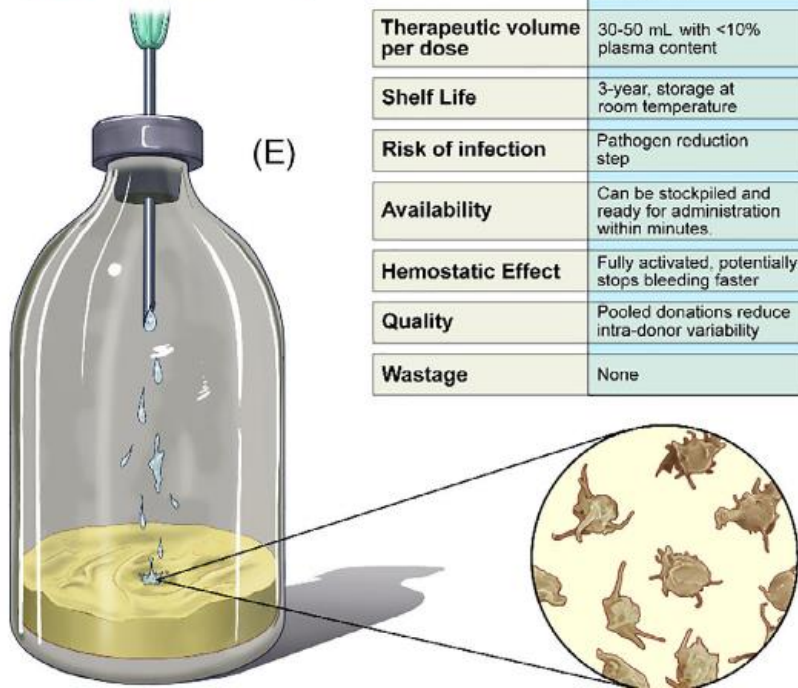
- Pooled from up to 1500 donors
- Donors screened and tested
- Pathogen inactivated
- Used throughout S. Africa and surrounding nations

Thrombosomes

- Freeze dried group – O platelets
- Stable for 3 years at room temp
 - Trehalose stabilized
- Pooled from up to 10 donors
- Heat treated for viral infections
- Cultured prior to use for bacteria
- Rehydrated in sterile water



	Thrombosomes	Platelets
Supply	Multiple doses from one platelet unit	Relies on stream of volunteers
Therapeutic volume per dose	30-50 mL with <10% plasma content	~250 mL with 100% plasma content
Shelf Life	3-year, storage at room temperature	2.5 day average hospital supply
Risk of infection	Pathogen reduction step	1:1000 to 1:2500 units are bacterially contaminated
Availability	Can be stockpiled and ready for administration within minutes.	Requires special storage and not available in rural hospitals.
Hemostatic Effect	Fully activated, potentially stops bleeding faster	Not fully activated for 24 h
Quality	Pooled donations reduce intra-donor variability	High variability between donors, variable clinical effect.
Wastage	None	344,000 units wasted annually



Additional Potential Advantages

- 15% of collected platelets wasted
 - \$178,000,000 in 2017
- Rapid reconstitution, 2 – 3 minutes
- Lower plasma content
- Not thrombogenic or immunogenic
 - Rabbits, swine, canine, NHPs

Ohanian et al. *AJH* 2021;97:256 – 266.

Phase I Clinical Study

- 24 hematologic malignancy patients
- Platelet counts 5000 – 70,000/uL
- 9.45×10^7 – 3.78×10^8 particles/kg
- No identified adverse events
- WHO bleeding scores stabilized or improved

Ohanian et al. *AJH* 2021;97:256 – 266.

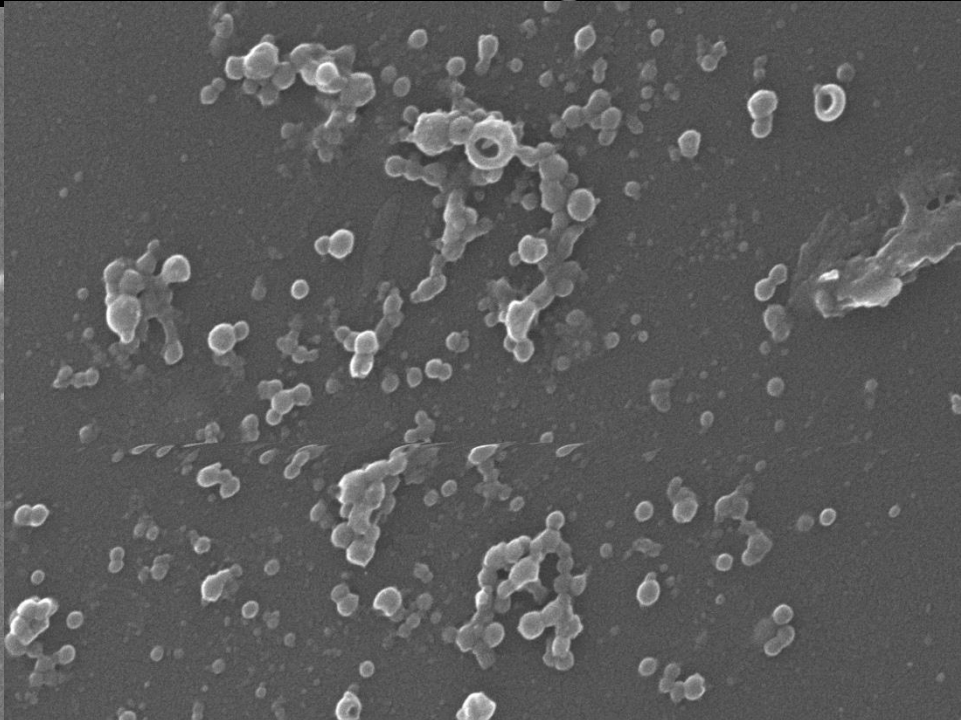
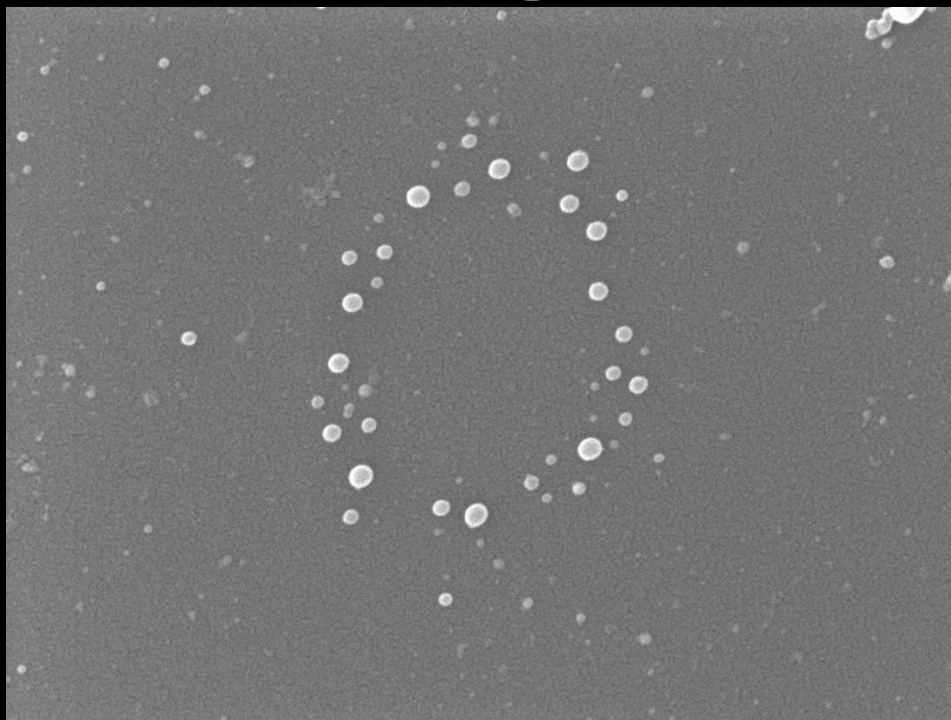
Additional Trials

- **Phase 2 trial**
 - Bleeding thrombocytopenic patients
- **Phase 2a trial**
 - Aortic dissection patients undergoing operations

Platelet Extracellular Vesicles

- Particles secreted from platelets
- Express surface receptors
- Range in size from 10 – 1000nm
- Procoagulant GPIIb/IIIa, TF, PS receptors
- Long shelf life from -80C to 40C
- Rehydrated in 10cc
- Known for close to 50 years

Scanning Electron Micrographs



SEM HV: 10.0 kV	WD: 4.02 mm		VEGA3 TESCAN
SEM MAG: 100 kx	Det: SE	1 μm	<i>NanoCraft</i>
View field: 5.55 μm	Date(m/d/y): 10/19/22		

SEM HV: 20.0 kV	WD: 4.00 mm		VEGA3 TESCAN
SEM MAG: 100 kx	Det: SE	1 μm	<i>NanoCraft</i>
View field: 5.55 μm	Date(m/d/y): 10/19/22		

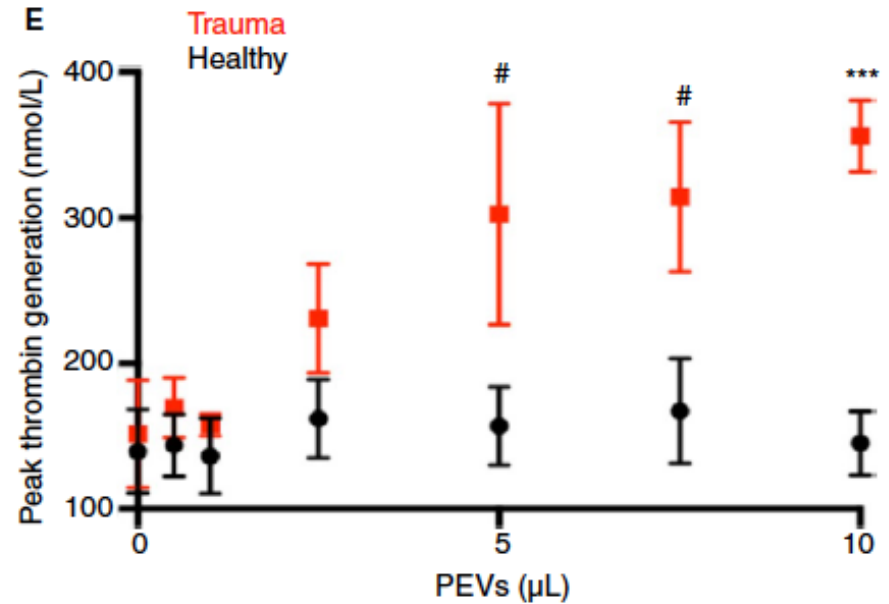
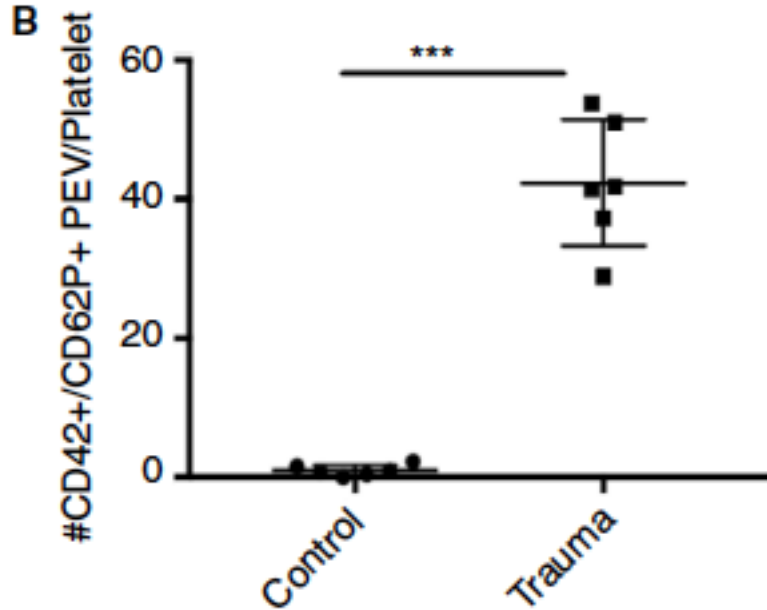
Potential Advantages

- Lyophilized
- Stable for 2 – 4 years
- Pasteurized – reduced bacterial load
- Reduced expression HLA antigens
- May be effective in refractory patients
- No RBCs or WBCs

Available Studies

- Mice, rats, rabbits, swine
- Phase I
 - Infusion 2 – 6 mg/kg in normal people
 - People given ASA
- Phase II trials
 - 31 Pts, mucosal bleeding and Plts < 50
 - Platelets or 2 – 6 mg/kg of PEVs

Human Derived PEVs

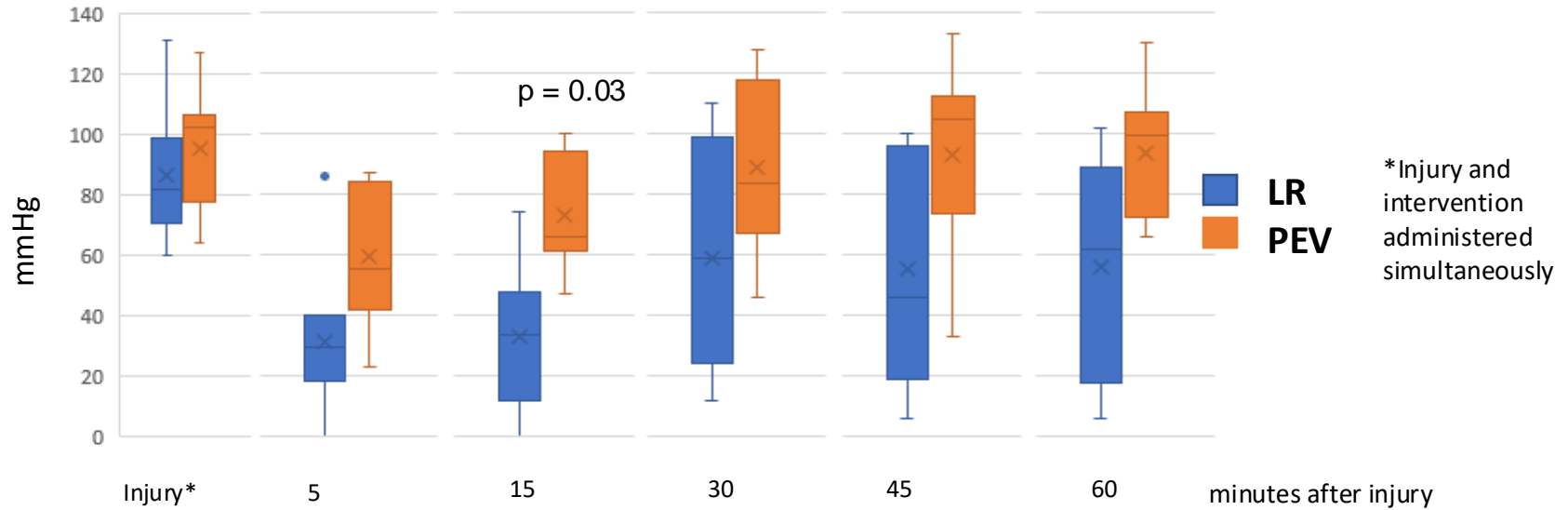


Dyer MR. JTH 2019;17:1733 - 1745.



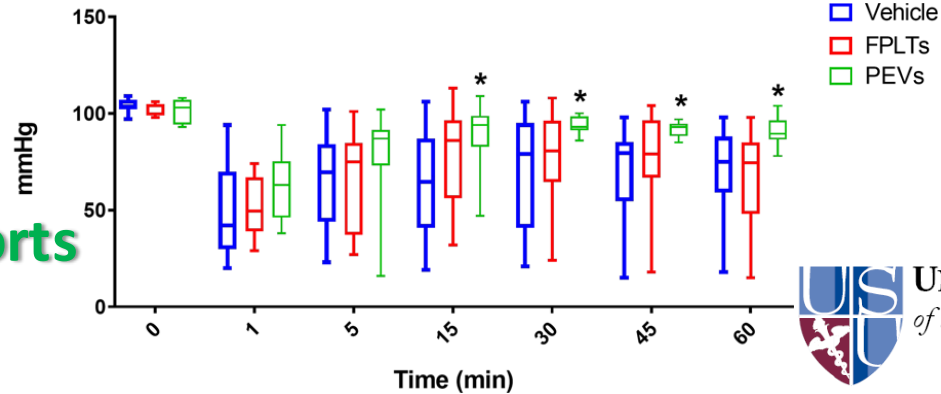
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Mean Arterial Pressure



B)

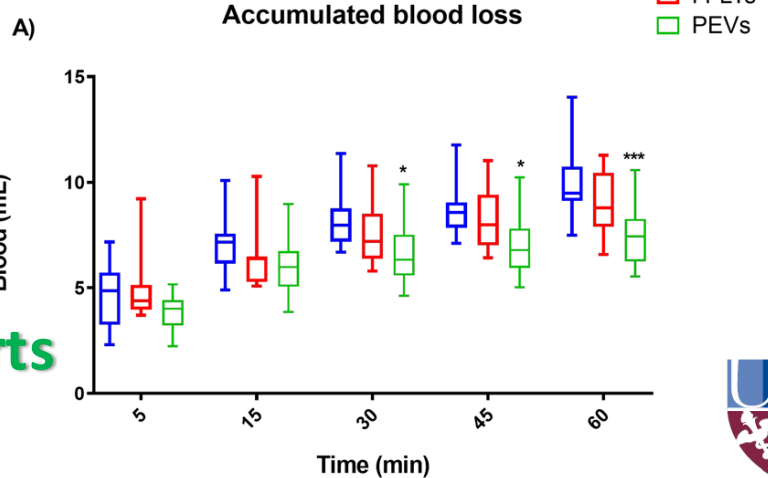
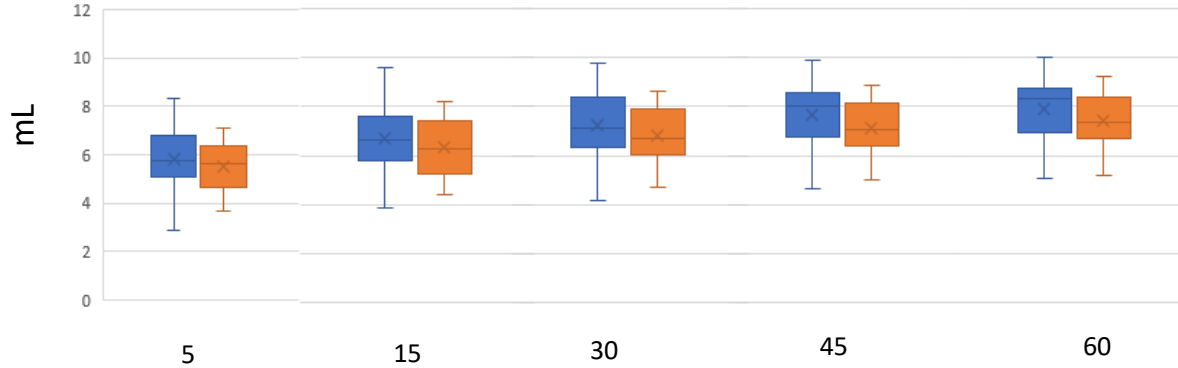
MAP



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Lopez et al.
Scientific Reports
2019;9:17676.

Cumulative Blood Loss

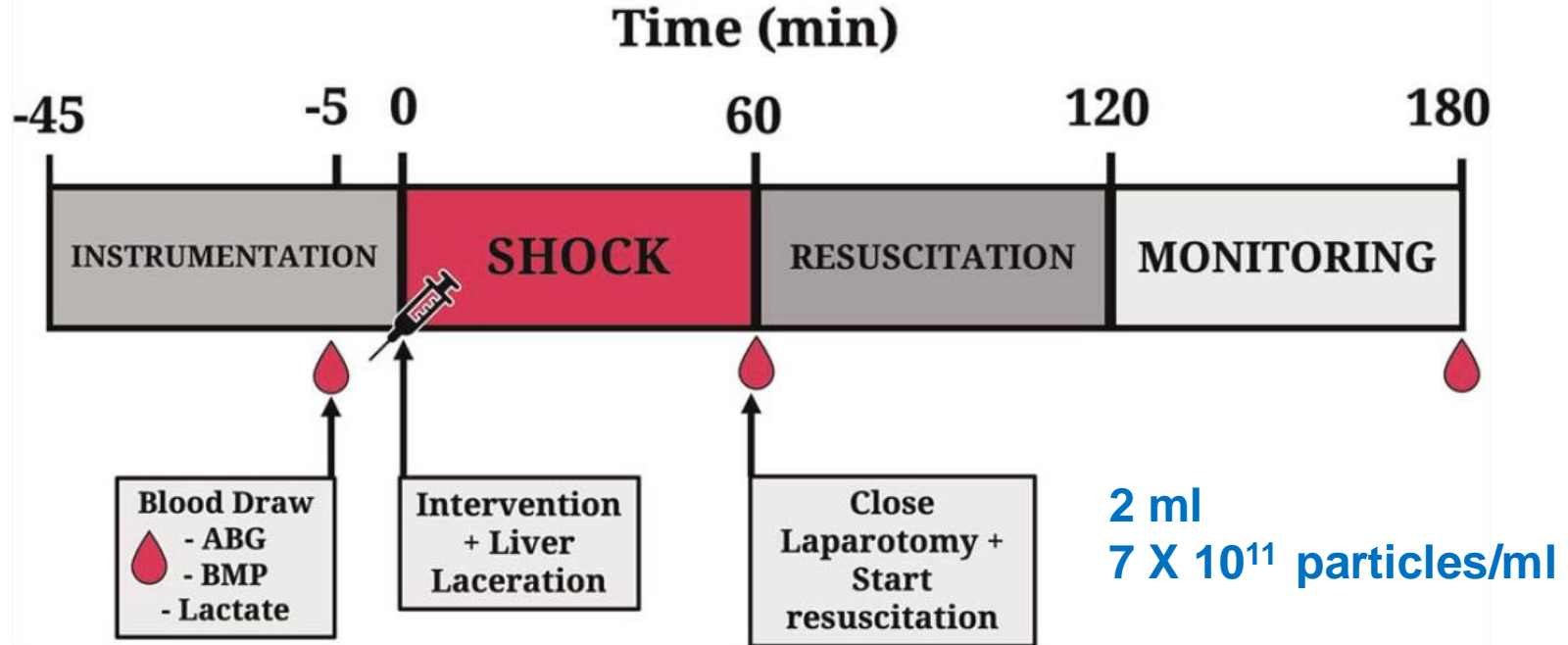


Lopez et al.
Scientific Reports
2019;9:17676.

Pilot study of frozen platelet extracellular vesicles as a therapeutic agent in hemorrhagic shock in rats

Samantha Durbin, MD, Lindsey Loss, MD, Lydia Buzzard, BS, Karen Minoza, MD, Marissa Beiling, DO, Carmen Karsonovich, Moqing Liu, PhD, Joseph Garay, PhD, Alexander Fields, PhD, Michael Mathews, BS, Benjamin Kuhn, BS, MS, Keith Moskowitz, PhD, MPM, Byron Miyazawa, BS, Alpa Trivedi, PhD, Lucy Kornblith, MD, Michael Fitzpatrick, PhD, Shibani Pati, MD, PhD, and Martin Schreiber, MD,
Portland, Oregon

EXPERIMENT TIMELINE

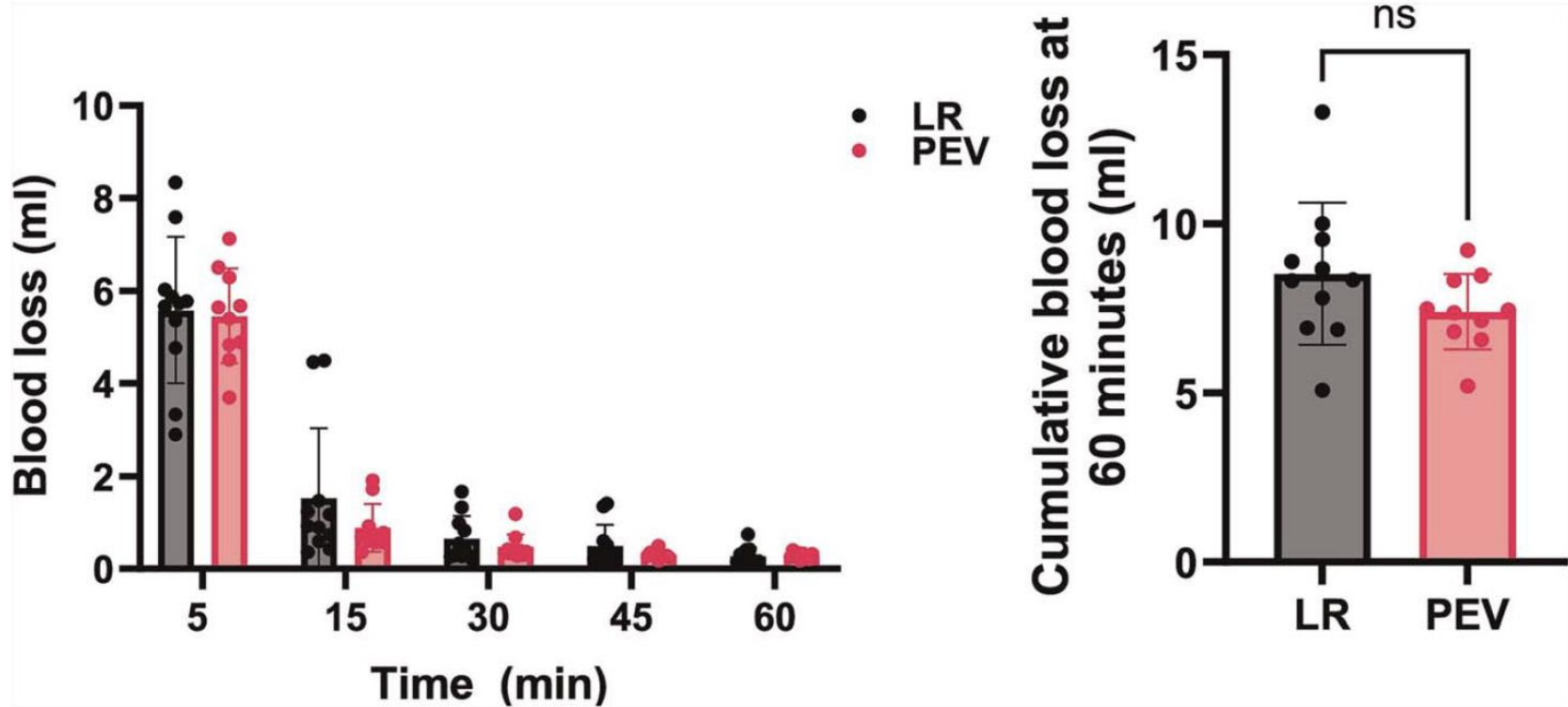


Durbin et al. *JTACS* 2024;96: 364–370.



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Blood Loss

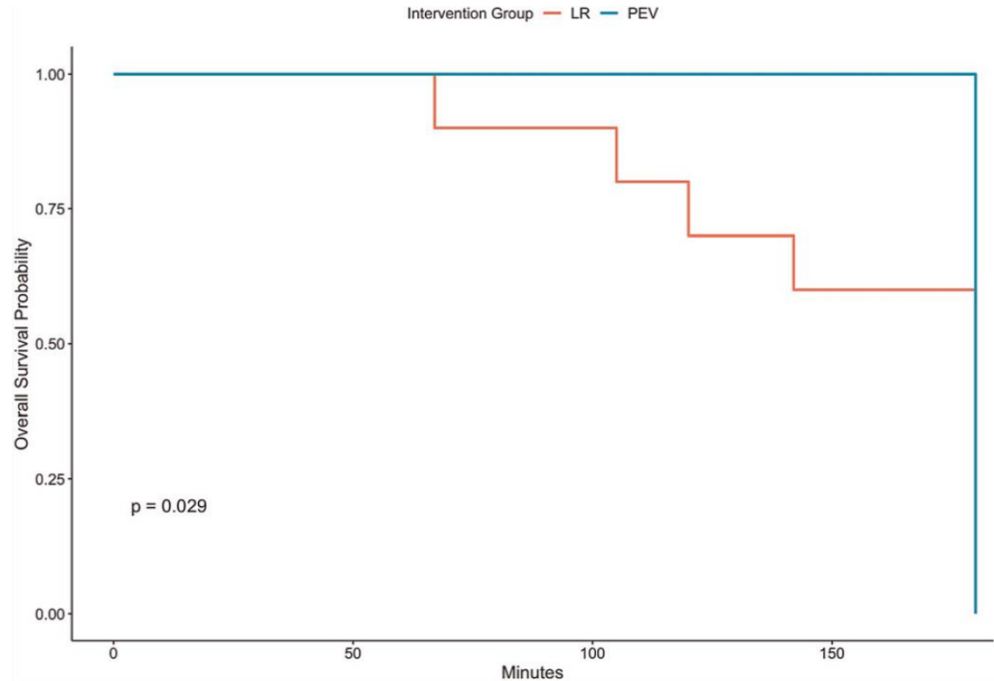
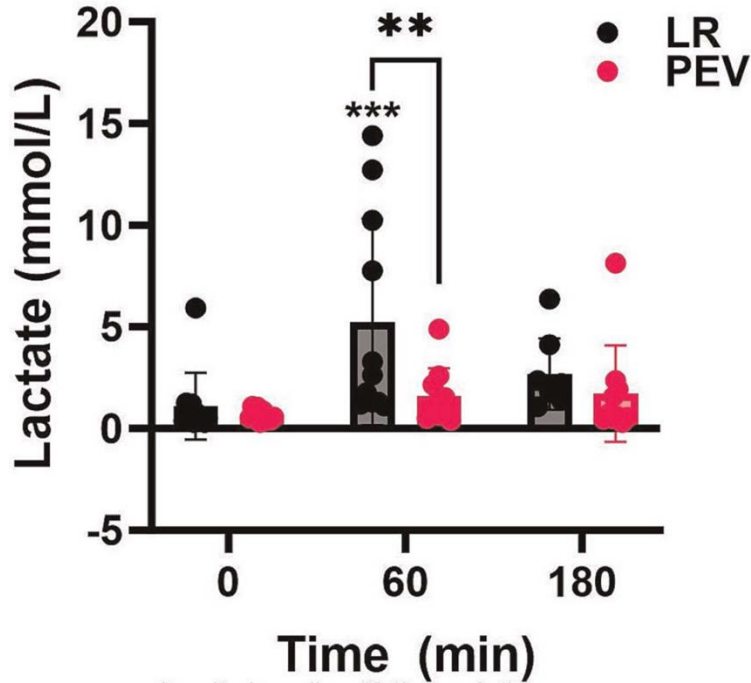


Durbin et al. *JTACS* 2024;96: 364–370.



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Lactate and Mortality



Durbin et al. *JTACS* 2024;96: 364–370.



REVIEW ARTICLE

Biopreservation of red blood cells – the struggle with hemoglobin oxidation

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1 Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada

2 Research and Development, Canadian Blood Services, Edmonton, Canada



Available online at www.sciencedirect.com



Cryobiology 51 (2005) 290–305

CRYOBIOLOGY

www.elsevier.com/locate/ycryo

Phospholipid vesicles increase the survival of freeze-dried human red blood cells ☆

Azadeh Kheirrolomoom^{a,1}, Gyana R. Satpathy^{a,1}, Zsolt Török^a, Mitali Banerjee^a, Rachna Bali^a, Roberta C. Novaes^a, Erika Little^a, Danielle M. Manning^a, Denis M. Dwyre^c, Fern Tablin^{a,b}, John H. Crowe^a, Nelly M. Tsvetkova^{a,*}



What Will Tomorrow's Special Forces Medic Carry?

Conclusions

- Dried plasma and platelet products just about ready for prime time
- Can we create a combination of powdered products to replace WB?