



Similarities and differences between Centrifugal plasma exchange vs DFPP and clinical applications

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DISCLOSURE

- During the last 3 years the presenter have recieved honoraria from the companies listed below for congress invitation, lectures, consultancy or research grants:
 - Infomed, Fresenius, Baxter, Sanofi, GSK, Astra-Zeneca, Astellas
- No writing fees, stock royalties endowed chair or gifts.



OUTLINE

Therapeutic plasmapheresis: procedures & modalities

Comparison of SPE by centrifugation with DFPP (pilot study)

Clinical implications



THERAPEUTIC PLASMASPHERESIS (TP)

Core Curriculum 2008 by Kaplan AA AJKD, 2008

- **Extracorporeal blood purification= remove substance with specific characteristics**
 - A large molecular weight (>150 kDa)
 - A prolonged half life with slow rate of formation and low volume of distribution
 - Acute toxic effect with resistance to conventional therapy
- **Exemple:** auto-antibody, immune complexes, paraproteins, lipoproteins, toxins



THERAPEUTIC PLASMAPHERESIS (TP) PROCEDURES

- **NON SELECTIVE TP:** *SINGLE PLASMA EXCHANGE* (SPE) (1960)
- **SEMI SELECTIVE TP:** *DOUBLE FILTRATION PLASMAPHERESIS* (DFPP) (1980)
- **SELECTIVE TP:** *PLASMA ADSORPTION* (IA) (1990)

THE MOLECULES REMOVE ARE DIFFERENT ACCORDING TO PROCEDURES



Conventional Apheresis Therapies: A Review

David M. Ward^{1,2,3*} *Journal of Clinical Apheresis* 26:230–238 (2011)

SINGLE PLASMA EXCHANGE

Centrifugal TPE

- Citrate (usually)
- Lower blood flow rate
- Peripheral veins or central line
- Process ~1.5 x blood volume
- Plasma extraction ~80%

Membrane TPE

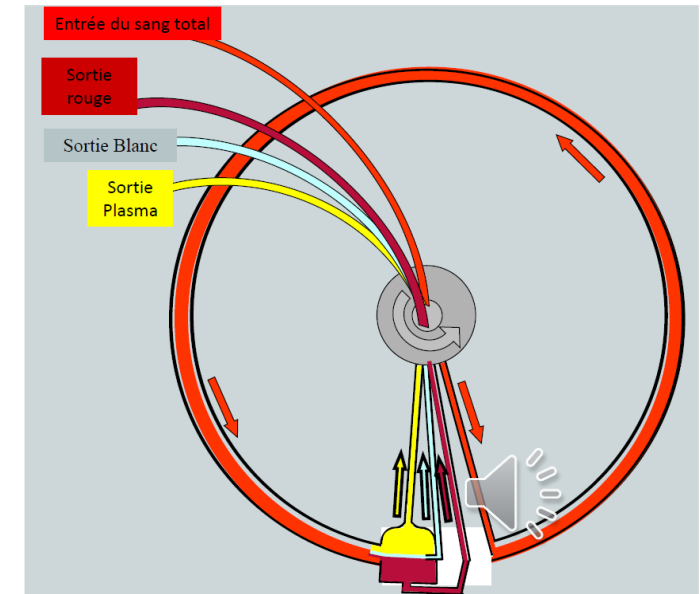
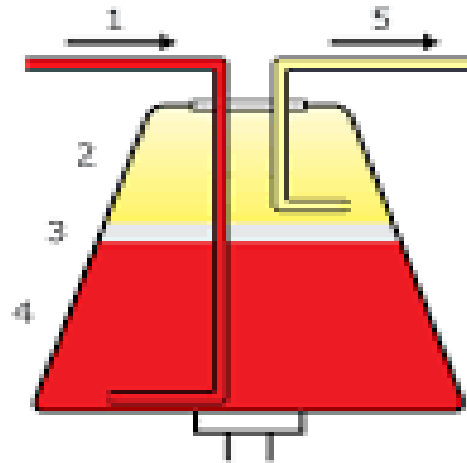
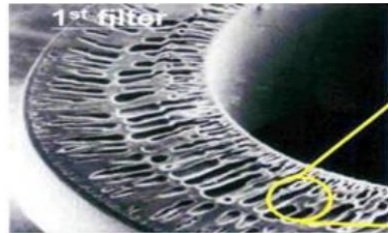
- Heparin (usually)
- Higher blood flow rate
- Central venous line
- Process ~3 x blood volume
- Plasma extraction ~30%



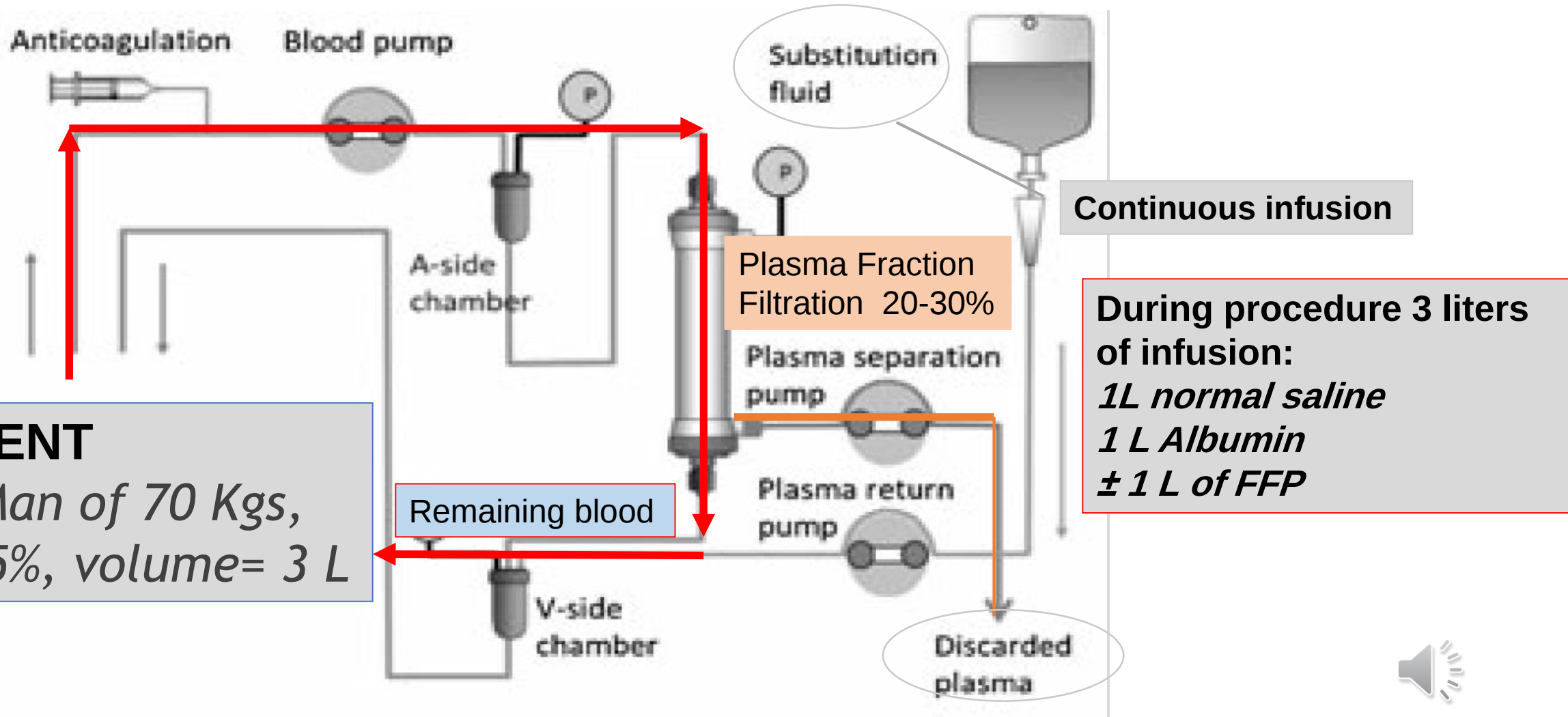
Non specific treatment with subtraction of plasma and injection of a substitution fluid



MODALITIES OF THERAPEUTIC PLASMAPHERESIS



NON SELECTIVE THERAPEUTIC PLASMAPHERESIS: SPE WITH FILTRATION



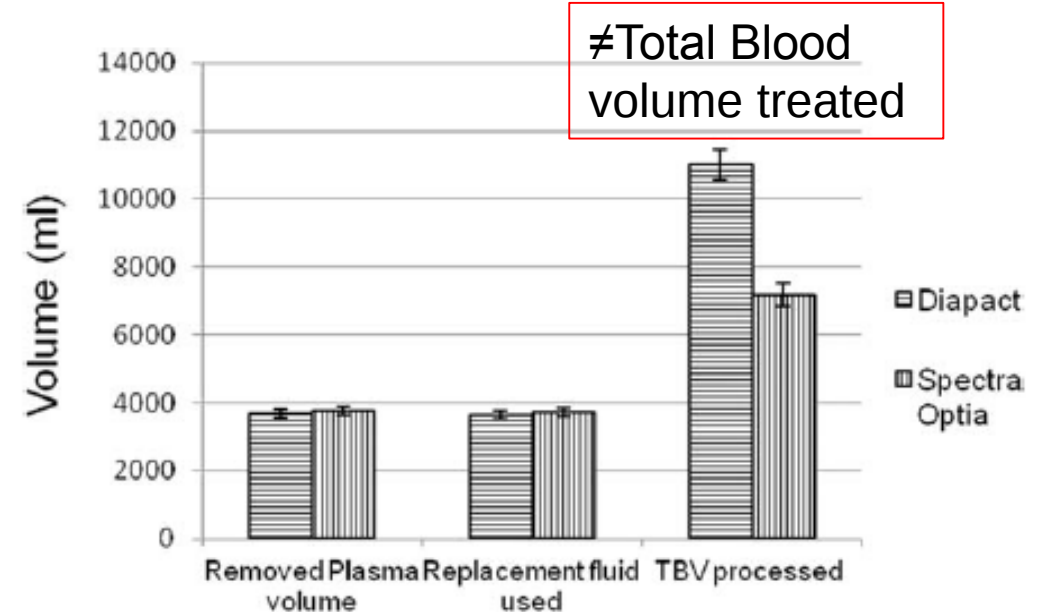
A randomized crossover study comparing membrane and centrifugal therapeutic plasma exchange procedures

TRANSFUSION 2016;56;3065–3072

Petar Kes,¹ Michiel Etienne Janssens,² Nikolina Bašić-Jukić,¹ and Milića Kljak¹

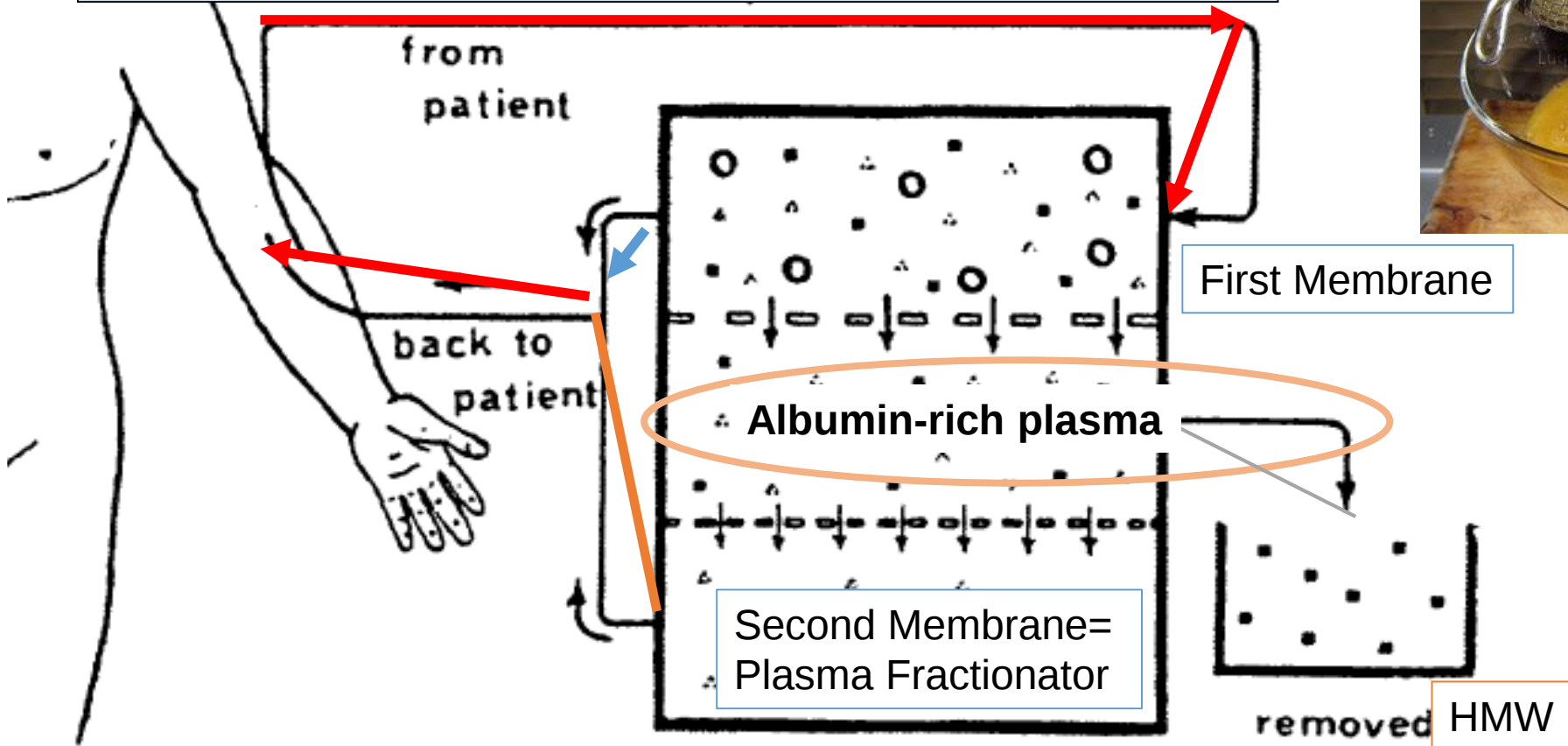
TABLE 2. Summarizing table of several comparative variables analyzed on 27 patients in this study*

Variable	Diapact	Spectra Optia
TBV (L)	4,574 ± 793	
Total plasma volume (L)	2,945 ± 515	2,976 ± 554
Setup time (min)†	7 ± 1	5 ± 1
Priming time (min)†	16 ± 1	6 ± 1
Preparation time (min)†	23 ± 2	11 ± 1
Procedure time (min)†	134 ± 26	91 ± 25
Total time (min)†	157 ± 26	102 ± 25
Time to remove 1 L of plasma (L/min)†	36.9 ± 5.5	24.5 ± 6.5
Mean flow rate (mL/min)	82.4 ± 11.8	80.6 ± 11.8
Removed plasma volume (mL)‡	3,676 ± 635	3,745 ± 641
Replacement fluid used (mL)§	3,624 ± 658	3,722 ± 635
TBV processed (mL)†	11,004 ± 2,427	7,181 ± 1,777
PLT loss (%)	9.68 ± 15.5	10.5 ± 16.53
IgG removal efficiency (%)	69.49 ± 9.48	72.17 ± 9.74
Fibrinogen removal efficiency (%)†	62.95 ± 16.14	72.32 ± 8.54
PRE (%)†	53.21 ± 6.59	83.02 ± 4.85



CONCLUSION: This study shows that, although both systems perform adequate and safe TPE procedures, those on the Spectra Optia in comparison to the Diapact are more efficient in terms of plasma removal and significantly shorter.

SEMI SELECTIVE PLASMAPHERESIS DOUBLE FILTRATION PLASMAPHERESIS (DFPP)



Remove
Plasma from
Blood (20-30%)

Remove protein
from plasma



FIG. 1. The drawing shows the principle of DFPP (2).

Man of 70 kgs, Hc 35%; Filtration 3 L; no substitution fluid during Procedure. Infusion at the end of session: Albumin 20%: 100mls



Feasibility, Efficacy, and Safety of Peripheral Venous Access for Chronic Double-Filtration Plasmapheresis with Regional Citrate Anticoagulation

Antoine Cardinale^a Emilie Pambrun^a Camelia Prelipcean^a Ziyad Messikh^a
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Protocol of comparison of the effects of single plasma exchange and double filtration plasmapheresis on peripheral lymphocyte phenotypes in patients with Chronic Inflammatory Demyelinating Polyradiculoneuropathy: a monocentric prospective study with single-case experimental design

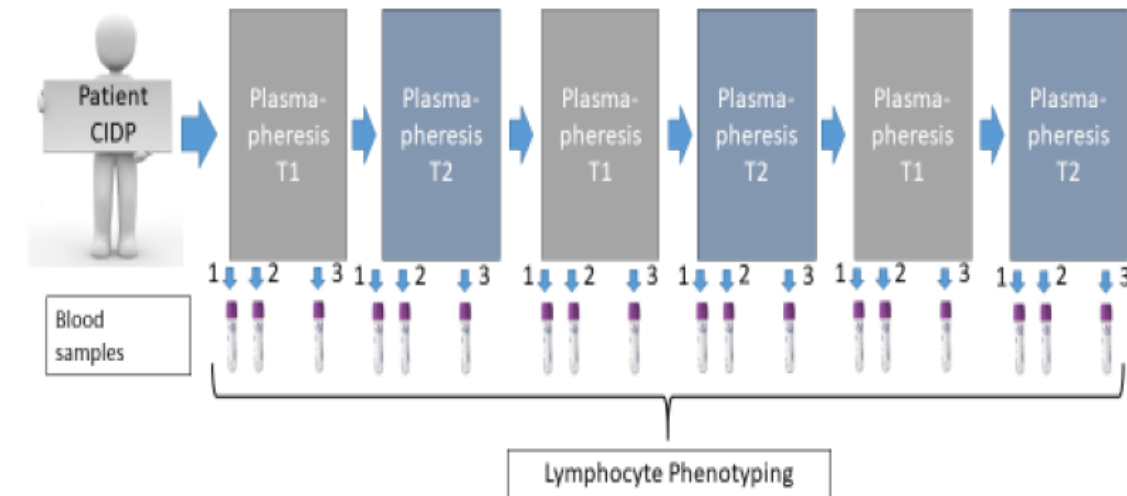
O. Moranne^{1,2*} , IM. Ion³, R. Cezar⁴, Z. Messikh¹, C. Prelipcean¹, S. Chkair⁵, E. Thouvenot^{3,6}, Tu Anh Tran⁷, P. Corbeau⁸ and T. Chevallier^{2,5}

➤ Secondary objective:
comparison of time procedure & tolerance for
SPE-C vs DFPP



POPULATION & METHODOLOGY

- Monocentric prospective **single-case study**
- **5 patients with CIPD**, depending on TP
- Evaluation of 6 sessions for each patient with alternatively SPE-C and DFPP and first treatment randomised



- Primary Objective: Lymph T phenotype variation with TP
- **Secondary Objective:** comparison procedures EPS/centrifugation vs DFPP

THERAPEUTIC PLASMAPHERESIS PROTOCOL

➤ SPE with Centrifugation

- Centrifugation: Comtec® (Freseinus Kabi)
- 100% substitution fluid Alb 4%
- Citrate regional anticoagulation (CRA) with infusion of CaCl
- PVA or CVA according to patients.

➤ DFPP

- Infomed HF440® (Infomed SA, Geneva, Switzerland)
- Primary filter, Granopen50® (Infomed SA, Geneva, Switzerland)
- Secondary Filter, EC30® (Asahi Kasei, Tokyo, Japan)
- Infusion 500ml of 4% alb continuously (20g)
- Anticoagulation was for
- PVA: CRA with CaCl
- CVA: bolus and continuous NHF



Comparison SPE-Centrifugal and DFPP

➤ POPULATION:

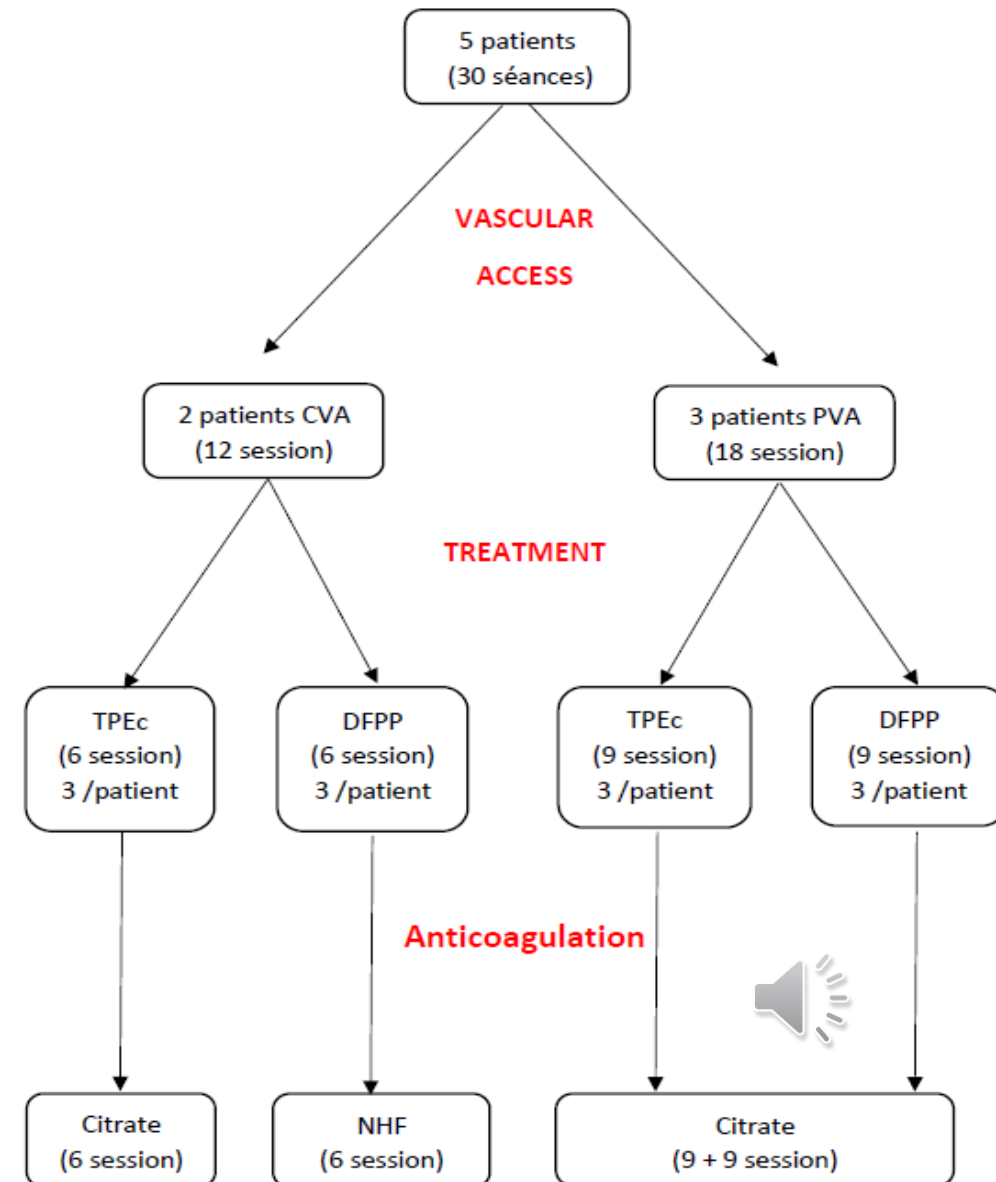
- **Male 100%; Age 62 [56-68];**
- **Weight 95 kgs[78-96]; BMI 27 [23-31];**
- Diabetes: 2 (40%); ISRE: 3(60%); none with IS treatment

➤ Vascular access & Anticoagulation:

- CVA: 2 pts with (NFH/ CRA)
- PVA: 3 pts (CRA)

➤ Outcomes:

- Procedure (Time duration; blood and Plasma flow)
- Clinical Tolerance
- Biological variation



5 patients with 6 sessions each alternatively SPE & DFPP	SINGLE PLASMA ESCHANGE CENTRIFUGATION	DFPP	p
N sessions	15	15	
Peripheral vascular access (PVA)	9 (60%)	9 (60%)	
Regional citrate Anticoagulation	15 (100%)	9 (60%)	
Blood volume process (ml)	9474 [9328 ; 10689]	19500 [17310 ; 25850]	<.001
Treated plasma volume (ml)	4500 [4461 ; 5000]	4500 [4470 ; 5000]	NS
Plasma Fraction filtration (en %)	51 [43 ; 53]	25 [18 ; 26]	<.001
Weight variation (After-Before)	0.4 [0.0 ; 0.5]	1.0 [0.5 ; 1.5]	.04
Serum Albumin 4% Infusion Albumin (g/L)	4500 [4500 ; 5000] 180 g	500 [500 ; 500] 20 g	<.001

	CENTRAL VENOUS ACCESS		p	PERIPHERAL VENOUS ACCESS		p
Traitement	SPEc	DFPP		SPEc	DFPP	
Patients n	2			3		
Session n	6	6		9	9	
Anticoagulation	Citrate 6 (100%)	HNF 6 (100%)		Citrate 9 (100%)	Citrate 9 (100%)	
TP procedure						
Mean Blood flow (ml/min)	94 [92 ; 94]	173 [168 ; 185]	.03	65 [63 ; 66]	121 [116 ; 128]	.01
Blood volume treated (ml)	10227 [9330 ; 11533]	26725 [24480 ; 28690]	.03	9474 [9328 ; 9650]	17370 [16160 ; 19270]	.004
Plasma Fraction Filtration (%)	47 [43 ; 51]	17 [16 ; 19]	.02	52 [47 ; 53]	26 [25 ; 26]	.004
Plasma Blood Flow (ml/min)	43 [40 ; 48]	31 [29 ; 34]	.03	34 [28 ; 35]	30 [30 ; 32]	.03
Overall Timing session						
Time preparation	29 [23 ; 38]	23 [20 ; 27]	.03	37 [32 ; 40]	28 [25 ; 30]	.03
Time Device	110 [99 ; 123]	148 [142 ; 155]	.03	148 [135 ; 150]	143 [132 ; 161]	.99
Time restitution	4 [3 ; 7]	6 [5 ; 7]		4 [4 ; 5]	4 [3 ; 5]	
Time before living	19 [10 ; 24]	16 [16 ; 17]	.75	16 [14 ; 20]	21 [17 ; 25]	.04
Total time session	163 [152 ; 174]	192 [187 ; 200]	.06	201 [189 ; 213]	199 [183 ; 211]	NS

No difference between groups for Plasma Volume treated

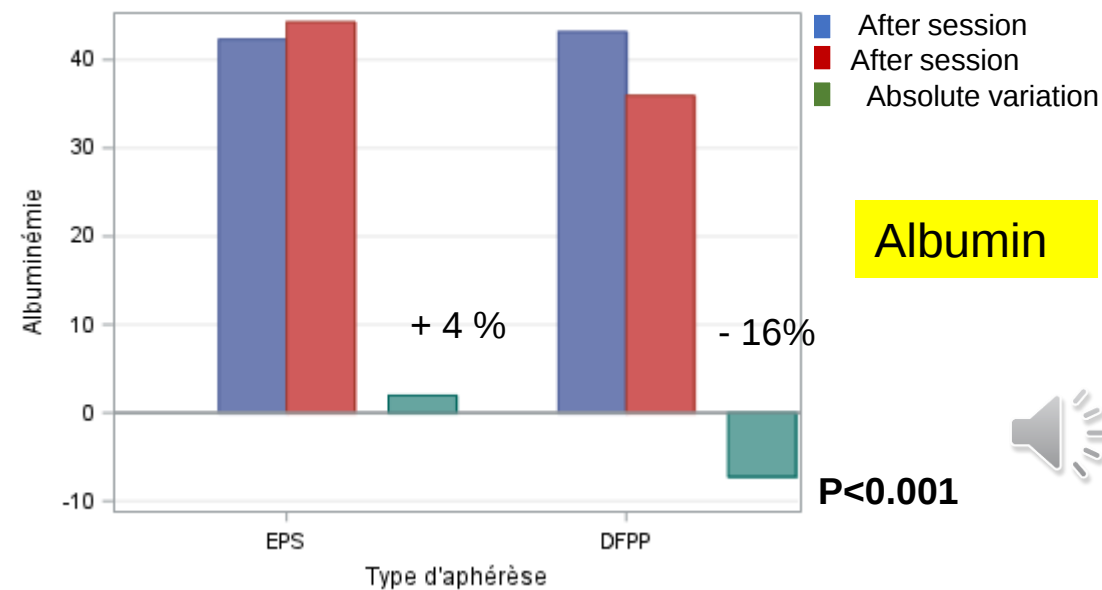
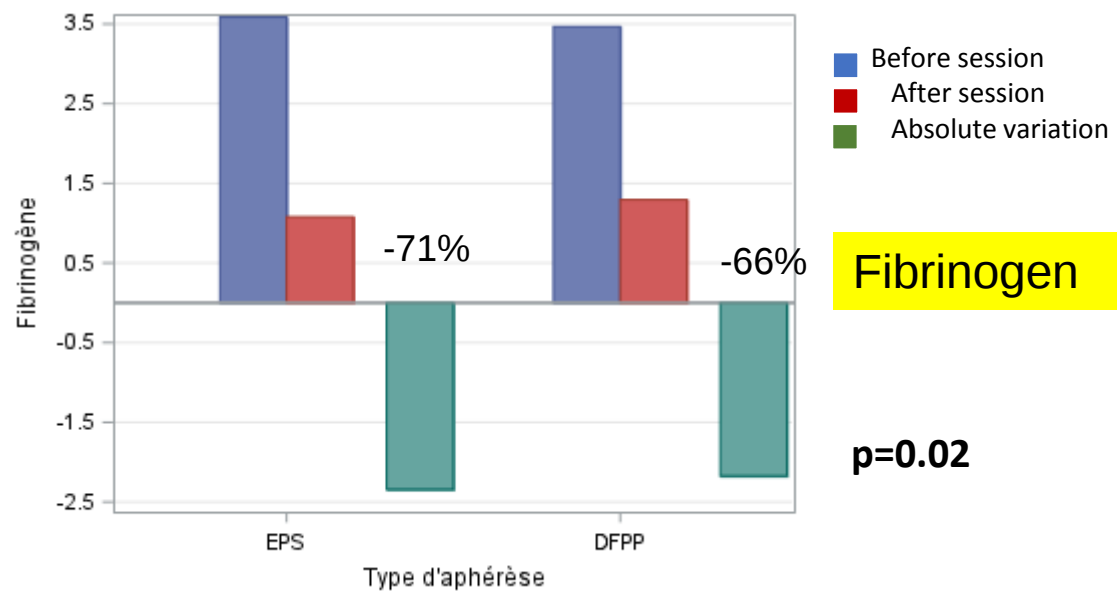
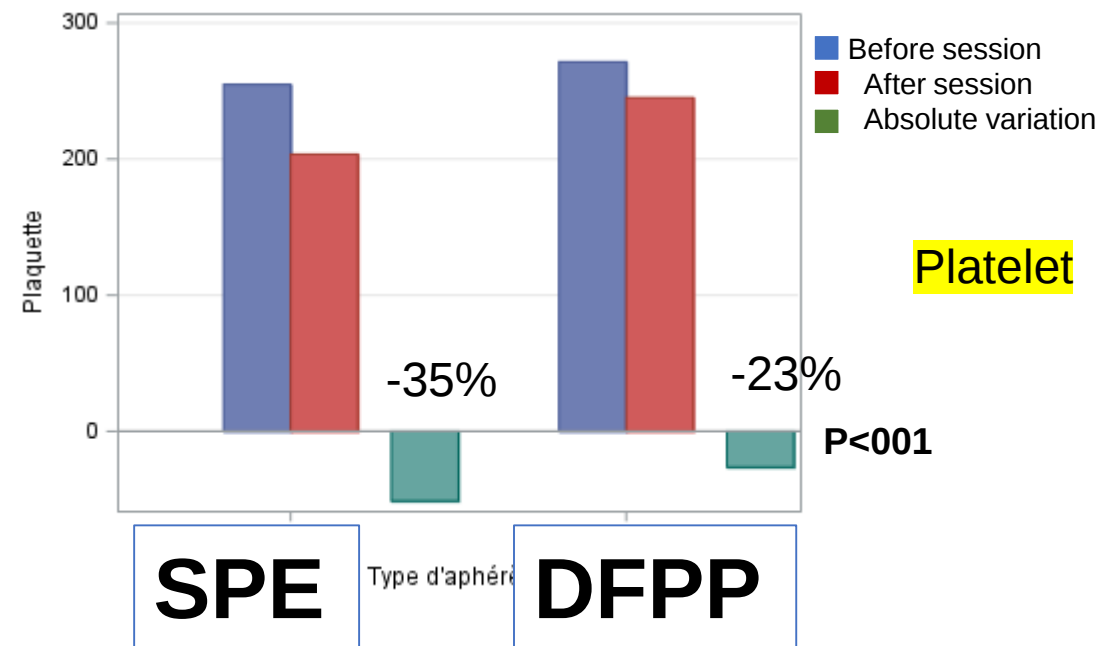
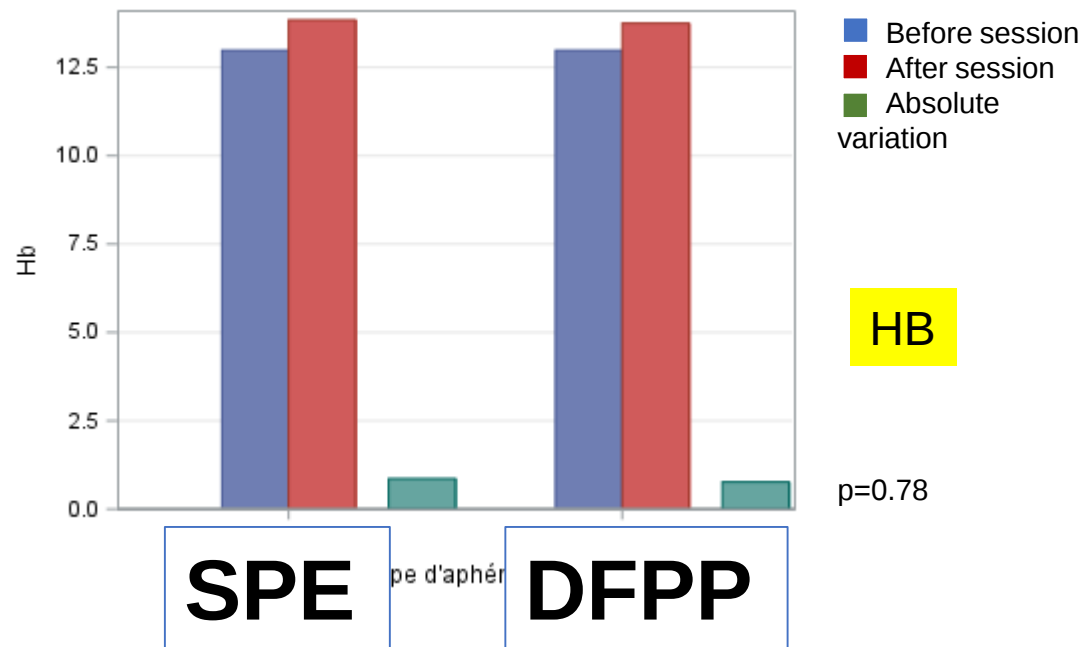
CLINICAL TOLERANCE

- No clinical adverse events during study
- No Hypocalcemia with RCA

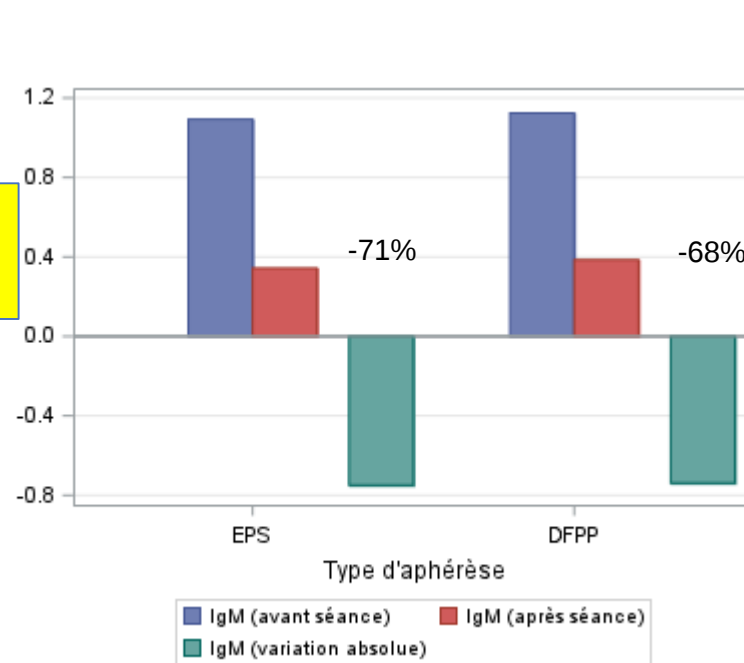
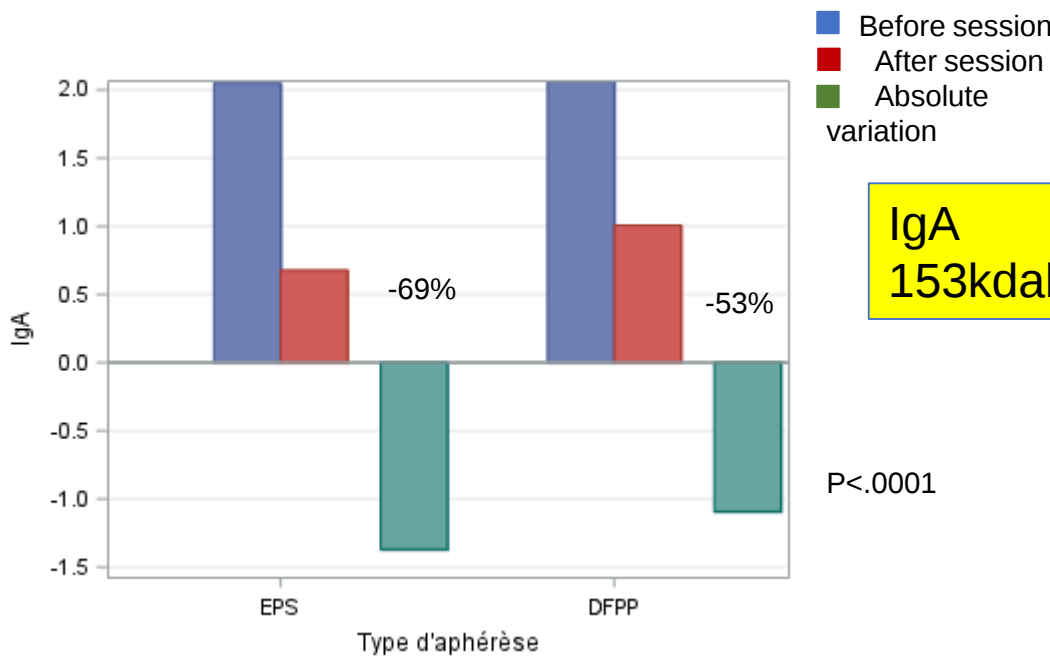
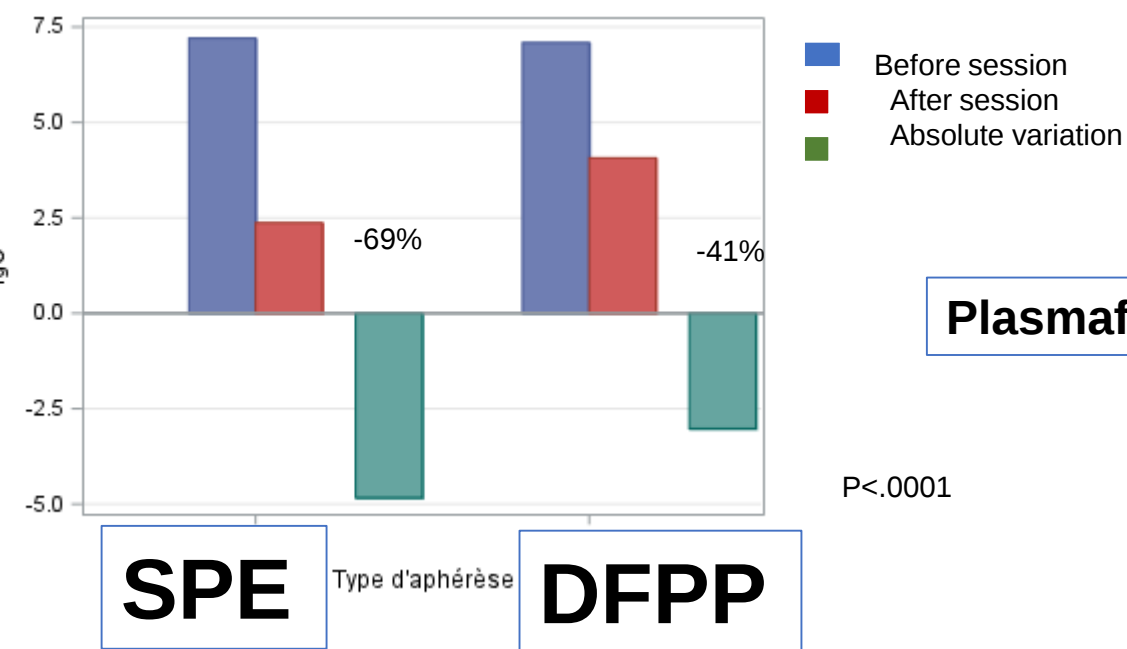
BIOLOGICAL VARIATION

- Variation during session of: Hb, Platelets, fibrinogen, Albumin, IgG/A/M





**IgG
146kdalton**



MESSAGES FOR COMPARISON SPE-C against DFPP

- Vascular access and procedures are associated to total time session
- Serum Albumin infused is higher with SPE
- No differences observed for clinical tolerance between procedures
- For the same PVT statistical significant difference for reduction of biological blood value (Fibrinogen, IgG and IgA) between procedures



Clinical Applications for SPE & DFPP

- **Choice of SPE to infuse therapeutic substitution fluid** (TTP, Liver Failure, Sepsis..)
- **Choice of Procedure according to the size of molecules to remove:**
 - Examples:
 - Thyrotoxicosis (FT4 & FT3 < Albumin); Myeloma (lambda/kappa) = SPE
 - Auto-immun disease with auto-antibodies : SPE / DFPP (Plasma volume treat ?)
- **Choice according to Serum Albumin availability:** less consumption of Serum Albumin with DFPP





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