

IMUGARD[®] III Leukocyte Removal Filter

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 - IMUGARD III-PL
 - High Platelet recovery
 - Higher concentrates of Platelet after filtrating with IMUGARD III
 - Keeping PLT aggregation ability
 - Less pH change
 - IMUGARD III-RC
 - Less affected by blood temperature

Leukocyte depletion

Background

- Leukocytes or White Blood Cells (WBC)
 - Cellular element present in Whole Blood and Blood Components such as CRC, PC and Plasma
 - Concentration of WBC depends upon component
 - Ave. CRC unit = $2.0 - 5.0 \times 10^9$ cells/unit
 - * $10^9 = 1,000,000,000$ cells = 1 billion
 - Ave. PC unit = $0.5 - 2.5 \times 10^8$ cells/unit

Leukocyte depletion

- What is it?
 - Removal of leukocytes from Whole Blood or Blood Components
 - FDA requirement (AABB)
 - Less than 5.0×10^6 cells/unit
 - COE requirement (Council of Europe)
 - Less than 1.0×10^6 cells/unit

Leukocyte depletion

- Why do it?
 - Objective : Decrease incidence of adverse transfusion reactions
 - Nonhemolytic febrile transfusion reactions
 - Alloimmunization to Human Leukocyte Antigens (HLA)
 - Viral infection (Cytomegalovirus - CMV)

What is complication with WBC?

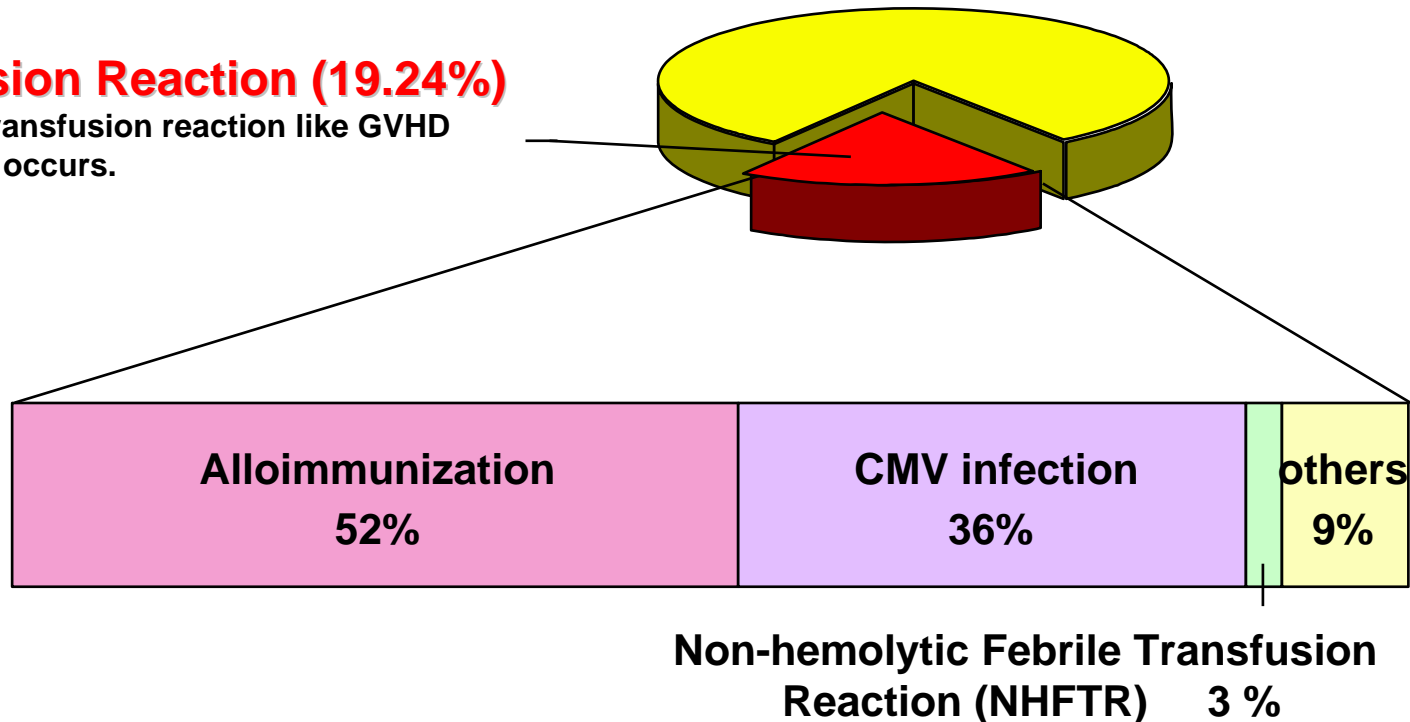
There are four major types of complications ;

- **Non-hemolytic febrile transfusion reaction**
- **Alloimmunization & PLT Refractoriness**
- **Viral infection (Cytomegalovirus)**
- **GVHD (Graft-versus Host Disease)**

Transfusion Reactions

Transfusion Reaction (19.24%)

Excluding Transfusion reaction like GVHD which rarely occurs.

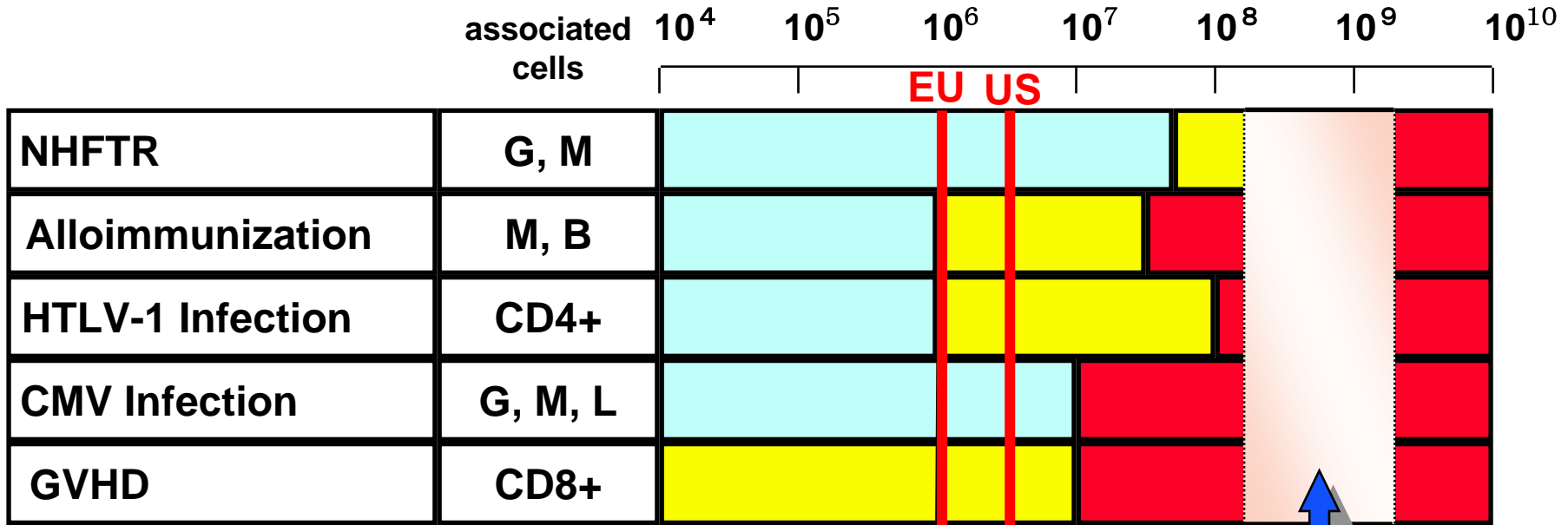


91% of Transfusion Reaction is associated to WBC

WALKER : A.J.C.P. 88(3):374-378,1987.

Transfusion Reactions by Leukocyte

Transfusion Reaction (WBC associated)



High Occurrence
 Unknown
 Preventable

↑ ↑
↑

Number of leukocyte contained in Blood Products

Standard of residual leukocyte number for leukocyte reduction component of each EU(1x10⁶) and US(5x10⁶) guideline

G:Granulocytes, M:Monocytes, L:Lymphocytes, B:Lymphocytes-B, CD:Leukocyte antigens

Non-hemolytic Febrile Transfusion Reaction (NHFTTR)

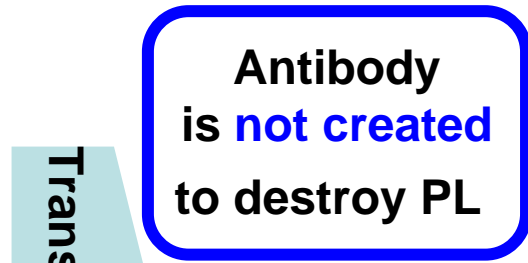
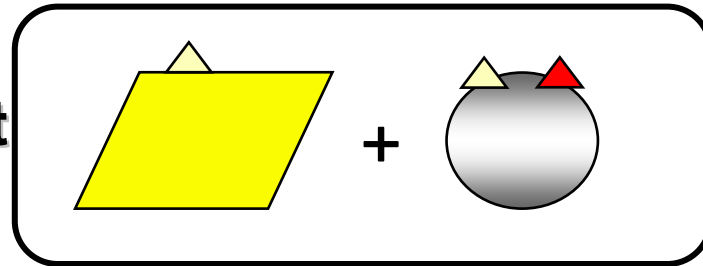
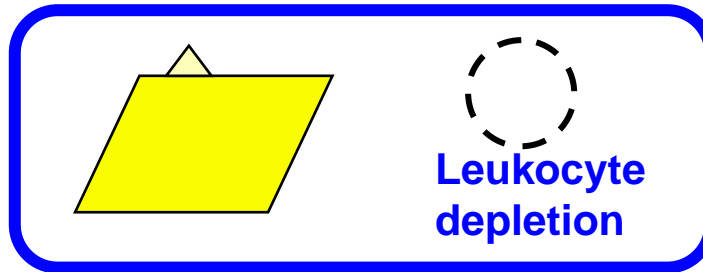
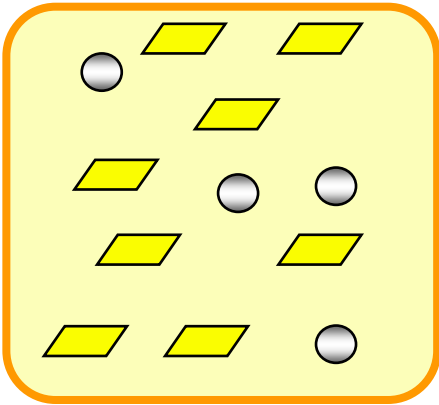
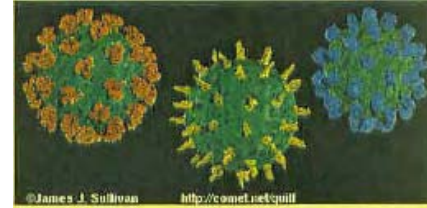
Flu-like symptoms of chills, cold sensation, rigors (shaking), headache and nausea.

On occasion, fevers can approach 40 degrees.

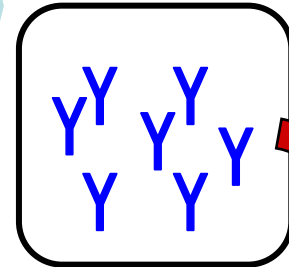
Leukocyte is the cause. However the mechanism is unknown.

Alloimmunization causes refractoriness to platelet transfusion.

Creating the antibody against the antigen on Platelet & WBC



Transfusion



Platelet component

○ Leukocytes

▭ Platelets

△ Human Leukocyte Antigen

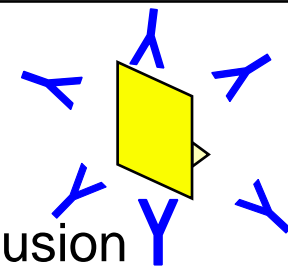
▲ Human Platelet Antigen

Y Antibody

Antibodies **destroy transfused PLT**

(more than 80%)

From 2nd or later transfusion

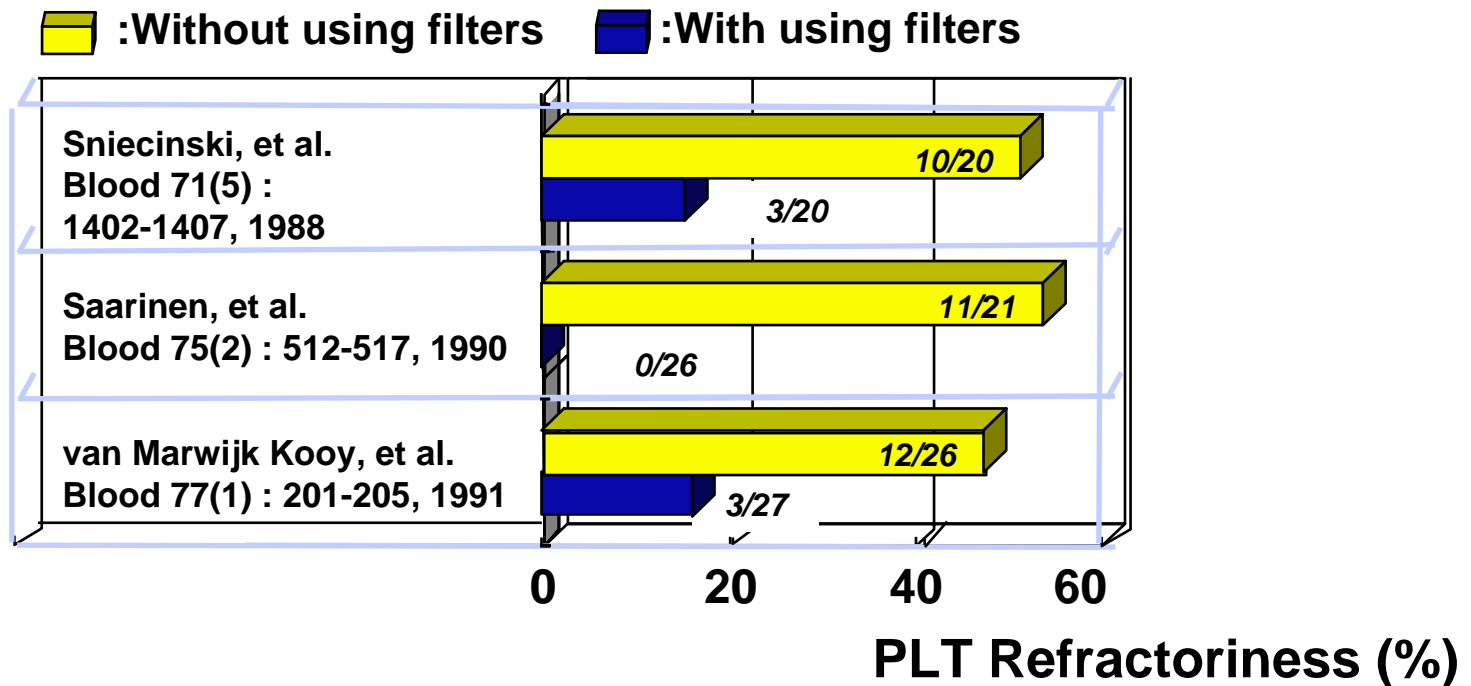


Platelet refractoriness

Welsh, et al. : Eur.J.Immunol. 7 : 267-272, 1977.

Prevent PLT refractoriness by filtration

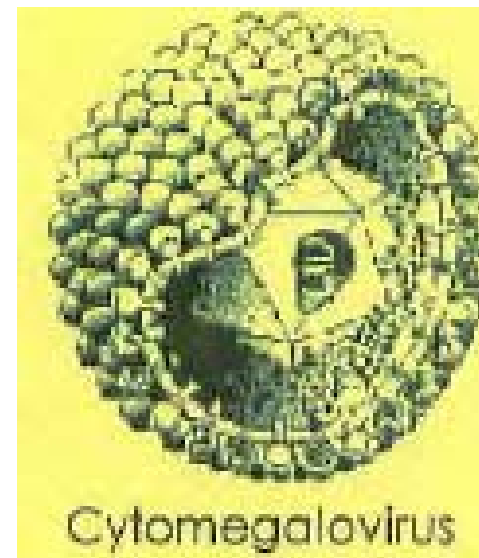
- Leukocyte-depleted PLT transfusions reduce the frequency of patients developing platelet refractoriness.



CMV infection

Inactive infections in WBC of individuals who carry the disease but do not have symptoms.

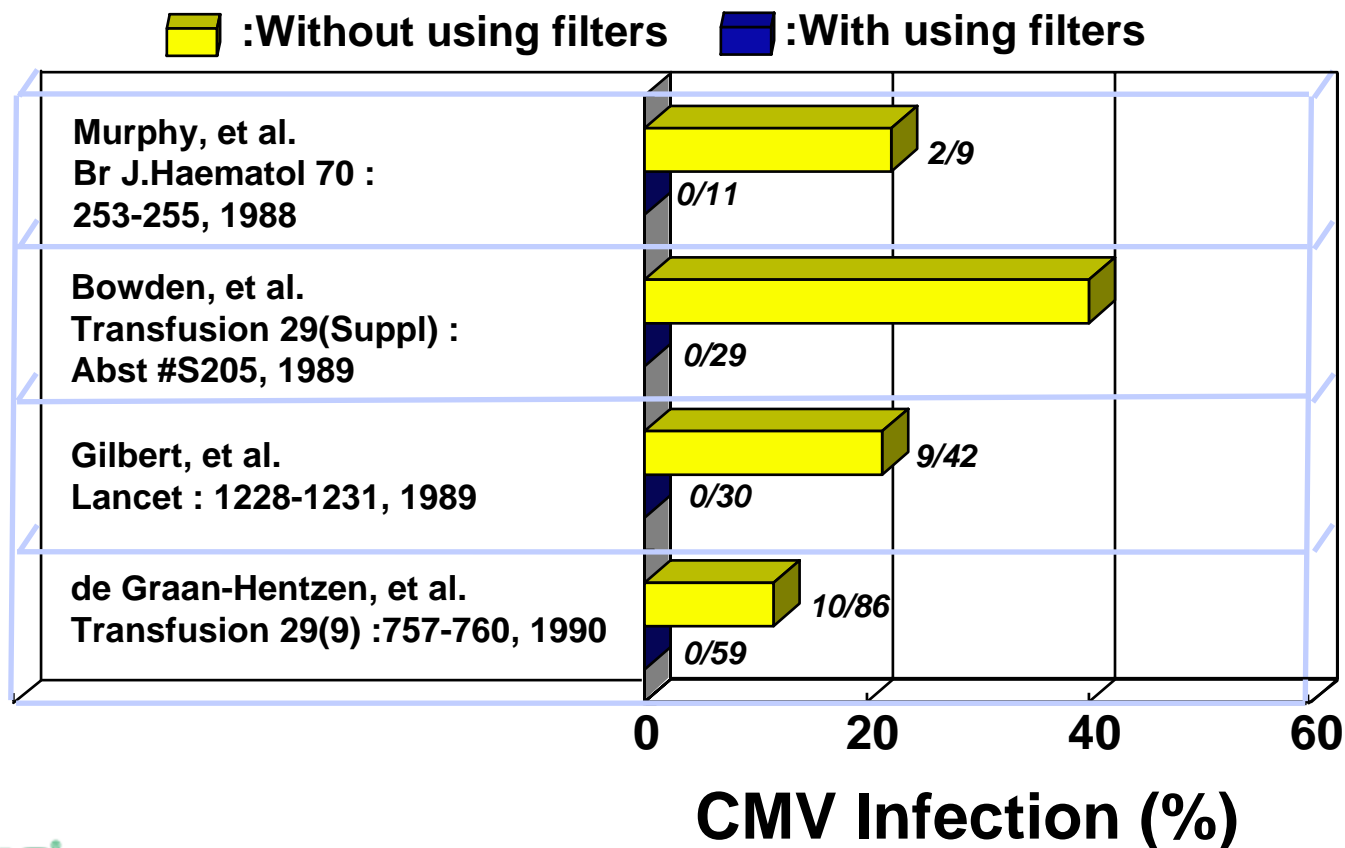
CMV is one of the viruses that resides exclusively in WBC. In certain patient populations, CMV infection can cause fever, hepatitis, pneumonia and severe brain damage, and can ultimately lead to death.



Cytomegalovirus

Prevent CMV infection by filtration

- Reducing **CMV** infection by leuko-deplete filtration



Stages of leukocyte depletion by filtration

- 1st stage : Bedside

- Less Process Control

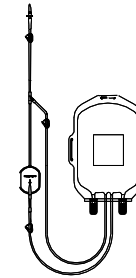


Post storage

- 2nd stage : Dockable

- Under the Process Control

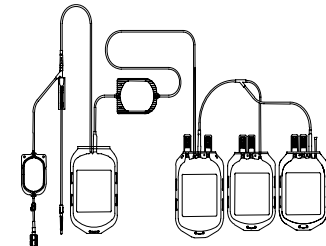
*Dockable = Dock + Able



Dockable filtration within 24hrs after collection is Pre storage filtration.

- 3rd stage : Inline

- Under the Process Control
- During or shortly after collection (generally, <24hrs)



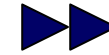
Pre storage

Stages of leukocyte depletion by filtration

Bedside

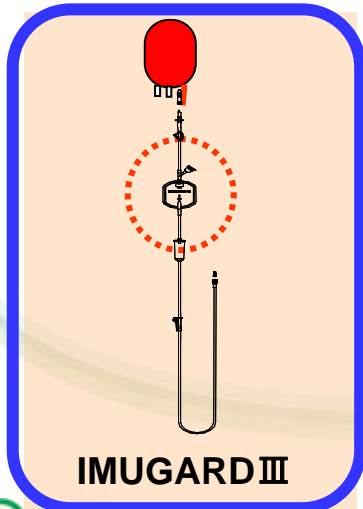
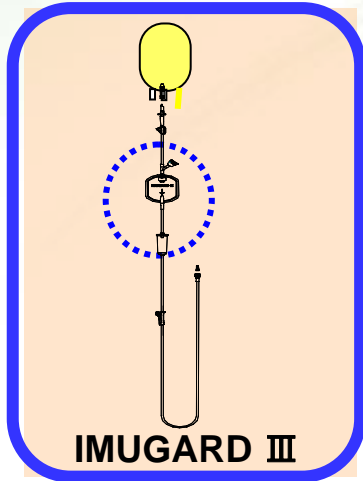


Dockable

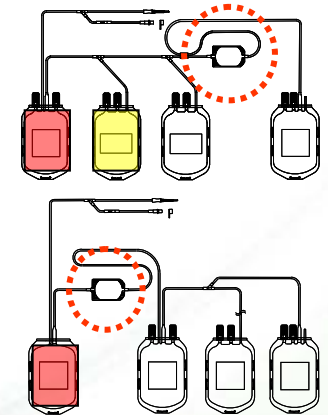
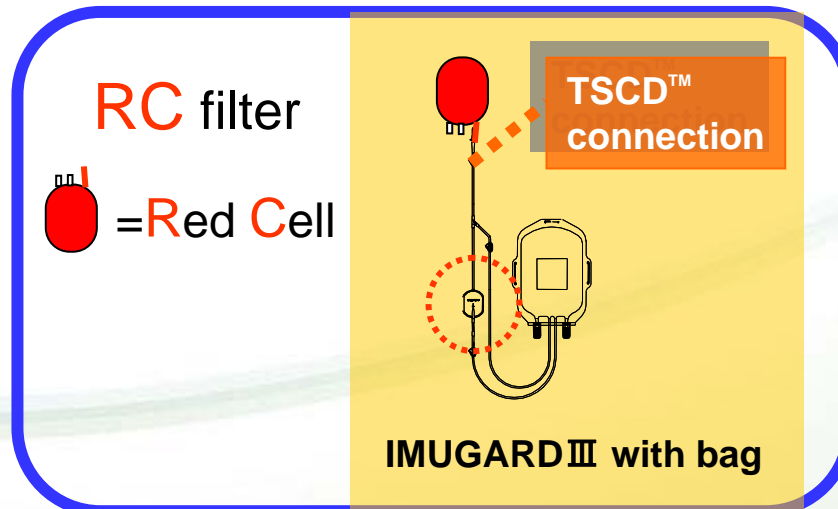
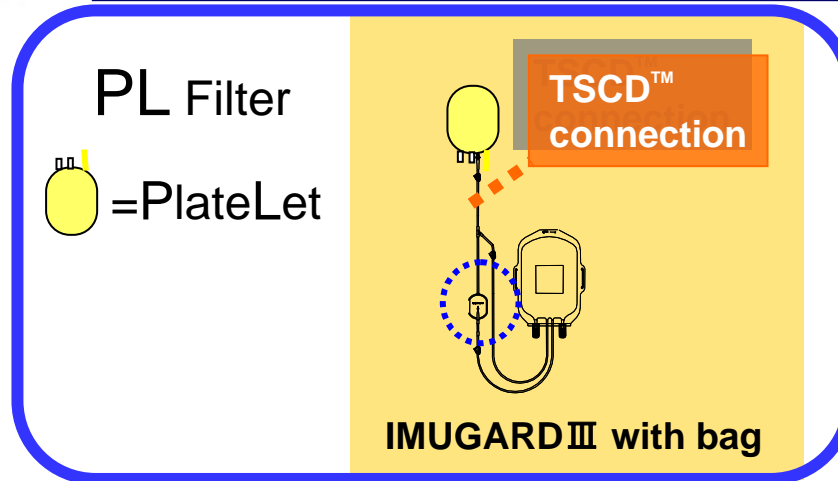


Inline

At hospital



At blood center



IMUFLEX™

Stages of leukocyte depletion by filtration

Bedside

IMUGUARDIII

Dockable

IMUGUARDIII (with bag)

Inline

IMUFLEX

LD
implementation
rate

100%

50%

0%

Western Europe, Can,
NZ, JPN, AUS

USA

China

Korea, Taiwan, HK

Saudi Arabia

Used in advanced
university HPs

Gulf region, South Africa

Brazil

Thailand, Malaysia

Vietnam, Philippine, Chile

India, Mexico

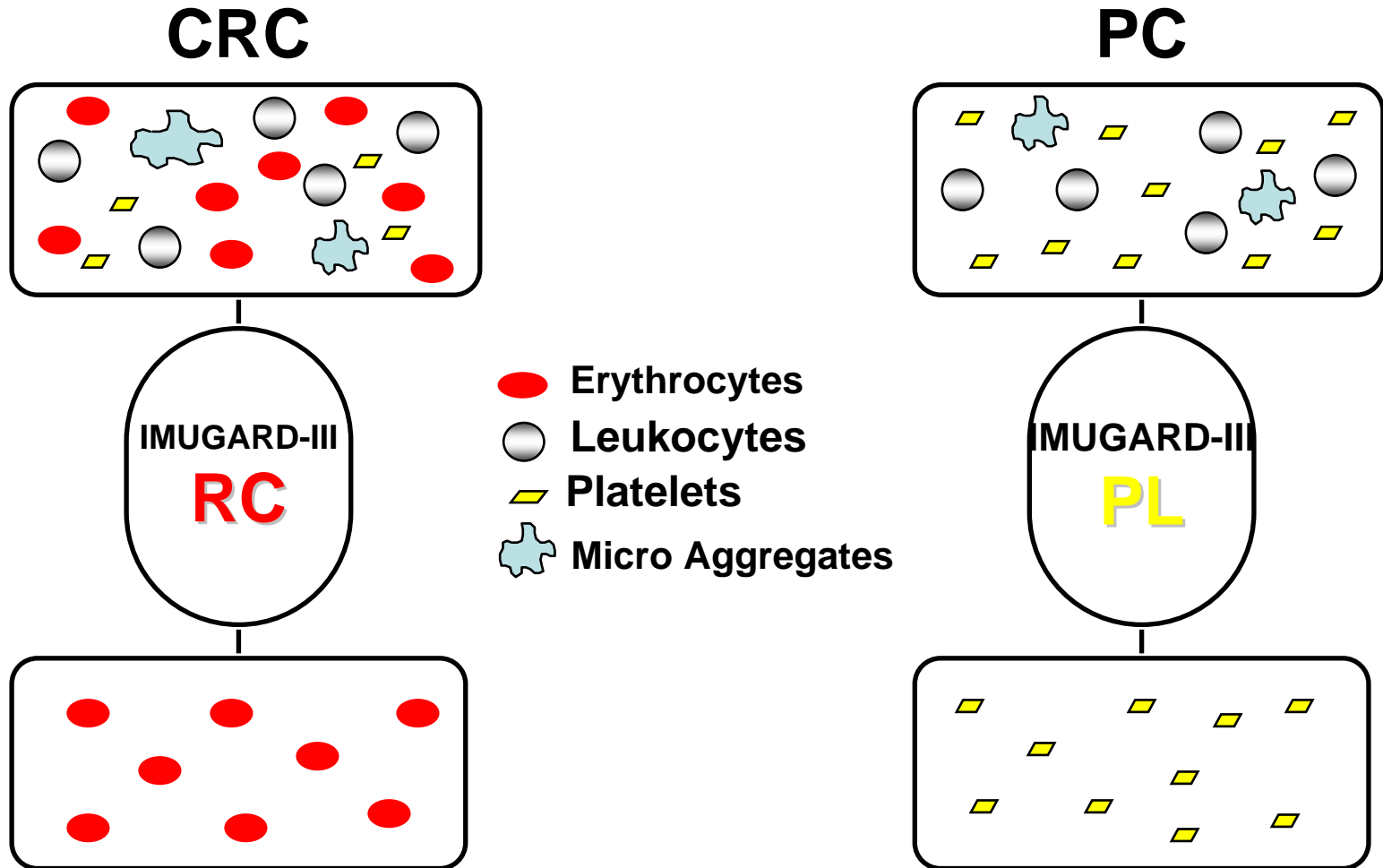
Indonesia

Leukocyte Removal Filter

IMUGARD® III-PL

IMUGARD® III-RC

Blood substances to be removed



IMUGARD III-PL Specification

- Filter Material : **Micro Porous Polyurethane**
- Housing : **Polycarbonate**
- Dimensions : **76 mm x 56 mm x 9 mm**
- Priming Vol. : **17 ml**
- Sterilization : **Ethylene Oxide Gas**
- Capacity : **PCs up to 10 units***

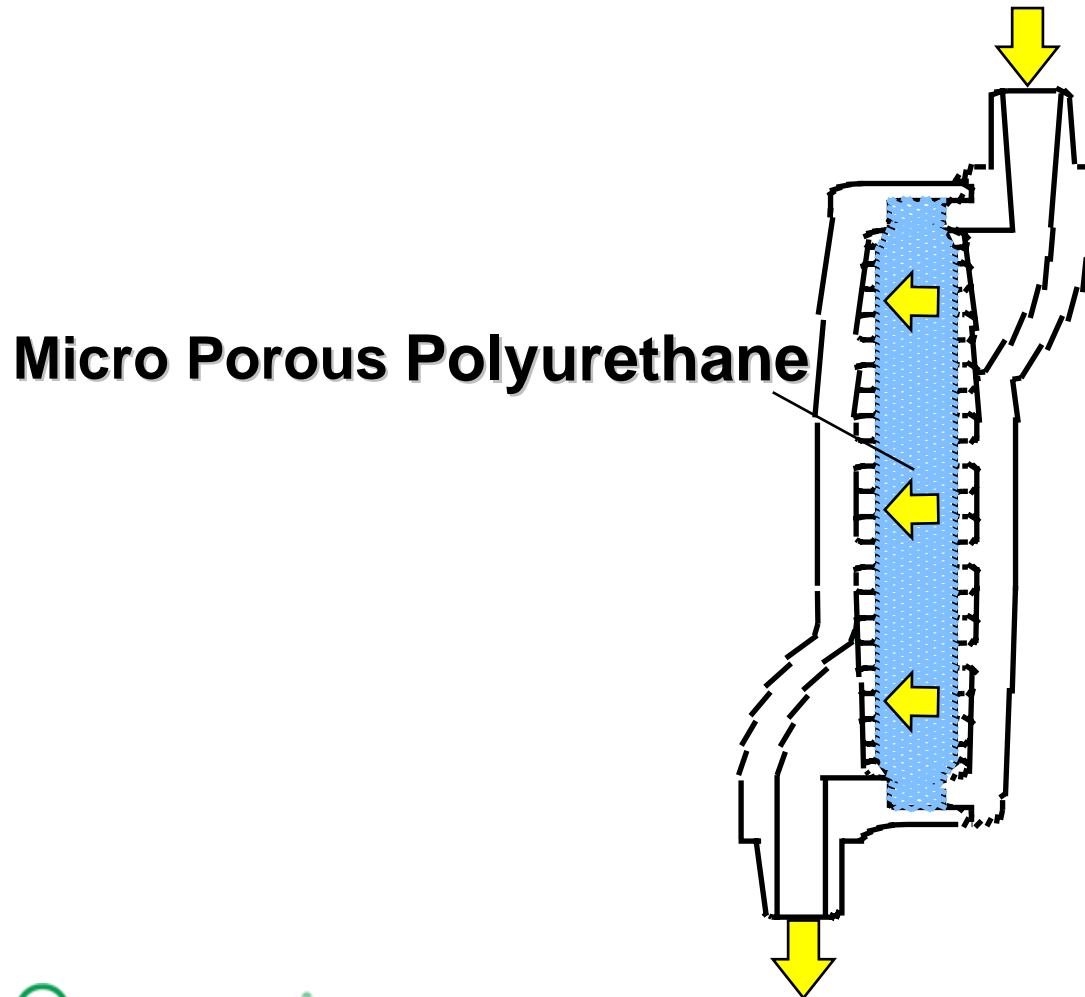
* 1 unit : PC derived from 450ml blood collection

IMUGARD III-RC Specification

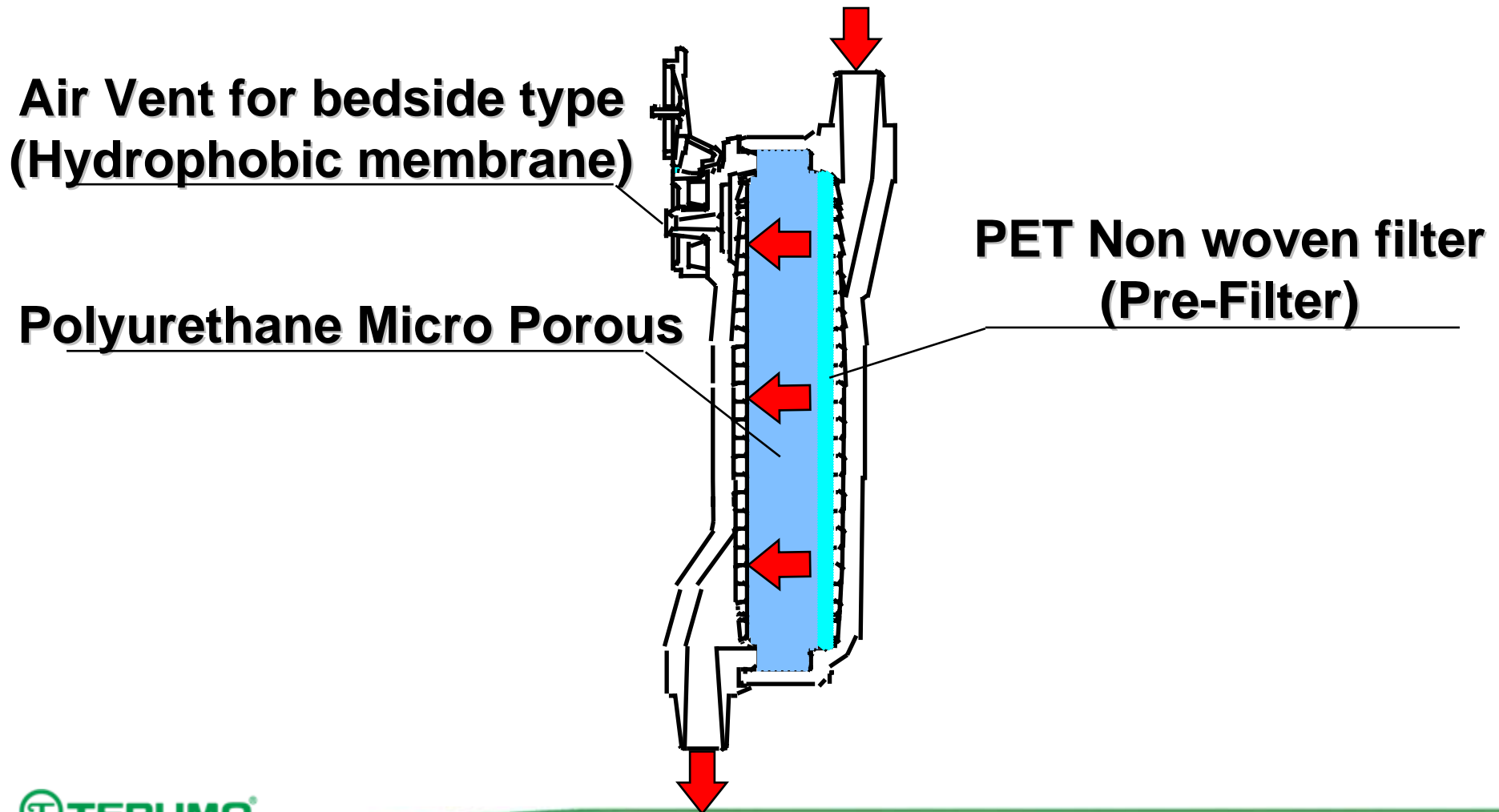
- Filter Material : **Micro Porous Polyurethane**
- Housing : **Polycarbonate**
- Dimensions : **93 mm x 70 mm x 15 mm**
- Priming Vol. : **38 ml**
- Air Vent : **0.2 um hydrophobic membrane**
- Sterilization : **Ethylene Oxide Gas**
- Capacity : **RBC 1 unit ***

* 1 unit : RBC derived from 450ml blood collection

IMUGARD III-PL Cross-Section



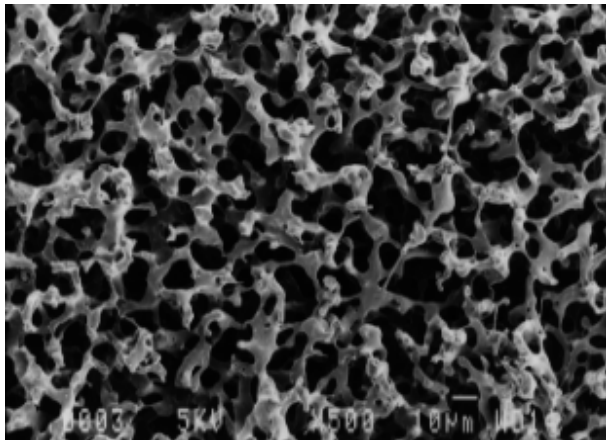
IMUGARD III-RC Cross-Section



IMUGARD III (PL/RC) Filtration Mechanism

IMUGARD III

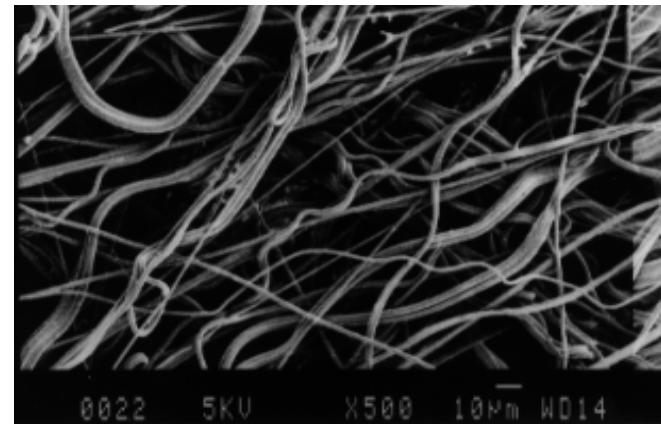
3-Dimensional structure
Trapping : “Sieve”



Polyurethane

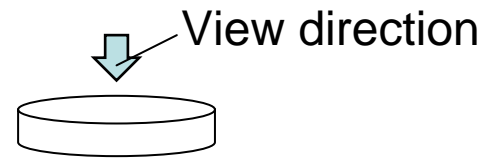
Competitors

2-Dimensional structure
Trapping : “Adhesion”

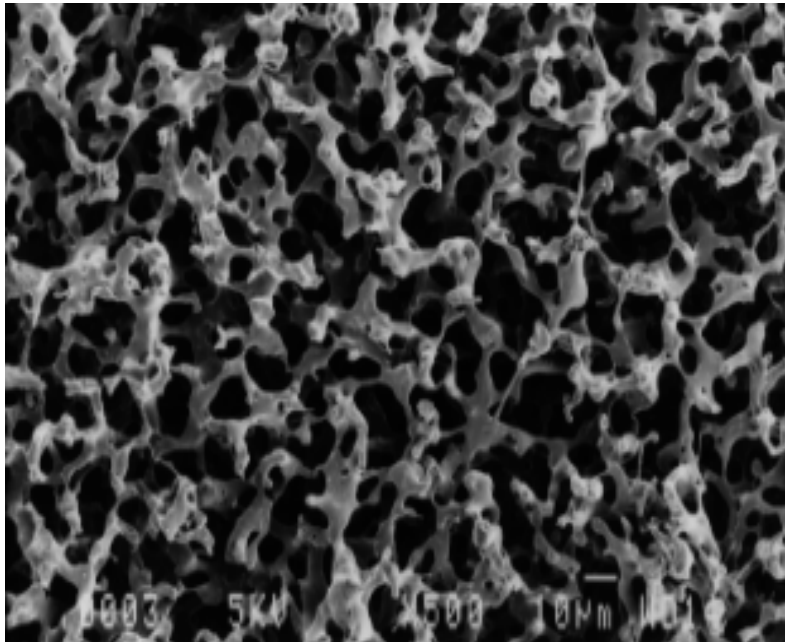


PET = Polyethylene Terephthalate

Difference : Filter material

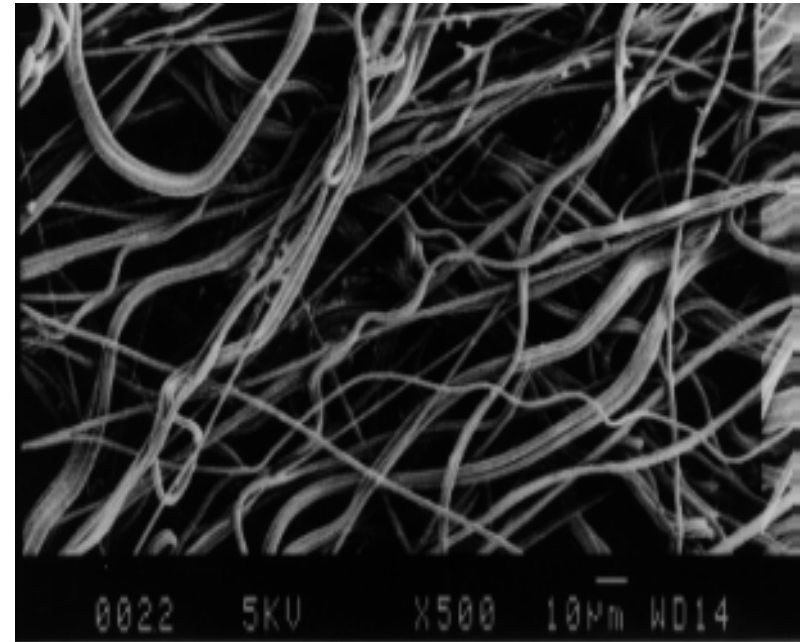


IMUGARD III



Polyurethane

Competitors



PET = Polyethylene Terephthalate

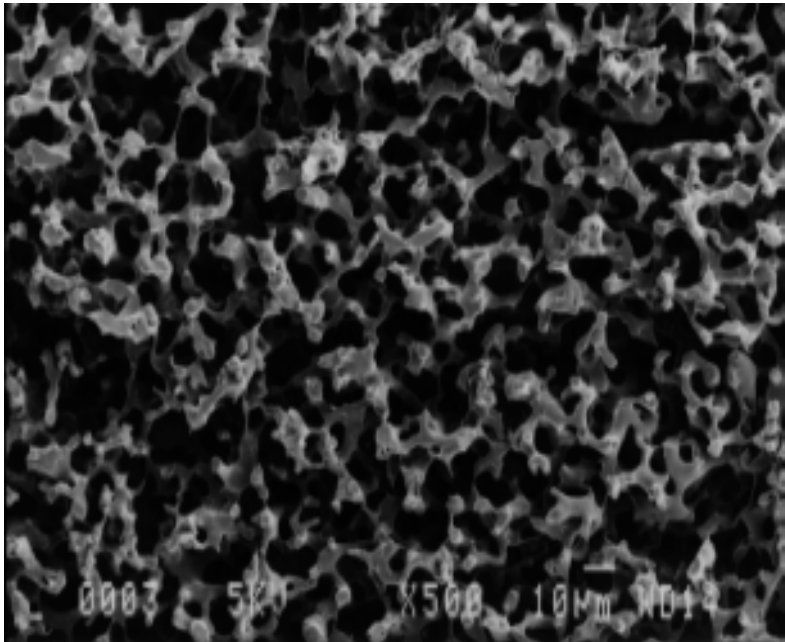
Difference : Filter material

View direction

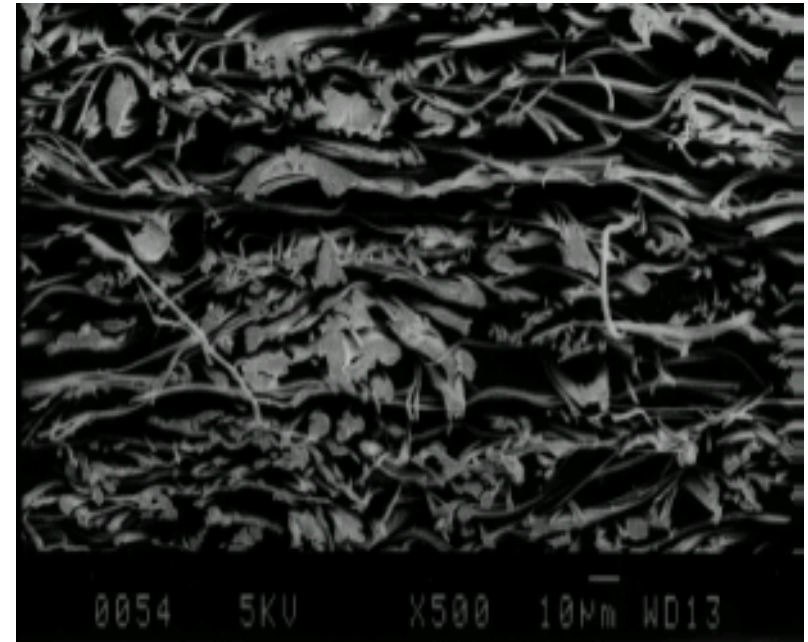


IMUGARD III

Competitors

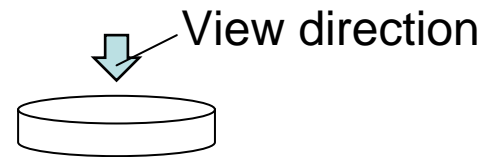


Polyurethane



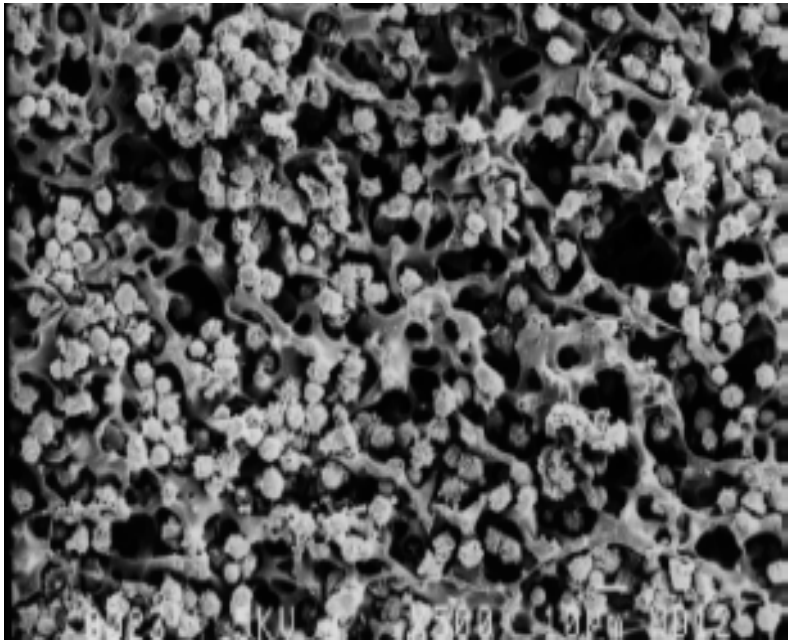
PET = Polyethylene Terephthalate

Post filtration

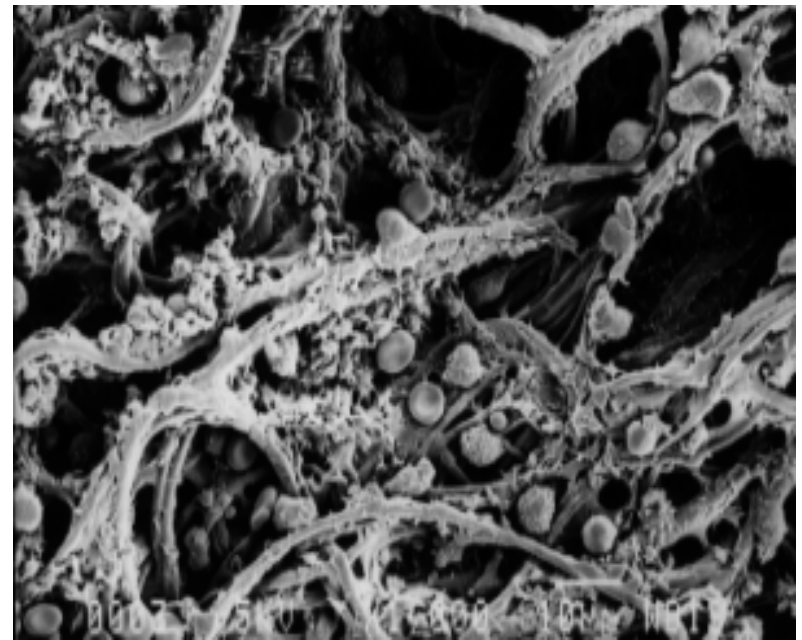


IMUGARD III

Competitors



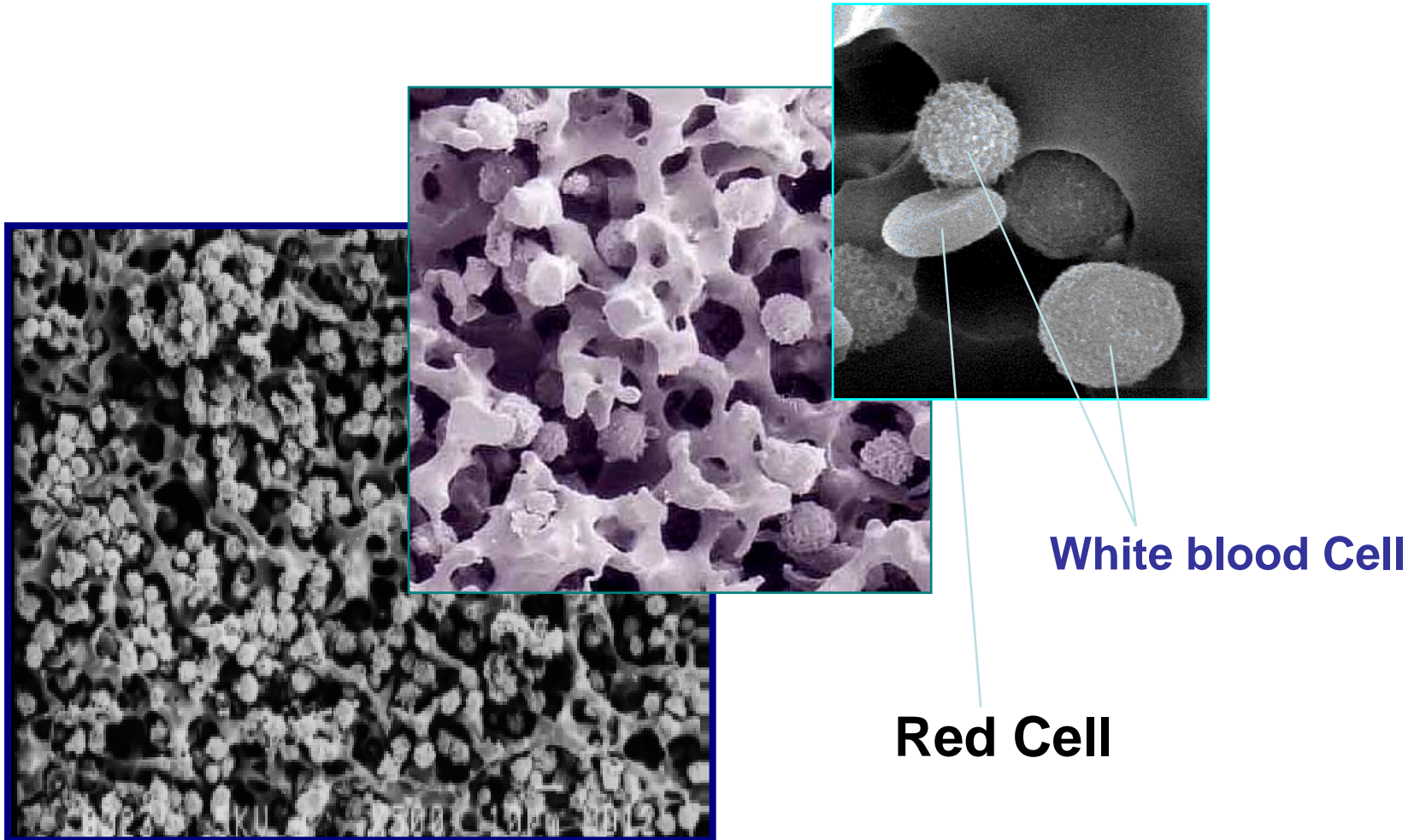
Polyurethane



PET = Polyethylene Terephthalate

Post filtration

IMUGARD III



IMUGARD III-PL Advantages

Thanks to Polyurethane material,

1. Superior recovery rate
2. High bio-compatibility

Comparison study of different type of filter

- Investigated the effects of surface treatment of filters on PLT function. 4 types of leukocyte reduction filter were used, namely negatively and neutral charged filters.

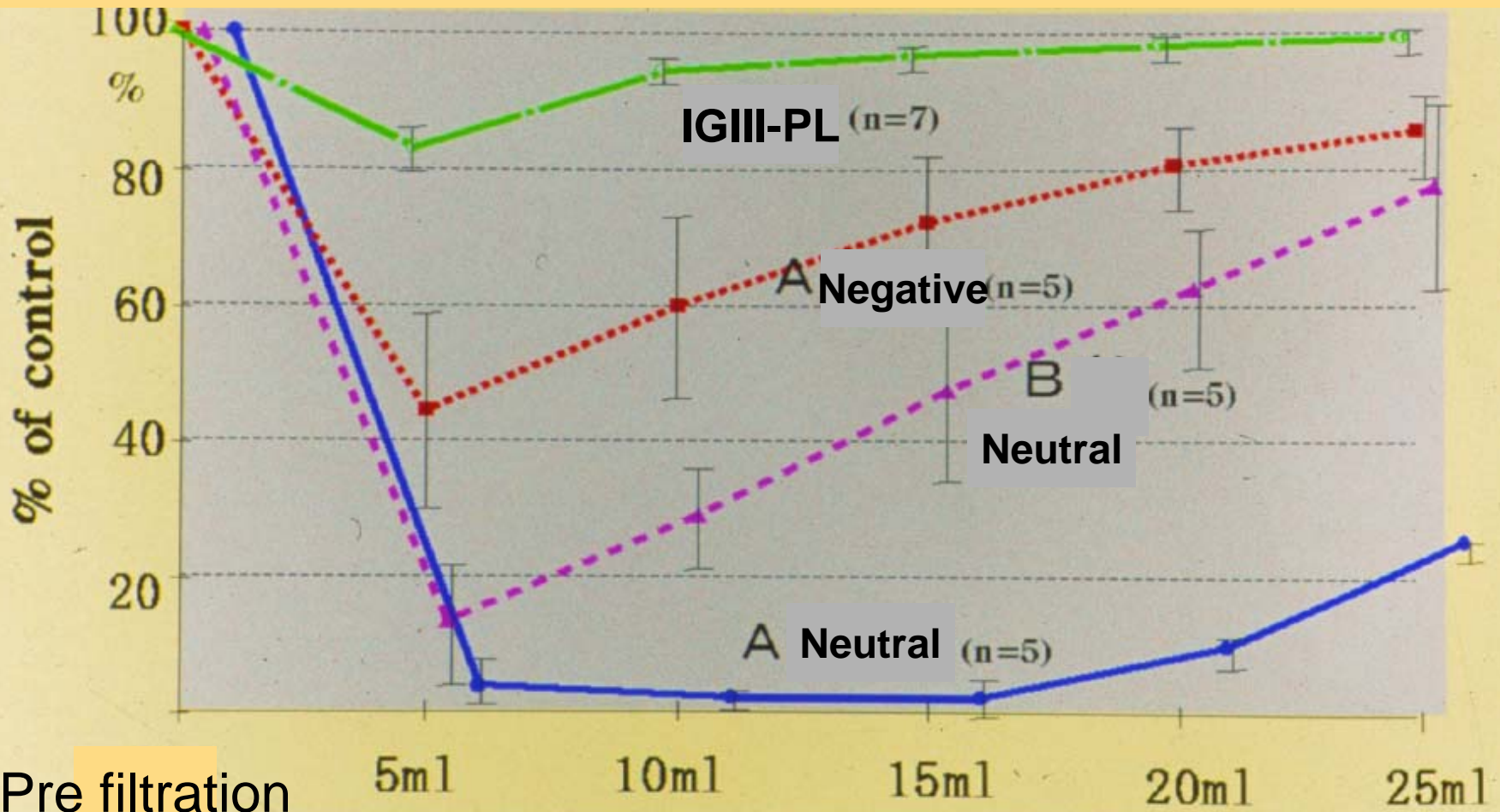
[Filters] (material; charge)

- Terumo IMUGARDIII-PL (PU; Neutral)
- A company (PET; Negatively)
- A company (PET; Neutral)
- B company (PET; Neutral)

[Result]

- Filter material and charge cause significant changes in PLT recovery and function, especially for first small portion of filtration.
- PU filters are superior to PET filters both negative and neutral charged in relation to PLT recovery and aggregation function.

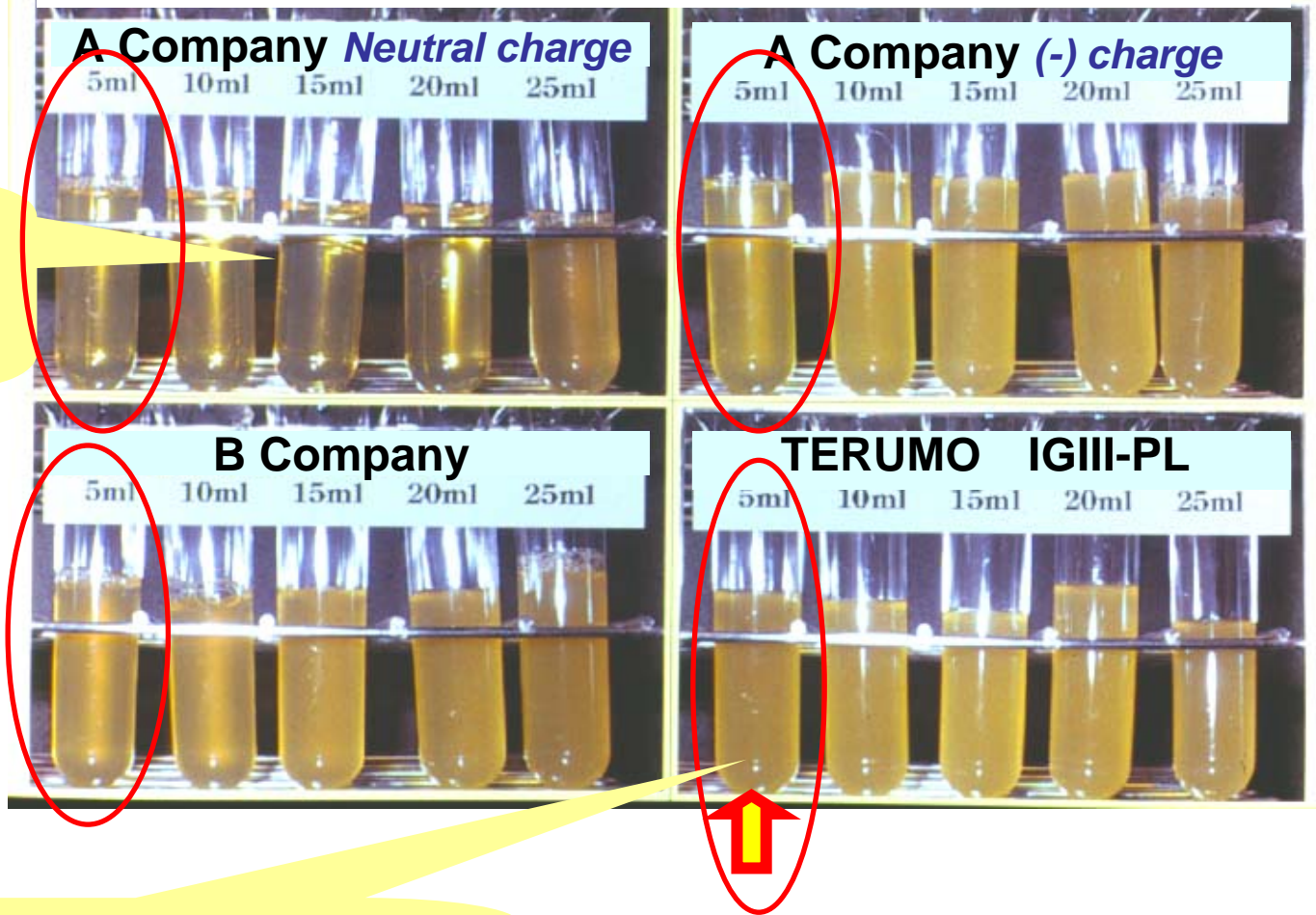
High Platelet Recovery



IGIII-PL shows higher PLT recovery from the beginning of filtration

Difference in appearance of PC after filtration by each filter

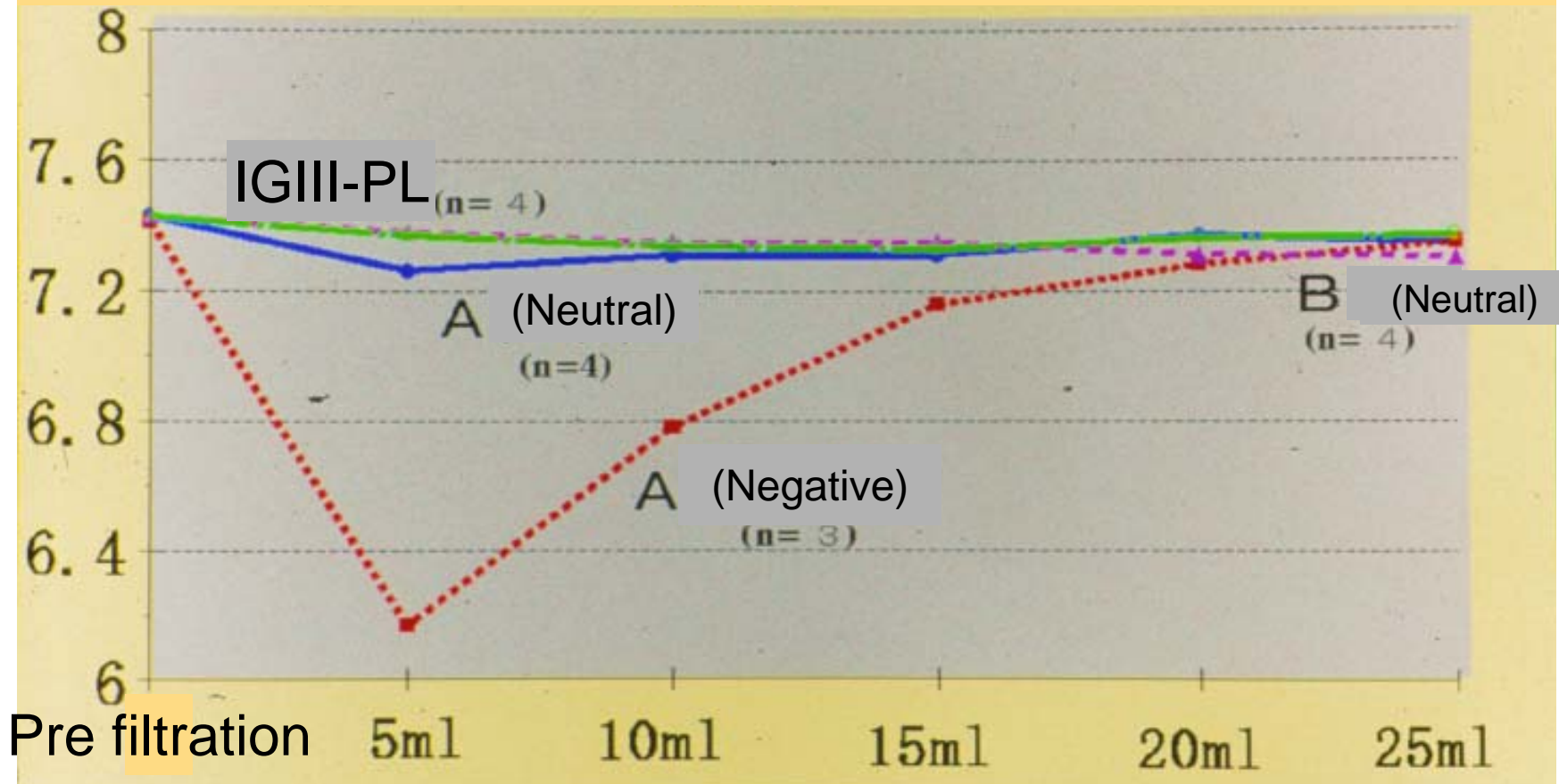
Transparent liquid
shows lower PLT
concentrate.



IGIII-PL can achieve higher PLT
recovery from the beginning of filtration

Ryo Kikuchi, Junichi Tsukada, and Hisahiro Sakamoto et.al, Platelet function in preservation and apheresis. 51th Japanese Transfusion Medicine Congress. Japanese Transfusion Medicine, Vol.49, No.2, 2003

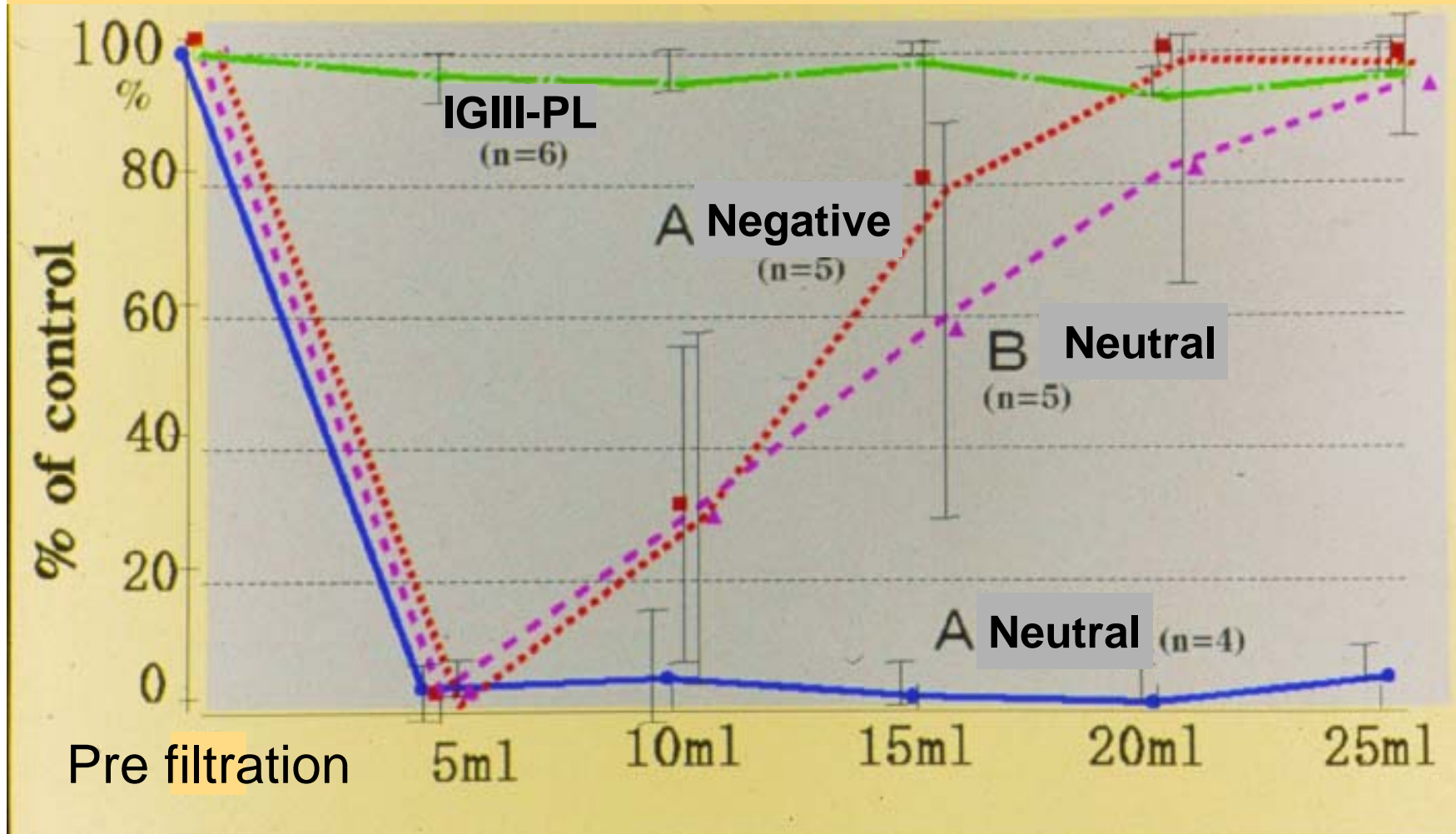
pH



Only A company's filter is negatively charged.

pH after filtrating with A filter fell at the beginning of filtration

IGIII-PL keeps ability of PLT aggregation

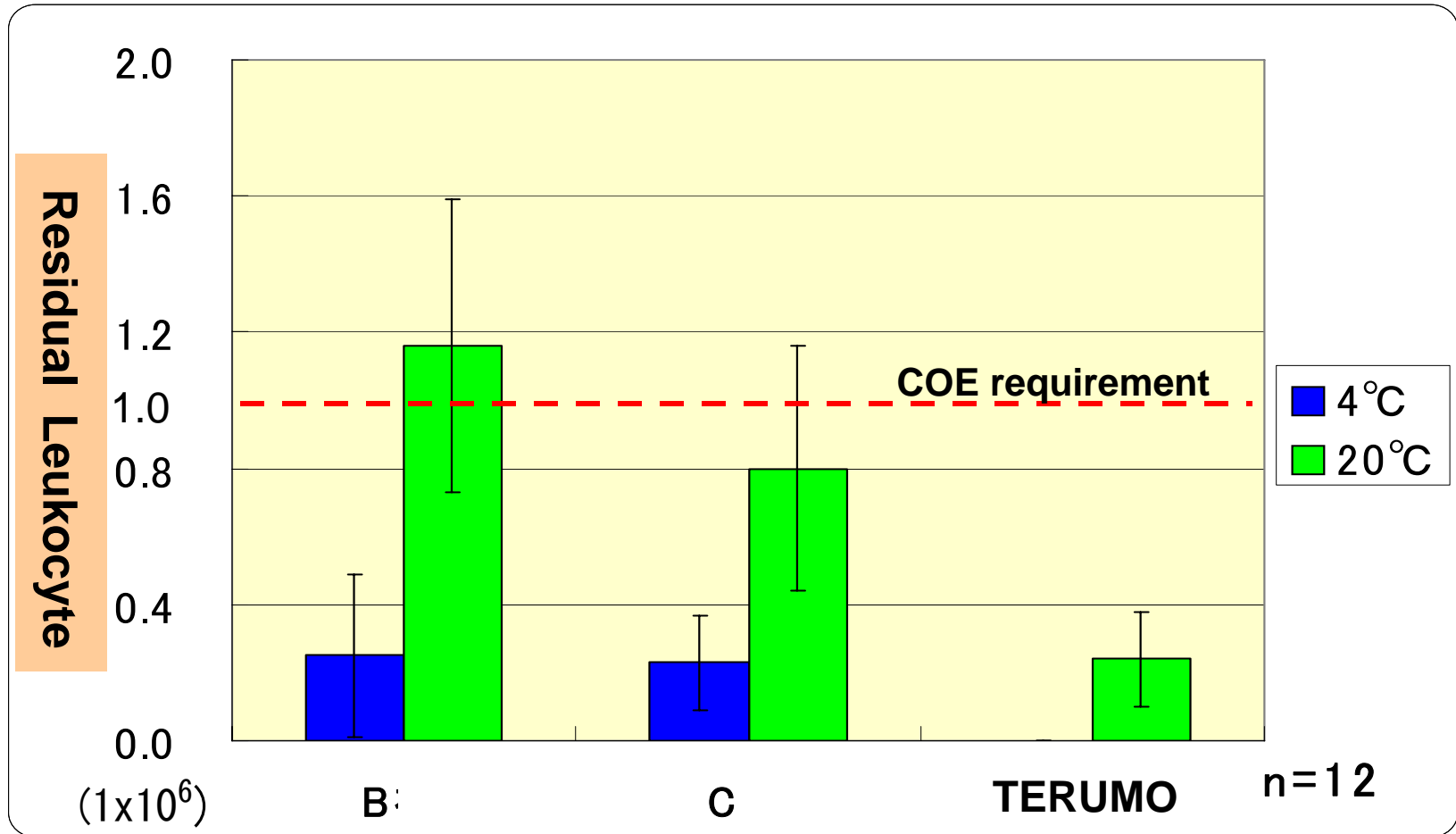


Ryo Kikuchi, Junichi Tsukada, and Hisahiro Sakamoto et.al, Platelet function in preservation and apheresis. 51th Japanese Transfusion Medicine Congress. Japanese Transfusion Medicine, Vol.49, No.2, 2003

IMUGARD III-RC Advantages

- 1 : Stable performance even in room temperature.
- 2 : Easy priming / recovery

Effect of blood temperature on WBC reduction



No data shown for 4°C with TERUMO filter in the original article.

IMUGARD at room temperature well conforms to the COE requirement.

Six filters for the removal of white cells from red cell concentrates, evaluated at 4 °C and/or at room temperature P.F.van der Meer et al., Transfusion 1999;39:265-270



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