Principles of Blood Separation and Apheresis Instrumentation

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Apheresis History
Apheresis History
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Apheresis

- From the Greek - “to take away”
- Blood separation
  - Donor apheresis
  - Therapeutic apheresis
Principles of Blood Separation

- Filtration
- Centrifugation
- Combined centrifugation and filtration
Membrane Separation

- Blood is pumped through a membrane with pores allowing plasma to pass through whilst retaining blood cells.
- Available as a hollow fiber membrane (older devices used parallel-plate membranes)
- Pore diameter for plasma separation: 0.2 to 0.6μm.
- A number of parameters need to be closely controlled
Detail of Membrane Separation

Figure 1-15. Comparative sizes of blood components. Note the large size difference between the largest plasma constituent and the smallest cellular elements. (Courtesy of Gambro BCT, Inc.)
Membrane Blood Separation
Trans Membrane Pressure (TMP)

Too High = Hemolysis
TMP Too Low = No Separation
Optimal TMP = Good Separation
Membrane Apheresis in the US

- PrismaFlex (Gambro – Baxter)
- NxStage
- BBraun
Filtration vs. Centrifugation Apheresis

**Filtration**

- Minimal availability in the USA
  - Poor industry support
- Limited to plasma exchange
  - Low efficiency

**Centrifugation**

- The standard in the USA
  - Very good industry support
- Multiple procedures (cytapheresis)
  - Opportunity to provide cellular therapies
# Centrifugation vs. Filtration Apheresis

<table>
<thead>
<tr>
<th></th>
<th>Centrifugation Apheresis</th>
<th>Filtration Apheresis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Flow</td>
<td>10 – 100 ml/min</td>
<td>150 ml/min</td>
</tr>
<tr>
<td>Efficiency of Plasma Removal</td>
<td>60 – 65%</td>
<td>30%</td>
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</tbody>
</table>
Apheresis in Clinical Practice and Blood Banking

- Sickle Cell Disease
- Falciparum Malaria
- Thrombocytosis
- Leukemias
- Cell Therapies
- TTP-HUS
- Guillain Barre Syndrome
- Myasthenia Gravis
- CIDP
- Autoimmune Renal Disease
- Hyperviscosity Syndromes
Centrifugal Separation

- Based on the different specific gravity of the blood components.
- In some instruments, also based on the cellular size (Elutriation).
- All apheresis devices need to be able to control the Separation Factor.
Separation by Specific Gravity

Platelets (1040)

Lymphocytes (1050-1061)

Monocytes (1065 - 1069)

Granulocyte (1087 - 1092)

RBC
Separation Factor (SF)

- Is a combination of **centrifugal acceleration** (g) and **centrifugation time** (dwelling time)
  - *Or also*

- The “centrifugal experience” that determines the degree of cell separation and sedimentation

- A.K.A. **Packing Factor** (same concept, different units)
G and SF correlate if dwelling time or inlet flow are constant.
Current Separation Technology

- Plasma
- Buffy Coat
- RBC

- Lymphocyte
  - B-cells
  - T-cells
- NK cells
- Stem Cells
- Dendritic cells
Elutriation

Centrifugal force

Fluid

Centrifugal force

Cells
Centrifugal Separation

**Discontinuous**

- Blood is processed in batches of a size that can be tolerated by the subject.
- Once the separation of that blood is completed, the separation chamber must be emptied to repeat the process (cycle) again.
- Large extracorporeal volume (ECV).
- Pediatric tubing sets (with smaller ECV) must be used with small patients.

**Continuous**

- Blood is processed and separated in a continuous way.
- Once the tubing set is primed, the separation chamber is not emptied till the end of the process.
- Medium – small ECV.
- No pediatric tubing sets are necessary; instead, a blood prime is performed with smaller patients.
Centrifugal Apheresis Systems

- Intermittent / Discontinuous Flow
  - **Haemonetics**: PCS-2, MCS+ 8150 and 9000, Cymbal
  - Therakos UVAR-XTS

- Continuous Flow
  - **TerumoBCT**: COBE Spectra, Trima, Trima Accel, Spectra Optia
  - **Fenwal (Fresenius Kabi)**: Amicus, Alyx.
  - **Fresenius Kabi**: AS 104, Com.Tec
**Latham bowl; Plasma (and RBC) collection process**

**HOW THE BOWL WORKS**

1. Whole blood is pumped down the feed tube and enters the bowl at the bottom.

   ![Diagram](image1)

   Anticoagulated Whole Blood → Air

2. Centrifugal force spins the denser cellular components to the outside, leaving plasma in the inner band.

   ![Diagram](image2)

   Anticoagulated Whole Blood → Plasma

3. When the bowl is full, plasma flows out of the effluent tube into the collection bag.

   ![Diagram](image3)

   Anticoagulated Whole Blood → Plasma

4. After the draw is completed, the bowl stops spinning and RBCs are pumped up through the feed tube and returned to the donor or transferred to an RBC storage bag or reservoir bag.

   ![Diagram](image4)

   Packed Red Cells → Air

Courtesy of Haemonetics Corp.
Haemonetics Devices

PCS 2

MCS+

Cymbal

Courtesy of Haemonetics Corp.
TerumoBCT

• COBE Spectra
  • Platelet collection & depletion (*ELP, ELP LRS*) (DN, SN)
  • Plasma Exchange (*TPE*) (DN, SN)
  • WBC collection and depletion (DN)
    • Mononuclear Cells (*MNC, AutoPBSC*)
    • Granulocytes (*PMN*)
  • RBC exchange and depletion (*RBCX*) (DN)

• Trima and Trima Accel
  • Platelet, Plasma and RBC (dRBC) collection (SN)

• Spectra OPTIA
  • TPE
  • Cytapheresis
    • *RBCX, MNC collections, PLT collection*
Trima

Courtesy of CaridianBCT
COBE Spectra

- Launched in the US in 1988
- FDA cleared for all standard apheresis procedures, including Plt collection and TPE in SN.
- Bone Marrow Processing protocol
- Continuous Flow device
- Automated AC management system
- Based on IBM technology
- Weight 385 Lbs.

Courtesy of CaridianBCT
Spectra OPTIA

- Launched in the US in 2007
- Will ultimately replace the COBE Spectra for all therapeutic procedures.
- FDA cleared for TPE and MNC collections; all-new software & disposable.
- Will do all procedures with two disposables and one filler.
- AIM System
- Touch screen
- Weight 202 lbs.
- Connectable to external printer or computer.

Courtesy of CaridianBCT
Fenwal (Fresenius Kabi)

- **Amicus**
  - Platelet & plasma collection (DN, SN; +1 concurrent RBC in SN as an option)
  - MNC collection (DN)
  - TPE

- **Alyx**
  - Double RBC & plasma collection (SN)

Courtesy of Fenwal, Inc.
Fenwal Amicus® Separator
TPE and MNC Procedures

• Conserves patient platelets

• Automated interface control system

• Operator ease of use
Aurora (Auto-C), Fenwal

Automated plasma collection

Uses both centrifugation and membrane technology

Used extensively in plasma collection centers
Blood Banking Instrument Choices
TA Instrument Choices
Double Filtration
(Cascade Plasmapheresis)

• First filter
  – Separates plasma from whole blood

• Second filter
  – Removes a specific plasma component
Double Filtration (Cascade Plasmapheresis)

Whole blood

Plasma filter

2nd filter

Cells
Specific Removal of Substances from Plasma

Immunoadsorption

Protein A

IgG
Kaneka LDL Apheresis
• **Liposorber LA-15** column
• **Plasma Separator MA-01**

*Plasma is removed with a hollow fiber membrane device (MA-01).*

*Plasma is subsequently filtered with the LA-15 column that keeps the LDL cholesterol by selective adsorption, then returned to the patient.*

*Most HDL cholesterol is returned to the patient in the filtered plasma.*
Kaneka MA - 03
**H.E.L.P. System**

- **Heparin-induced Extracorporeal LDL Precipitation**
- Plasma is removed by membrane filtration.
- Heparin in an acid Acetate solution (pH 4.85) is added, causing a selective precipitation of LDL cholesterol.
- The LDL precipitate is removed by filtration and finally, plasma is returned to the patient after being ultra-filtered and dialyzed.
H.E.L.P.
The Therakos® Photopheresis Process

1. Whole blood drawn and separated via centrifugation.
2. Plasma and RBCs immediately returned to patient.
3. Leukocyte (WBC) enriched Buffy Coat isolated and collected.
4. Methoxsalen added to Buffy Coat and exposed to UVA light.
5. Photoactivated Buffy Coat returned to patient.

Therakos® Photopheresis delivers photopheresis therapy in a single, integrated device.
THERAKOS® CELLEX® Photopheresis System

Physical Dimensions
- Dimensions (Height x Width x Depth)
  - 163 cm x 58.4 cm x 79 cm
  - 64 in x 23 in x 31 in
- Working Height
  - 84 cm (33 in) from floor to pump deck surface
- Weight
  - 155 kg (341 lb)
- Recommended Operating Surface
  - 25.4 cm (10 in) clearing on all sides
Treatment Times

Instrument Mean Treatment Times (min)

<table>
<thead>
<tr>
<th>Instrument</th>
<th>DNM-SNM*</th>
<th>SNM</th>
<th>DNM</th>
</tr>
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<tbody>
<tr>
<td>CELLEX</td>
<td>108</td>
<td>103</td>
<td>74</td>
</tr>
</tbody>
</table>

DNM=double-needle mode; SNM=single-needle mode.

*Started DNM and converted to SNM.

Additional Information

• Principles of Apheresis Technology, ASFA 2014
• Ed Burgstaler presentation at ASFA 2015
• dkiprov@DobriKiprov.com
• www.Apheresis101.com
Dali (removes LDL from whole blood)
Protein A Columns (ProSORBA)
Multifunctional

Major Applications

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Myasthenia Gravis</td>
<td>Guillain-Barré Syndrome</td>
<td>Chronic Inflammatory Demyelinating Polyneuropathy</td>
<td>Multiple Sclerosis</td>
<td>Systemic Lupus Erythematosus</td>
</tr>
<tr>
<td>Pemphigus</td>
<td>Pemphigoid</td>
<td>Stevens-Johnson Syndrome</td>
<td>Familial Hyperlipidemia</td>
<td>Thrombotic Thrombocytopenic Purpura</td>
</tr>
<tr>
<td>Arteriosclerosis Obliterans</td>
<td>Severe Blood-type Incompatibility Pregnancy</td>
<td>Primary Macroglobulinemia</td>
<td>Glomerulosclerosis</td>
<td>Allergic Renal Transplantation</td>
</tr>
<tr>
<td>Fulminant Hepatitis</td>
<td>Acute Hepatic Failure</td>
<td>Toxic Epidermal Necrolysis</td>
<td>Postoperative Hepatic Failure</td>
<td>Ulcerative Colitis</td>
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<td></td>
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<td>Crohn's Disease</td>
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Plasma Exchange (PE)

Plasmaphlo™

Double Filtration Plasmapheresis (DFPP)

Plasmaphlo™

Plasmaphlo™

Cascadeflo™ Rheofiltes™

Leukocytapheresis (LCAP)

Cellsorba EX™

Plasmaphlo™

Plasmaphlo™

Immurosorba™ Plasorba™

Plasmaphlo™
Removes LDL from whole blood