Specification of Plasma Fractionator Evaflux 2A

Model		2A10	2A20
Hollow fiber	Material	Ethylene vinyl alcohol copolymer	
	Inner diameter	175 μm	
	Wall thickness	40 μm	
Housing	Material	Polycarbonate resin	
	Membrane surface area	1.0 m^2	2.0 m^2
	Outer dimension	45 ϕ x 280 L mm	57 ϕ x 280 L mm
Priming volume	Outside hollow fibers	Approx. 85 mL	Approx. 108 mL
	Inside hollow fibers	Approx. 82 mL	Approx. 150 mL
Filled liquid		Sterile water	
Sterilization method		Gamma-ray irradiation	

2A10

2A20

Note

*Please read instructions carefully when using the product.

*Evaflux™ is a trademark of SB-KAWASUMI LABORATORIES, INC.

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CE 0123

MANUFACTURER

SB-KAWASUMI LABORATORIES, INC.

3-25-4 Tonomachi, Kawasaki-ku, Kawasaki-shi, Kanagawa 210-8602, Japan

TEL +81-44-589-8070 URL www.sb-kawasumi.jp

Authorised representative in the European community

MPS Medical Product Service GmbH

Borngasse 20 35619 Braunfels Germany

Manufacturing facility

Kawasumi Laboratories (Thailand) Co., Ltd.

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SB-KAWASUMI

Therapeutic Plasmapheresis in autoimmune neurological disorder using Plasma Fractionator Evaflux™

New treatment option for drug refractory cases or crisis stage

SB-KAWASUMI LABORATORIES, INC.

What is autoimmune neurological disorders ?

Autoimmune neurological disorders are believed to be inhibition of tissue due to antigen-specific autoimmune response which targets central nervous system, peripheral nerves and neuromuscular junction.
Clinical conditions are mainly divided into “primarily antibody mediated” and “T-cell mediated”, and other substances like cytokines, chemokines, immune complex and adhesion molecules are also considered to be involved.

Autoantibody targets in autoimmune neurological disorders

Autoimmune neurological disorder	Clinical condition	Target	
Myasthenia Gravis (MG)	Autoimmune disease of the neuromuscular junction	① anti acetylcholine receptor (AChR) antibody ② anti muscle specific receptor tyrosine kinase (MusK) antibody	① IgG_1, IgG_3 ② IgG_4
Guillain-Barré Syndrome (GBS)	Acute progressive paralyzing illness affecting both motor and sensory peripheral nerves Autoimmune disorder of ganglioside of myelin sheath (spontaneous recovery in most patients)	anti ganglioside antibody	IgG_1, IgG_3 IgM, IgA
Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)	Autoimmune disorder of ganglioside of myelin sheath (progress and relapses for over two or more months)	anti ganglioside antibody	IgG_1, IgG_3 IgM, IgA
Multiple Sclerosis (MS)	Autoimmune disorder of central nervous system white matter demyelination involved by cellular immunity	anti myelin basic protein (MBP) antibody, anti myelin oligodendrocyte glycoprotein (MOG) antibody, etc.	IgG_1,IgM
Neuromyelitis Optica (NMO) / Devic' syndrome	Autoimmune disorder of optical nerve and spinal cord involved by humoral immunity	anti aquaporin 4 (AQP4) antibody	IgG_1
Lambert-Eaton syndrome Myasthenic Syntrome (LEMS)	Autoimmune disorder of the neuromauscular junction and nerve ending	anti voltage-gated calcium channel (VGCC) antibody	IgG_1

New treatment option: Therapeutic Plasmapheresis in autoimmune neurological disorders

Therapeutic Plasmapheresis is a method for removing pathogenic antibodies from patients' blood. In autoimmune neurological disorders, it is generally performed when drug therapy is not effective, or in acute exacerbation stage to normalize or to improve the symptoms.

What is the benefit of Therapeutic Plasmapheresis in autoimmune neurological disorders ?

- **Shorten remission time**
  → reduce residual disability and hospital stay
- **Reduce dosage (steroid etc.)**
  → alleviate adverse side effect
- **Apply to drug refractory cases or to patients who can not tolerate**
- **When immediate effectiveness is needed (e.g. crisis stages)**

What is Double / Cascade Filtration ?

Double/Cascade Filtration is one of the Therapeutic Plasmapheresis methods.

It's principle is to selectively deplete a plasma fraction that contains disease associated high molecular weight substances and to reduce or eliminate the requirement for substitution fluid such as albumin.

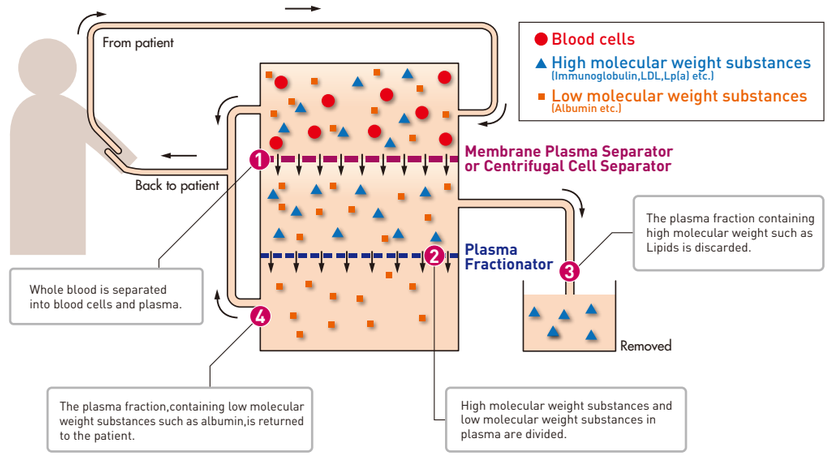
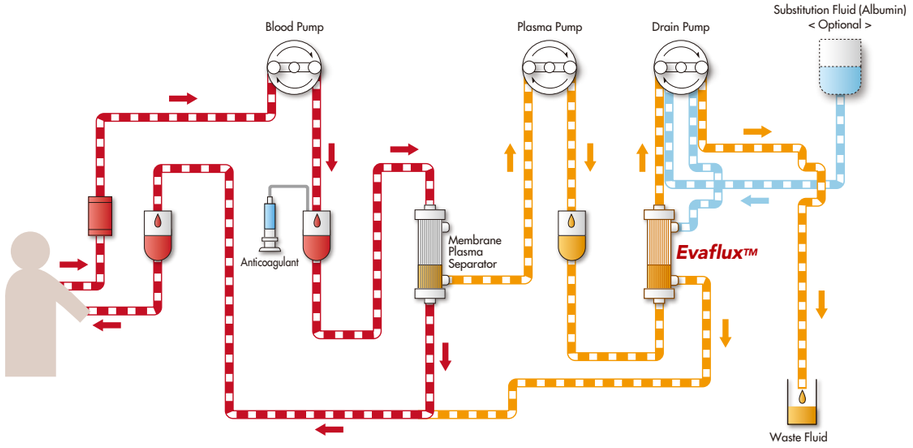


Fig 1: Principle of Double / Cascade Filtration
(Conceptual diagram was proposed by Prof.Agishi)

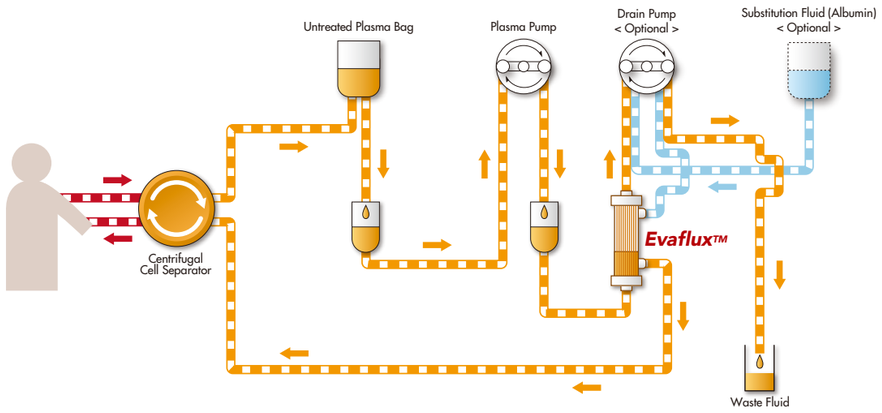
*Therapeutic Apheresis 4 (1):29-33, 2000

Flow Diagram of Double Filtration Plasmapheresis (DFPP)



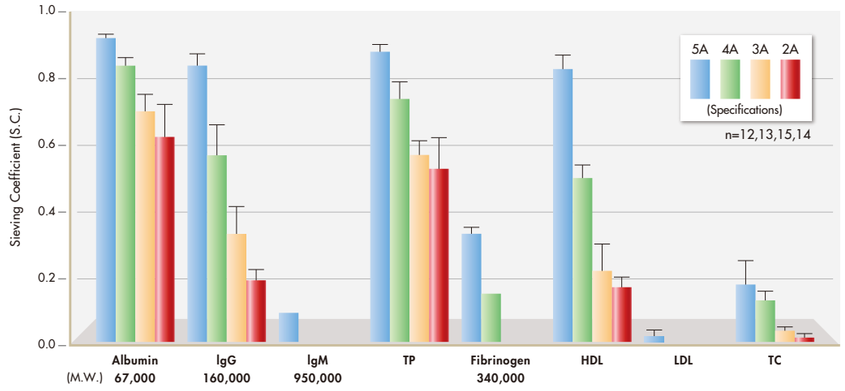
Flow Diagram of Cascade Filtration (CF)

[in combination with Centrifugal Cell Separator]



Performance of Plasma fractionator Evaflux™

- Selective from 4 different pore sizes according to diseases -

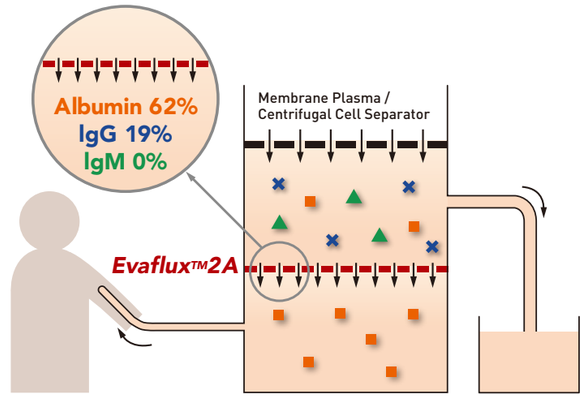


S.C.is a parameter indicating the membrane permeability at a certain point.

Fig 2: Sieving Coefficient of "Evaflux"
(When 1,000 ml of plasma was processed)

Evaflux™ 2A can remove Immunoglobulins while allowing Albumin to be returned

Evaflux™ 2A	Alb. ■	IgG ✖	IgM ▲
S.C.	0.62	0.19	0.00



Clinical effects of DFPP: Guillain-Barré Syndrome

Controll study of 12 patients with GBS, who have quadriparesis and unable to stand unaided .

(* T. Jyoichi et al, Clin. Neurol., 27:479-486, 1987)

Plasmapheresis-pulse therapy group	n=6	Received DFPP followed by pulse therapy [DFPP] 1 – 3 times (every 7 days) per patient, using Evaflux 2A [Pulse therapy] methylprednisolone 1,000mg/day
Supportive care group	n=6	Only rehabilitation

Effect on clinical condition improvement

→ In plasmapheresis-pulse therapy group, 5 of 6 patients improved to the point able to walk, although in supportive care group only 1 of 6 patients could.

Fig 3: Clinical course of the both groups

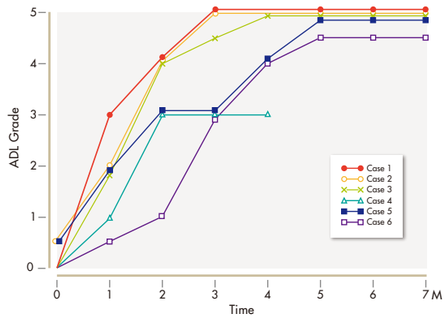


Fig 3a: plasmapheresis-pulse therapy group

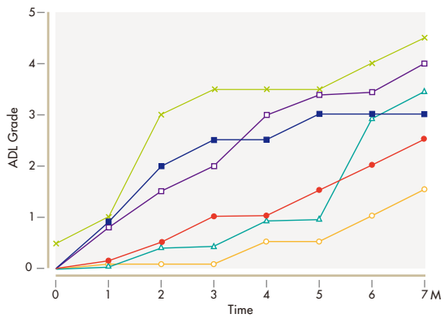


Fig 3b: supportive care group

< Grading Scale for ADL >

0: Bedridden	3: able to walk with aid
1: Able to stand with support	4: Unstable walk with effort
2: Able to stand without support but unable to walk	5: Normal

Effect on serum immune factors

→ Immunological suppression were observed in all the patients with Plasmapheresis-pulse therapy.

Fig 4: Difference of serum immune factors pre and post DFPP in plasmaphereis-pulse therapy group