TERUMO BLOOD AND CELL TECHNOLOGIES

Therapeutic Plasma Exchange

Technology Overview

Spectra Optia™ Apheresis System

Centrifugal therapeutic plasma exchange (cTPE)

The Spectra Optia system and other cTPE systems use differences in the specific gravity and sedimentation velocity of blood cells and plasma to separate specific blood components. Red blood cells (RBCs), white blood cells (WBCs), and platelets are centrifuged to separate components into layers, allowing plasma to be removed and replaced. Because the plasma is not filtered, there is no preferential removal of small proteins. With continuous flow centrifugation, blood is continuously added into the centrifuge; blood cells are separated from plasma, mixed with replacement fluid, and returned to the patient.[1]

Membrane therapeutic plasma exchange (mTPE)

In mTPE, a membrane filtration system (membrane system) is used to separate blood components based on differences in particle size. The plasma is separated from the cellular elements by pumping whole blood through a filter that allows plasma to pass through but retains blood cells. Depending on the characteristics of the membranes, there is differential removal of proteins based on size. The majority of modern membrane filters use hollow-fiber technology, which offers a greater filter surface area than the older parallel-plate technology.[1]

Therapeutic plasma exchange (TPE) with secondary plasma processing

TPE with secondary plasma processing (also known as online plasma processing or plasma regeneration) has become common for some disease indications. It is used with both centrifugation and membrane systems by adding a secondary plasma processing device to the primary plasma separation device. The process of TPE first separates plasma from a patient's blood and then, in a second step, secondary plasma processing is performed. In this step, the plasma is passed through a column-shaped device containing either a membrane filter (cascade or double-filtration plasmapheresis) or an adsorption matrix (adsorption or immunoadsorption plasmapheresis) that provides selective removal of targeted disease mediators. The treated plasma is then returned to the patient.[2,3]

Table 1: Spectra Optia system and membrane plasmapheresis distinctions

Attributes	Spectra Optia System	Membrane Systems	Benefits
Procedure time			
Setup and priming	11 minutes[4,5]	23 to 40 minutes[5,6]	The setup and priming time for mTPE differs depending on the device (can take up to 40 minutes) and is longer than 11 minutes.[4-6]
Time to exchange 1 L of plasma	24.5 to 33 minutes[5,6,8] Median of 30.6 minutes with a minimum of 10.7 minutes[7]	36 to 37 minutes[5,6,8]	The total procedure time depends on the amount of plasma volume exchanged, which is influenced by the hematocrit (Hct), the total blood volume of the patient, and the clinician's choice. Procedure time is directly related to plasma removal efficiency (see next row).
Plasma removal efficiency	80% to 87%[5,8-12]	27% to 53.2%[2,5,8]	▪ Plasma removal efficiency (PRE) represents the volume of plasma that can be removed per volume of plasma that is processed by a specific device[5,9]; PRE = (Plasma removed/Plasma processed) × 100. ▪ Because centrifugal systems are more efficient than membrane systems, they remove 2 to 3 times more plasma per volume of whole blood processed. This allows for shorter procedure times and/or lower whole blood flow rates as desired.[2,8] ▪ In general, higher blood flow rates are used on mTPE devices, which can partially compensate for the plasma removal efficiency.[5]
Blood flow rate and access			
Inlet/blood flow rate	Inlet flow rate up to 142 mL/min For small patients, a flow rate of 5 mL/min or less can be used.	mTPE procedures require blood flow rates of at least 40 mL/min (depends on the filter type used).[13]	
Access	Multiple venous access options: ▪ Peripheral venous access ▪ Central venous catheter (CVC) ▪ Arteriovenous (AV) fistula or AV graft ▪ Implanted ports Lower blood flow rates can be supported via peripheral venous access on the Spectra Optia system, making the procedure less invasive if needed.	Multiple venous access options: ▪ Peripheral venous access ▪ Central venous catheter (CVC) ▪ Arteriovenous (AV) fistula or AV graft ▪ Implanted ports mTPE devices require higher blood flow rates (see above) so it is often advised to use venous access through a CVC for a successful TPE procedure with this type of device.[14]	▪ The Spectra Optia system allows a single- or dual-needle option. If venous access or one of the lines of the catheter is compromised, the Spectra Optia system provides the option to perform the procedure with only single-needle access. ▪ TPE with peripheral venous access instead of CVC reduces the risk of infection up to 80%.[2,14,15]
Anticoagulant	Citrate	Heparin in most cases, but citrate is often in the replacement fluid.	▪ Because citrate anticoagulates the extracorporeal circuit in cTPE procedures, citrate-induced adverse events (which occur during 0.08% to 1.2% of procedures)[16] tend to be mild and self-limiting. These adverse events may be treated with prophylactic calcium.[14,17] ▪ Heparin-induced adverse events are rare but serious: ▪ Because citrate is neutralized as soon as it mixes with systemic blood, there is no systemic bleeding risk as there is with heparin.[18] ▪ Heparin-induced thrombocytopenia occurs in 0.5% to 5% of procedures.[14,17,19]

			▪ The half-life of citrate in the blood of a patient with normal renal and hepatic functionality is around 36 minutes.[20] For heparin, the half-life in the human system is 30 to 150 minutes, depending on the dose infused to the patient.[21] ▪ The Spectra Optia system regulates the rate of citrate infusion to minimize hypocalcemia. ▪ When citrate is used with a membrane system, citrate toxicity is more likely because more citrate is needed in proportion to the higher flow rate and larger volume of blood processed.[2]
Clotting	No clotting event resulting in premature ending of a procedure or obliged use of an additional tubing set has ever been reported on the Spectra Optia system in the peer-reviewed literature.	High frequency of filter clotting. Clotting events resulting in premature ending of a procedure or obliged use of an additional tubing set have been observed in 7% to 33% of the procedures in five separate reports and studies.[5,6,8,22,23]	Filter clotting in mTPE is very time-consuming and results in patient inconvenience and/or premature ending of the procedure. Alternatively, it may require the use of an additional (part of a) tubing set. In some studies, an average of up to 50% additional tubing sets per procedure has been reported.[6] This results in higher cost.

Table 2: General comparison of adverse events between the two types of procedures

Attributes	Centrifugal Systems	Membrane Systems	Benefits
Adverse events (in % of procedures with reported adverse events)	6%[24]	11%[24]	▪ Therapeutic plasma exchange, like other therapeutic treatments, is associated with a low occurrence of adverse events.[24,25] Adverse events related to access, fluid balance, immune reactions, and infection are common to cTPE and mTPE devices. While hemolysis can occur with both cTPE and mTPE, hemolysis related to high transmembrane pressure is seen only in mTPE procedures.[6,26] ▪ Filters cannot exceed certain maximum transmembrane pressure requirements per manufacturer recommendation; if the recommended requirement is exceeded, fibers may rupture, resulting in blood contamination of the plasma.[27] ▪ Possible bleeding[16] and complement activation have also been described only in mTPE and not in cTPE.[28,29]

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