Literature Review on Spectra Optia® Apheresis System Therapeutic Plasma Exchange (TPE)

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TERUMO BLOOD AND CELL TECHNOLOGIES

Introduction

TPE is a non-pharmacological treatment that removes a large volume of a patient's plasma after separating it from the cellular components of the blood. The plasma removed is concomitantly replaced with appropriate fluids.[1,2,3,4,5] For TPE to be an effective therapy, a disease or disorder must be induced and/or exacerbated by a pathological substance that can be effectively removed with the plasma in order to reduce symptoms. TPE is used to remove or decrease the level of circulating antibodies, antigen-antibody complexes, cytokines, abnormal plasma proteins, cholesterol, metabolic waste products, and plasma-bound toxins and drugs.[2,4,6,7,8,9,10] Reducing the levels of pathological factors circulating in the patient's plasma is the mechanism of action of TPE to eliminate symptoms or prevent further destruction of the involved organ or system.[2,7,11] Alternatively, TPE can be used to replace a deficient factor, as in systemic thrombotic microangiopathy.[5] It can be used as a standard treatment or as an adjunct therapy in combination with drugs and/or surgery.[4]

TPE can be performed manually, where blood is extracted in repeated cycles and centrifuged ex vivo. The supernatant (plasma) is then discarded, and the remainder of the blood is returned with a replacement fluid.[12] Alternatively, standard TPE can be performed by automated devices and is categorized into two distinct groups: centrifugal (cTPE) and membrane filtration (mTPE).

cTPE separates blood components based on the density of the individual elements. Exposing whole blood to a centrifugal field results in the separation of plasma from cellular components. A replacement fluid is mixed with the blood and returned to the patient.[1,9,11]

With mTPE, the patient's blood is pumped through a parallel-plate or hollow-fiber filter. The pores of the filter membranes have a specific diameter sufficient to allow passage of plasma, isolating it from the cellular components of the blood.[2,3,4]

The Spectra Optia system, a next-generation therapeutic apheresis platform, has been available on the market for several years with an approved cTPE protocol. Since then, several researchers and physicians have published five papers and more than 20 abstracts regarding TPE. The following is a summary of these publications, including major outcomes.

Plasma Removal Efficiency (PRE)

TPE is based on the premise that circulating disease mediators can be decreased more effectively than through the body's own mechanism to maintain homeostasis. Patients could benefit from the replacement fluid used and the removal of pathological substances, which in turn could regulate other immune mechanisms.[11]

General Concept

PRE is an established metric to analyze the performance of an apheresis device during a TPE procedure.[13,14,15] PRE can be simply stated as:

$$PRE = \frac{Vol_{RP}}{Vol_{PP}} \times 100$$

Vol_{RP}: Volume of plasma and anticoagulant (AC) that is removed
Vol_{PP}: Volume of plasma and AC that is processed

The Vol_{PP} is:

$$Vol_{PP} = (V_{IN} - V_{AC}) \times (1 - Hct) + V_{AC}$$

Hct: Venous hematocrit of the patient (ideally, an average of pre- and post-procedure values)

V_{IN}: Volume of inlet blood processed

V_{AC}: Volume of AC used

The following complete formula was used by several authors both for the Spectra Optia system and the comparison to other cTPE devices:[8,13,14,15]

$$PRE = \frac{Vol_{RP}}{[(V_{IN} - V_{AC}) \times (1 - Hct) + V_{AC}]} \times 100$$

Using this calculation, PRE shows the volume of plasma that can be removed per volume of plasma that is processed with a specific apheresis device; in other words, the fraction of the processed plasma that is actually removed. Logically, PRE should be rather independent of the amount of blood processed. However, short procedures tend to have lower PREs than longer procedures, as apheresis devices require time to build up the blood levels to the necessary requirements while replacing the priming fluid. During this starting phase, blood, and therefore plasma, is already being processed while there is no removal of plasma yet.

The Spectra Optia system is the only existing device using an Automated Interface Management (AIM) system, which continuously monitors and interprets the position of the interface (the distinguishable boundary between plasma and cells in centrifuged blood). It does this by evaluating the position of the interface on approximately every other rotation of the centrifuge, depending on the speed of the centrifuge. When the AIM system is enabled, it makes

Table 1: *Summary of published average values for procedures performed on the Spectra Optia system. In the PRE/PE column, assume that PRE is used unless PE is indicated. When a parameter is not shown for a specific publication, the authors did not report it. Publication references in bold are peer-reviewed papers; the others are abstracts published at conferences and meetings. The last row shows the range for each parameter.*

Publication	Parameters (Average Values)				
	PRE/PE (%)	Procedure Time (Min)	Platelet Loss (%)	ACD-A Infused (mL)	ACD-A Used (mL)
Balint, et al, 2013 a&b[21,22]	86		1.2	58	414
Burgstaler and Winters, 2013 (ratio 13)[23]	86.6	62		71	
Burgstaler and Winters, 2013 (ratio 26)[23]	83.2	55		44	
Cid, et al., 2014[15] and Cid, et al., 2013[24]	82.9	115			687
Cole, et al, 2014[25]		116			644
Douglas, et al, 2008[16]	86 (PE)	109		68	
Golla, et al, 2011[26] and Hafer, et al, 2013[27]	84		7		
Hequet, et al, 2014[14]	80-86	91	3.4		461
Kim, et al, 2013[28]	91	102			
Lambert, et al, 2011[8]	83.2 (PE)	82	1.6		
Lefevre and Poullin, 2008[17]	88 (PE)		0.3		
Opitz, et al, 2008[29]	86	109			
Perotti, et al, 2008[18]	85.8 (PE)	135	1.1		
Puppe and Kingdon, 2014[30]		113		63	
Roxby, et al, 2008[31]	87	128	1		
Snyder, et al, 2007[32]	87				
Theunissen, et al, 2007 a&b[19,20]	84.6 (PE)		1.6		
Tormey, et al, 2010[13]	87	81	1	60	461
Range	**80–91**	**55–135**	**0.3–7**	**44–71**	**414–687**

adjustments to the plasma pump flow rate to maintain the optimal position of the interface, when reliably identified (the Spectra Optia system rarely might not "see" the interface during a TPE procedure, causing the interfaces not to be reliably identified during those occasional moments). Theoretically, this allows the Spectra Optia system to safely remove more plasma when compared to procedures that are based solely on a hematocrit algorithm.

In general, cTPE devices significantly outperform mTPE devices in terms of PRE, as previously described.[3,11] Published data show that flow rates for mTPE are typically much higher than for cTPE, which suggests that practitioners of mTPE devices counter the typically lower PRE by increasing the flow rate in order to reach similar procedure times for both device types.

PRE Versus Plasma Exchange Efficiency (PE)

In addition to PRE, other names for efficiency of plasma removal exist, such as plasma exchange efficiency (PE). However, PE does not necessarily mean the same as PRE. Nevertheless, some authors use PE interchangeably with PRE with a similar formula as described above.[8] Several abstracts describing the use of the Spectra Optia system in TPE also use the term PE instead of PRE, although the formula is not explained.[16,17,18,19,20] It remains a question whether the authors really refer to one or the other. Therefore, this review will treat the PRE and PE in a similar way, although when PE is used instead of PRE, it will be clearly stated. Despite the apparent confusion in the literature, PRE is the preferred way to describe TPE performance.

General Variables

PRE and Procedure Time

Table 1 compiles the data for the main parameters described in the majority of the publications on the Spectra Optia system. The PRE on the Spectra Optia system ranges from 80 percent to 91 percent, and in 10 of the 15 publications, it is calculated above 85 percent. Comparisons with other devices will be discussed later in this review, but Ward summarizes that centrifugal apheresis devices in general have a PRE of 80 percent.[3] As demonstrated in Table 1, the Spectra Optia system meets or exceeds 80% in every case but one in which PRE is measured.

Another important parameter reported in many publications is procedure time. The range of procedure times in the different abstracts and papers is wide. The reason is that procedure time depends on many factors, such as blood inlet flow rate, inlet:AC ratio used, AC infusion rate, total plasma volume (TPV) treated, type of replacement fluid used, pauses during the procedure and so on. Therefore, procedure time provides a standard basis for comparison when devices are compared for the same patients with similar conditions for the treatment. Additionally, it can be concluded that procedures can be finished quickly (within an hour) on the Spectra Optia system, especially when a high inlet:AC ratio is used.[23] Conversely, with lower flow rates and/or higher TPVs treated, TPE procedures could take up to more than two hours, ranging from 55 to 135 minutes.[18,31]

Platelet Loss

When performing TPE procedures, it is an important patient safety concern to have minimal cellular loss. Because platelets have the lowest specific gravity of all human blood cells, they have the highest probability of residing in the plasma fraction and can be the most affected in a TPE procedure. Furthermore, platelet activation and platelet aggregation mechanisms could contribute to an additional loss of platelets. In general, platelet loss is calculated using this formula:

$$\frac{\text{Quantity of platelets in waste bag}}{\text{Quantity of platelets initially in patient's circulation}} \times 100$$

When looking at the results of the platelet losses, the majority of the authors measure a platelet loss of 0.3 percent to 1.6 percent. Only two groups published higher platelet losses.[14,27] Hequet and colleagues use a different calculation method:

$$\frac{\text{(Pre-apheresis value - Post-apheresis value)}}{\text{Pre-apheresis value}} \times 100$$

It should be noted that many of the described publications do not explain how they calculate platelet loss, so Hafer, et al. may also have used some other method, but this remains unknown.[27] In the publications where platelet loss is known to be calculated by the first formula shown above, it did not exceed 1.6 percent. Compared to other devices, these numbers are low (see the following sections).

Anticoagulant (AC)

The validated AC used in the Spectra Optia system is ACD-A (acid citrate dextrose formula A), which is known to potentially induce citrate toxicity. Therefore, it is important to control the AC infusion rate and the total amount of ACD-A used. Typically, total amounts of ACD-A used are much higher than the ACD-A that is actually infused (administered to the patient): only 44 mL to 71 mL of ACD-A is infused versus 414 mL to 687 mL used during the average TPE procedure. This allows citrate-induced adverse events (0.08 percent to 1.2 percent of procedures) to be mild and self-limiting.[1] The low amount of ACD-A infused can be attributed to the high PRE result with the Spectra Optia system.

Inlet:AC Ratio Comparison

Burgstaler and Winters used the Spectra Optia system when comparing an inlet:AC ratio of 13:1 with 7,000 units of heparin to an inlet:AC ratio of 26:1 in combination with 10,000 units of heparin.[23] Each time, heparin was added to 1 L of ACD-A. However, for the procedures with an inlet:AC ratio of 13:1, the ACD-A was diluted with a saline solution to a 1-to-1 ratio, while for the 26:1 inlet:AC ratio procedures, non-diluted ACD-A was used (Terumo Blood and Cell Technologies does not recommend dilution of the ACD-A with the Spectra Optia system as this defeats the device's ability to control the citrate infusion rate). Consequently, similar AC concentrations were used in both types of procedures in the extracorporeal circuit. Still, when using the higher ratio (26:1), the authors reported a similar PRE (the difference was not significant; $p > 0.05$), but a shorter procedure time at a significantly higher blood flow rate ($p < 0.05$) was used. Additionally, significantly less anticoagulant was infused to the patient ($p < 0.05$). Due to dilution in the 13:1 inlet:AC ratio arm, the effective anticoagulation is unclear. No significant clotting was observed, and therefore no early termination of any procedure was reported.

Miscellaneous Parameters

Some publications also described different variables; one was pump accuracy of at least 97 percent.[13,28] Three publications reported the volume of whole blood processed, which ranged from 5,555 mL to 6,796 mL.[15,18,29] None of the published literature shows any serious adverse events (SAEs) experienced with procedures on the Spectra Optia system.

Performance in Comparison to the COBE® Spectra Apheresis System

The COBE Spectra system is the previous-generation apheresis device from Terumo Blood and Cell Technologies. Over 20 years of experience have been reported on this device, and it has been referred to as the "gold standard" in apheresis.[33] It is, therefore, not surprising that many of the publications compare the Spectra Optia system to the COBE Spectra system. Table 2 summarizes the results of this comparison.

PRE and Procedure Time

In general, the Spectra Optia system seems to outperform the COBE Spectra system in all cases. Average PREs on the Spectra Optia system ranged from 80 percent to 91 percent, while the COBE Spectra system's lowest PRE was 70 percent, and PRE never reached higher than 83 percent. Additionally, procedures on the Spectra Optia system were generally faster than those on the COBE Spectra system. One exception in which the COBE Spectra system was faster, was likely due to higher flow rates on the COBE Spectra system, although the flow rate is not specified in the article.[13] A higher PRE in combination with a similar blood flow rate should imply a shorter procedure time when, on the COBE Spectra system and Spectra Optia system, the apheresis procedures are continuous. Cid, et al. did not show a difference in procedure duration between the COBE Spectra system and the Spectra Optia system.[15] When looking at the results in detail, the operators chose to use an inlet:AC ratio of 10:1 on the Spectra Optia system, while on the COBE Spectra system the inlet:AC ratio was 12:1. The lower ratio on the Spectra Optia system resulted in a lower flow rate. Therefore, the procedure time is artificially longer than what it could be on the Spectra Optia system. The authors also mention that the inlet:AC ratio of 10:1 is in accordance with manufacturer's instructions, but it should be noted that this statement is not in any Terumo Blood and Cell Technologies documents.

Platelet Loss

Fewer platelets are lost in the Spectra Optia system than on the COBE Spectra system, as outlined in Table 2. In the abstracts and papers discussing the comparison of the two Terumo Blood and Cell Technologies devices, the average platelet loss on the Spectra Optia system does not exceed 1.2 percent, with one exception of 3.4 percent. On the other hand, the lowest average platelet loss measured on the COBE Spectra system was 3 percent, and losses range up to 16.4 percent. This could be due to the fact that the Spectra Optia system uses a higher packing factor during the TPE procedures and, therefore, platelets are more likely to be found in the buffy coat layer. Furthermore, when reliably identified, the AIM system on the Spectra Optia system constantly controls the interface, which potentially leaves less room for operator errors.

Anticoagulant

ACD-A is processed differently on the Spectra Optia system than on the COBE Spectra system. Both devices use comparable amounts of AC in the published data; however, as a result of the higher PRE on the Spectra Optia system, more ACD-A is also removed and thus less citrate is returned to the patient. This improves patient safety, as ACD-A can induce citrate toxicity.

Miscellaneous Parameters

Some additional parameters were analyzed in several publications. Roxby et al describe the setup time on the Spectra Optia system to be 15 minutes, while on the COBE Spectra system the operator needed

Table 2: *Summary of published average values for procedures performed on the Spectra Optia system compared with those performed on the COBE Spectra system. In the PRE/PE column, assume that PRE is used unless PE is indicated. When a parameter is not shown for a specific publication, the authors did not report it. Publication references in bold are peer-reviewed papers; the others are abstracts published at conferences and meetings. The last row shows the range for each parameter. When statistical significance is mentioned in the publication, it is shown in the table (p value or ^{NS} for not significant).*

Publication	Parameters (Average Values)									
	PRE/PE (%)		Procedure Time (Min)		Platelet Loss (%)		ACD-A Infused (mL)		ACD-A Used (mL)	
	Spectra Optia System	COBE Spectra System	Spectra Optia System	COBE Spectra System	Spectra Optia System	COBE Spectra System	Spectra Optia System	COBE Spectra System	Spectra Optia System	COBE Spectra System
Balint, et al., 2013 a&b[21,22]	86	79 ($p < 0.05$)			1.2	16.4 (in a) 4.2 (in b; $p < 0.05$)	58	114	414	518
Cid, et al., 2014 (also vs. Amicus Separator)[15]	82.9	70.4 ($p < 0.001$)	115	115^{NS}					687	647
Douglas, et al., 2008[16]	86 (PE)	77 (PE) ($p < 0.01$)	109	112				68	116	
Hequet, et al., 2014[14]	80–86	77–83 ($p < 0.05$)	91	95^{NS}	3.4	10.9 ($p < 0.05$)			461	473^{NS}
Kim, et al., 2013[28]	91	83 ($p < 0.001$	102	110 ($p = 0.001$)						
Roxby, et al., 2008[31]	87	83	128	145	1	7				
Snyder, et al., 2007[32]	87	79 ($p = 1.4 \times 10^{-8}$)								
Tormey, et al., 2010[13]	87	79 ($p < 0.0001$)	81	75 ($p < 0.05$)	1	3 ($p < 0.025$)	60	105	461	500 ($p < 0.001$)
Range	**80–91**	**70–83**	**81–128**	**75–145**	**1–3.4**	**3–16.4**	**58–68**	**105–116**	**414–687**	**473–647**

25 minutes to prepare the device.[31] In addition, the published data regularly show that in terms of complete blood count before and after the procedures, no significant differences were found between the COBE Spectra system and the Spectra Optia system.[13,14,15,22,28] Douglas et al reported an increased frequency of high-return-pressure alarms on the Spectra Optia system.[10] As with the Spectra Optia system, no SAEs were observed on the COBE Spectra system.

Comparing To Other Centrifugal Apheresis Devices

In Table 3, two devices manufactured by other companies are compared to the Spectra Optia system. Two groups compare it to the Amicus separator (Fresenius Kabi), while Lambert et al make the comparison to MCS®+ platelet collection system (Haemonetics).

Tonev et al compare the Spectra Optia system to COM.TEC® (Fresenius Kabi). This study comments only on the Spectra Optia system's higher mobility and lower platelet loss without showing any other results.[34]

Spectra Optia System Versus Mcs+

When the devices are analyzed side by side, the Spectra Optia system has a higher PRE than the MCS+. The procedure time is drastically higher on the MCS+, because this device works in a discontinuous way and uses only a single-needle procedure. Furthermore, the platelet loss is much higher in this study on MCS+ compared to the Spectra Optia system. The authors report a similar RBC loss post-procedure in both devices.

Spectra Optia System Versus Amicus

Amicus has been described by Cid and colleagues in both a peer-reviewed paper and an abstract as having comparable results to the Spectra Optia system.[15,24] Although the PRE is superior on the Spectra Optia system, the authors measured longer procedure times on the Spectra Optia system than on Amicus. In the same publications, they also compare the COBE Spectra system to the Amicus and, as mentioned above, they used a lower inlet:AC ratio on the Spectra Optia system, 10:1, versus 12:1 on both Amicus and the COBE Spectra system. Having more ACD-A per volume of blood processed implies that the overall blood flow rate goes down when the AC infusion rate remains the same; therefore, the procedure time logically increases. If similar blood flow rates had been used, a shorter procedure time could have been expected on the Spectra Optia system when processing the same amount of plasma, since the PRE was the highest on this device. Equivalent settings should be used to compare procedure times. This is the case for Cole et al, where the Spectra Optia system was the most efficient device in terms of procedure time in comparison to Amicus.[25]

In the article published by Cid et al in 2014, "anticoagulant infused" is used to mean "anticoagulant used" and not "anticoagulant administered to the patient"; therefore, it is put in the "anticoagulant used" column in Table 3. In this article, an average of 687 mL "anticoagulant infused" is reported, which is within the typical range used for a procedure — not all of that goes to the patient. (In contrast, for Ca^{++}–Mg^{++} solution "infused," the authors do mean "administered to patients").[15] To compensate for the loss of Ca^{++} in the patients, more Ca^{++}–Mg^{++} solution was used in the Amicus procedures (81 mL with Amicus versus 56 mL with the Spectra Optia system; $p < 0.001$), although anticoagulant used in the Spectra Optia system was the highest (which is to be expected with the lower inlet:AC ratio). The patient ionized Ca^{++} in the blood was not significantly different in the patients treated on both devices. Therefore, we can speculate that the infused volume of citrate used with the patients was significantly higher on Amicus than on the Spectra Optia system and COBE Spectra system during this study. This speculation is confirmed by Cole et al, who show on average 40 percent less infused volume of ACD-A when using the Spectra Optia system compared to Amicus.[25]

Finally, the comparison of the Spectra Optia system with Amicus shows a significantly higher plasma volume removed on the Spectra Optia system with a comparable volume of whole blood processed, probably due to a higher PRE on the Spectra Optia system.[15] Additionally, a higher drop in ion Ca^{++} concentration in

Table 3: *Summary of published average values for procedures performed on the Spectra Optia system compared with the MCS+ system and the Amicus separator. In the PRE/PE column, assume that PRE is used unless PE is indicated. When a specific parameter is not shown, the authors did not report it. Publication references in bold are peer-reviewed papers; the others are abstracts published at conferences and meetings. When statistical significance is mentioned in the publication, it is shown in the table (p value or NS for not significant).*

Publication	Parameters (Average Values)									
	PRE/PE (%)		Procedure Time (Min)		Platelet Loss (%)		Anticoagulant Infused (mL)		Anticoagulant Used (mL)	
	Spectra Optia System	Amicus	Spectra Optia System	Amicus	Spectra Optia System	Amicus	Spectra Optia System	Amicus	Spectra Optia System	Amicus
Cid et al, 2013[24] and **2014**[15] (also versus COBE Spectra system)	82.9	79.8	115	101[NS]					687	542 (p<0.001)
Cole, et al, 2014[25]			116	132 (p < 0.05)			111	186 (p<0.01)	644	560 (p<0.05)
	PRE/PE (%)		Procedure Time (Min)		Platelet Loss (%)		Anticoagulant Infused (mL)		Anticoagulant Used (mL)	
	Spectra Optia System	MCS+	Spectra Optia System	MCS+	Spectra Optia System	MCS+	Spectra Optia System	MCS+	Spectra Optia System	MCS+
Lambert et al, 2011[8] (p < 0.05 for all parameters)	83.2 (PE)	80 (PE)	82	148	1.6	7			542	566

Amicus versus the Spectra Optia system is possibly due to a lower AC infusion rate on the Spectra Optia system versus Amicus.[25]

Performance of the Spectra Optia System Compared to mTPE Devices

A last series of comparative studies between the Spectra Optia system and two mTPE devices is summarized in Table 4. Only two centers have reported on such a comparison. One discusses the performance of the Spectra Optia system against the Octo Nova device (DIAMED) using a Plasmaflo OP 05W filter (Asahi Kasei Medical, Japan) in two abstracts.[26,27] The other group discusses the Spectra Optia system and a Prisma device with the TPE2000 set (Gambro) in both an abstract and a peer-reviewed publication.[30,35]

In terms of PRE, the Spectra Optia system clearly outperforms the Octo Nova device. This corroborates with literature indicating that cTPE devices exceed mTPE devices in terms of PRE.[3] Higher flow rates used in mTPE devices do not always result in a difference of procedure time, as mentioned in the discussion above on the Spectra Optia system versus Amicus. Nevertheless, even with these settings, the Spectra Optia system outperforms both mTPE devices in procedure time. Platelet losses are significantly higher on the Octo Nova device, as well. Hafer et al describe a higher removal of fibrinogen and IgG with the Spectra Optia system (64 percent versus 56 pecent and 68 percent versus 63 percent in the Spectra Optia system and Octo Nova devices, respectively).[27] The Octo Nova device also had to process more than three times as much blood as the Spectra Optia system (19,855 mL versus 6,456 mL) for a similar volume of plasma exchange/removal.[27]

In nine procedures on the Prisma device, 13 filters were used due to clotting, while the Spectra Optia system required only one disposable set per procedure.[30] In this publication, clotting on the Prisma device occurred in a total of 33 percent of procedures. In other published data, 7.3 percent and 15.5 percent of mTPE procedures either resulted in premature ending of the procedure or required the use of an additional disposable set.[10,36] The percentage of clotting in the Puppe and Kingdon article is relatively high, which could be explained by possible differences in heparin usage. Nonetheless, clotting was never reported on the Spectra Optia system during a TPE procedure.[24]

Diseases Treated*

Several publications describe the disease types of the patients enrolled in the studies. Notably, it is specifically mentioned how many patients for each specific disease were treated on the Spectra Optia system (and other devices). Seventy out of 124 disorders are neurological (56 percent). The other main disease types are hematological (n = 30; 24 percent), renal and rheumatological (n = 15; 12 percent) and oncological (n = 12; 10 percent). Table 5 summarizes these findings.

Table 4: *Summary of published average values for procedures performed on the Spectra Optia system compared with mTPE devices. When a parameter is not shown for a specific publication, the authors did not report it. Publication references in **bold** are peer-reviewed papers; the others are abstracts published at conferences and meetings. When statistical significance is mentioned in the publication, it is shown in the table (p value or NS for not significant).*

Publication	Parameters (Average Values)							
	PRE		Procedure Time (Min)		Platelet Loss (%)		Disease Mediator Removal	
	Spectra Optia System	mTPE	Spectra Optia System	mTPE	Spectra Optia System	mTPE	Spectra Optia System	mTPE
Golla et al, 2011[26] and Hafer et al, 2013[27]	84	27 (p < 0.05)		10.5% longer than Spectra Optia system (p < 0.05)	7	15 (p < 0.05)	64% fibrinogen 67.8% IgG	56% fibrinogen (p < 0.05) 63.3% IgG[NS]
Puppe and Kingdon, 2014[30] and Puppe et al, 2013[35]			113	130[NS]				

Conclusion

From this literature review, we can conclude that the Spectra Optia system has proven its effectiveness compared to other existing apheresis systems. The Spectra Optia system shows better results than the COBE Spectra system for TPE procedures in terms of several parameters: it achieves higher PRE, lower procedure time and lower platelet loss. In addition, less anticoagulant is infused to the patient by the Spectra Optia system. Compared to other cTPE devices, the Spectra Optia system has been shown to outperform on all these parameters, with the exception of procedure time. In the case of Amicus, it requires a comparison using the same conditions on both machines (for example, using similar inlet:AC ratios and blood inlet flow rates). The Spectra Optia system also surpassed the mTPE devices that were tested on PRE, procedure time and platelet loss. In the abstracts mentioning disease mediator removal efficiency, it more effectively removed the larger protein fibronectin than the Octo Nova device.

Several authors have come to the conclusion that the Spectra Optia system is a preferred choice for TPE, citing several aspects of its performance. Balint et al conclude that "Spectra Optia is a more acceptable device for upcoming clinical TPE protocols than COBE Spectra," while Hafer et al advise that "especially in centers performing many procedures per year cTPE in contrast to mTPE can reduce treatment time without compromising treatment efficacy."[22,27] Lambert et al conclude that "the Spectra Optia has significantly higher extraction rate and exchange efficiency than the MCS+ allowing to remove the same amount of plasma in less time, by processing less blood," and Cole et al agree that "despite higher inlet flow rates, Amicus took an average of 14 minutes longer and processed 900 mL more blood to achieve similar exchange volume to Optia." [8,25]

**The Spectra Optia system is an option for therapeutic plasma exchange. While this system does not have a specific indication for any disease as an immunomodulatory therapy, plasma exchange is an identified therapeutic option and has been demonstrated to remove inflammatory mediators.[37,38,39] Use of this device must be evaluated and prescribed by the healthcare professional responsible for the patient's care.*

Table 5: *Reported number of patients treated in the abstracts and peer-reviewed publications of procedures performed on the Spectra Optia system.*

Disease Type	Disease	Number of Patients
Neurological	**Peripheral nervous system disorders**	**44**
	Myasthenia gravis	24
	Guillain-Barré syndrome	4
	Chronic inflammatory demyelinating polyradiculoneuropathy	7
	Other/non-specified auto-immune neuropathies	9
	Central nervous system demyelinating disorders	**23**
	Multiple sclerosis (Marburg's variant)	8
	Acute CNS inflammatory demyelinating disease	3
	Devic's syndrome/neuromyelitis optica	1
	Acute disseminated encephalomyelitis	1
	Central nervous system disorders	**3**
	Limbic encephalitis	2
	Stiff person syndrome	1
Hematological	Thrombotic thrombocytopenic purpura	14
	Cryoglobulinemia	11
	Monoclonal gammopathy (crossover with oncology)	5
Renal/Rheumatological	ABO-incompatible kidney transplantation	7
	Goodpasture's syndrome	3
	HLA-incompatible kidney transplantation	2
	Systemic lupus erythematosus	2
	Glycogenosis type 1—multi-organ failure and hypertriglyceridemia	1
	ANCA-associated small vessel vasculitis	1
Oncologic	Waldenström's disease (oncology)	6
	Myeloma (oncology)	1
Other	HELLP Syndrome	1
Total		**124**

References

1 Linenberger ML and TH Price, "Use of Cellular and Plasma Apheresis in the Critically Ill Patient–Part 1: Technical and Physiological Considerations." *Journal of Intensive Care Medicine* 2005; 20: 18–27.

2 Bramlage CP, et al., "Predictors of Complications in Therapeutic Plasma Exchange." *Journal of Clinical Apheresis* 2009; 24 (6): 225–231.

3 Ward D, "Conventional Apheresis Therapies: A Review." *Journal of Clinical Apheresis* 2011; 26 (5): 230–238.

4 Sanchez AP and DM Ward, "Therapeutic apheresis for renal disorders." *Seminars in Dialysis* 2012; 25 (2): 119–131.

5 Carter CE and NM Benador, "Therapeutic plasma exchange for the treatment of pediatric renal diseases in 2013." *Pediatric Nephrology* 2014; 29 (1): 35–50.

6 Tan HK and G Hart, "Plasma filtration." *Annals of the Academy of Medicine*, Singapore 2005; 34 (10): 615–624.

7 Yokoyama H, et al., "Advances in Apheresis Therapy for Glomerular Diseases." *Clinical and Experimental Nephrology* 2007; 11 (2): 122–127.

8 Lambert C, et al., "Plasma Extraction Rate and Collection Efficiency During Therapeutic Plasma Exchange with Spectra Optia in Comparison with Haemonetics MCS+." *Journal of Clinical Apheresis* 2011; 26 (1): 17–22.

9 Pusey D and JB Levy, "Plasmapheresis in Immunologic Renal Disease." *Blood Purification* 2012; 33 (1–3): 190–198.

10 Paton E and IC Baldwin, "Plasma Exchange in the Intensive Care Unit: A 10 Year Retrospective Audit." *Australian Critical Care* 2014; 27 (3): 139–144.

11 Madore F, "Plasmapheresis: Technical Aspects and Indications." *Critical Care Clinic* 2002; 18 (2): 375–392.

12 Abel JJ, et al., "Plasma Removal with Return of Corpuscles (Plasmaphaeresis): First Paper." *Journal of Pharmacology and Experimental Therapeutics* 1914; 5: 625–641.

13 Tormey CA, et al., "Improved Plasma Removal Efficiency for Therapeutic Plasma Exchange using a New Apheresis Platform." *Transfusion* 2010; 50 (2): 471–477.

14 Hequet O, et al., "Comparison of Plasma Exchange Performances Between Spectra Optia and COBE Spectra Apheresis Systems in Repeated Procedures Considering Variability and Using Specific Statistical Models." *Transfusion and Apheresis Science* 2014; 51 (1): 47–53.

15 Cid J, et al., "Comparison of Plasma Exchange Procedures Using Three Apheresis Systems." *Transfusion* 2015; 55 (5): 1001–1007.

16 Douglas KW, et al., "An Initial Single-Center Experience with Plasma Exchange on the Spectra Optia Cell Separator Machine: 106 Consecutive Optia Procedures Compared to 114 Consecutive COBE Spectra Procedures on the Same Patient Group." 29th Annual Meeting of the American Society for Apheresis (ASFA). Galveston, TX, USA. April 2008.

17 Lefevre PA and P Poullin, "Therapeutic Plasma Exchange with the New Continuous Blood Flow Separator Spectra Optia." 29th Annual Meeting of the American Society for Apheresis (ASFA). Galveston, TX, USA. April 2008.

18 Perotti C, et al., "Therapeutic Plasma Exchange Employing the New Spectra Optia 1.0 Device. The Italian Experience." 30th Annual Meeting of the International Society of Blood Transfusion (ISBT). Macao, China. June 2008.

19 Theunissen K, et al., "Birth of a New Generation of Therapeutic Apheresis Platforms: Interim Analysis of a Routine Use Experience With the Spectra Optia." 28th Annual Meeting of the American Society for Apheresis (ASFA). Nashville, TN, USA. April 2007.

20 Theunissen K, et al., "Interim Analysis of a Routine Use Trial of TPE Using the Gambro Spectra Optia, a New Generation of Therapeutic Apheresis Platforms." 60th Annual Meeting of AABB. Anaheim, CA, USA. October 2007.

21 Balint B, et al., "Immediate Benefit from Plasma Exchange in the Treatment of Severe Hypertriglyceridemia Using Spectra Optia System versus COBE Spectra System." 23rd Regional Congress of the International Society of Blood Transfusion (ISBT). Amsterdam, the Netherlands. June 2013.

22 Balint B, et al., "Plasma Removal/Exchange Efficacy: Spectra Optia System versus COBE Spectra System—A Comparative Preclinical Study." 34th Annual Meeting of the American Society for Apheresis (ASFA). Denver, Colorado, USA. April 2013.

23 Burgstaler EA and JL Winters, "A Technique Used to Improve Performance of the Terumo BCT Spectra Optia System for Therapeutic Plasma Exchange." 34th Annual Meeting of the American Society for Apheresis (ASFA). Denver, CO, USA. April 2013.

24 Cid J, et al., "Efficiency and Safety of Plasma Exchange using Three ApheresisSystems on the Same Patients." AABB Annual Meeting and CTTXPO. Denver, CO, USA. October 2013.

25 Cole N, et al., "Comparison of Fenwal Amicus and Terumo BCT Optia Cell Separators for Therapeutic Plasma Exchanges." ASFA & WAA Joint Conference. San Francisco, CA, USA. April 2014.

26 Golla P, et al., "Membrane versus Centrifuge Based Therapeutic Plasma Exchange—a Clinical Cross-over Comparison." German Society of Nephrology Annual Congress (DGFN). Berlin, Germany. September 2011.

27 Hafer C, et al., "Membrane versus Centrifuge Based Therapeutic Plasma Exchange—a Randomized Prospective Cross-Over Study." Joint British Transplantation Society and Renal Association Congress (BTS/RA). Bournemouth, UK. March 2013.

28 Kim S, et al., "Comparison of Two Apheresis Instruments in Plasma Removal Efficiency During Therapeutic Plasma Exchange Related to Kidney Transplantation." 23rd Regional Congress of the International Society of Blood Transfusion (ISBT). Amsterdam, the Netherlands. June 2013.

29 Opitz A, et al., "First Experience With the New Apheresis Platform Spectra Optia for Therapeutic Plasma Exchange." Joint Annual Congress of the German Society for Transfusion Medicine and Immunohaematology (DGTI) and the Interdisciplinary European Society for Haemapheresis and Haemotherapy (ESFH) in cooperation with the Société Française de Transfusion Sanguine (SFTS). Düsseldorf, Germany. September 2008.

30 Puppe B and EJ Kingdon, "Membrane and Centrifugal Therapeutic Plasma Exchange: Practical Difficulties in Anticoagulating the Extracorporeal Circuit." *Clinical Kidney Journal* 2014 ; 7 (2): 201–205.

31 Roxby D, et al., "Preliminary Experience Using the Spectra Optia Apheresis System for Therapeutic Plasma Exchange Procedures." 29th Annual Meeting of the American Society for Apheresis (ASFA). Galveston, TX, USA. April 2008.

32 Snyder E, et al., "In Vivo Evaluation of the Spectra Optia Apheresis System for Therapeutic Plasma Exchange (TPEX)." 28th Annual Meeting of the American Society for Apheresis (ASFA). Nashville, TN, USA. April 2007.

33 Soh T, et al., "Comparison Study Between Two Apheresis Machines: Cobe® Spectra Versus Spectra Optia®—A Single Center Experience." *Cytotherapy* 2013; 15 (4): S29–S30.

34 Tonev I, et al., "Thrombotic Thrombocytopenic Purpura (TTP) Using Different Approaches and Cell Separators." 34th Annual Meeting of the American Society for Apheresis (ASFA). Denver, Colorado, USA. April 2013.

35 Puppe B, et al., "Differences in Anticoagulation Strategies between Membrane and Centrifugal Therapeutic Plasma Exchange." Joint British Transplantation Society and Renal Association Congress (BTS/RA). Bournemouth, UK. March 2013.

36 Betz C, et al., "Regional Citrate Anticoagulation in Therapeutic Plasma Exchange with Fresh Frozen Plasma—A Modified Protocol." International Journal of Artificial Organs 2013; 36 (11): 803–811.

37 Reeves HM and JL Winters, "The Mechanisms of Action of Plasma Exchange." *British Journal of Haematology* 2013; 164 (3): 342–351.

38 Fuller L, et al., "Successful Treatment of a Patient With Severe Atopic Dermatitis and Severe Asthma by Centrifugal Therapeutic Plasma Exchange." *BMJ Case Reports* 2015; doi: 10.1136/bcr-2014-209008.

39 Lyu RK, et al., "Plasma Exchange Versus Double Filtration Plasmapheresis in the Treatment of Guillain-Barré Syndrome." *Therapeutic Apheresis* 2002; 6 (2): 163–166.

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