


# Effectiveness of a New Single-Needle Single-Pump Dialysis System with Simultaneous Monitoring of Dialysis Dose

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**Abstract:** To date, single-needle (SN) hemodialysis (HD) requires a dialysis machine equipped with two blood pumps—one controlling arterial blood flow (Qb) and one controlling venous Qb. B. Braun has developed an innovative single-pump SN HD system. Therefore, usability is improved by reducing complexity. The aim of this study was to compare dialysis parameters of the new single-pump SN HD system with a double-pump SN HD system available on the market (Fresenius Medical Care [FMC] 5008). In this two-armed crossover study, patients were randomized into two groups (B. Braun - FMC/FMC - B. Braun). Study period was 2 weeks (6 HD sessions) for each SN HD system. Both B. Braun and FMC dialysis machines were operated in the single-needle auto mode. With the FMC dialysis machines, Qb was optimized manually, whereas for B. Braun machines it was optimized automatically using the auto-mode functionality. A phase volume of 25 mL, treatment time, needle type and size, and dialyzer type and size were kept constant per patient throughout the study. Due to technical prerequisites in the SN mode, online dialysis adequacy ( $Kt/V$ :  $K$  - dialyzer clearance of urea;  $t$  - dialysis time;  $V$  - volume of distribution of urea) monitoring could only be performed in the B. Braun group. Twelve HD patients (5 male/7 female, mean age  $75.5 \pm 8.8$  years, mean time on dialysis  $4.97 \pm 3.86$  years,  $3 \times$  weekly HD) were enrolled. Total number of treatments performed:  $n = 132$  (65 B. Braun, 67 FMC) and the mean online  $Kt/V$  value in the B. Braun group was  $1.26 \pm 0.29$  ( $n = 63$ ). Mean dialysis time per session: B.

Braun  $253.4 \pm 19.9$  min, FMC  $251.6 \pm 18.8$  min. Mean phase volume: B. Braun  $25.1 \pm 0.2$  mL, FMC  $25.4 \pm 3.1$  mL. Mean cumulated blood volume (CBV): B. Braun  $55.0 \pm 5.5$  L, FMC  $40.5 \pm 5.9$  L ( $P < 0.0001$ ). Mean Qb: B. Braun  $217.8 \pm 12.9$  mL/min, FMC  $178.6 \pm 14.9$  mL/min (effective Qb) ( $P < 0.0001$ ), which corresponds to a difference of 39.3 mL/min (22.0%). Higher Qb has an influence on the CBV. To evaluate this effect, CBV was corrected for the difference in Qb by calculating the CBV/Qb rate. The mean CBV/Qb rate was  $252.2 \pm 19.4$  min (B. Braun) and  $226.8 \pm 27.6$  min (FMC) ( $P < 0.0001$ ) per session. This represents a highly significant difference of 11.4%. To support the in vivo data the dead time for opening/closure of the clamps of the FMC 5008 was measured, resulting in 364 milliseconds. Over a 240 min dialysis session, with a blood flow rate of 250 mL/min and a phase volume of 25 mL, it was estimated at about 14.56 min (6.1% of the session). Similarly, it was estimated that the dead time of the pumps of the FMC 5008 during 240 min dialysis session was 4.7 min (1.9% of the session). In case single needle therapy is the only practical option for a patient, the advantages of the new single-pump single needle system—namely the proven higher cumulative blood volume, the alarm-free auto-regulation of the blood flow and the easier handling for the nursing staff—ensure higher treatment efficiency than conventional double-pump single needle systems. **Key Words:** Single-needle hemodialysis—Dialysis adequacy—Cannulation complication—Vascular access.

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Dialysis adequacy in extracorporeal treatments depends on many factors, some of them related to medical prescription (treatment time, dialysate flow, type of dialysis membrane, surface of dialysis membrane, etc.), others mainly defined by patient characteristics (1), that is, extracorporeal blood flow. Blood flow is one of the most important factors associated with adequacy not only in terms

of low-molecular weight substances for achieving  $Kt/V$  ( $K$  - dialyzer clearance of urea;  $t$  - dialysis time;  $V$  - volume of distribution of urea) but also of middle molecule clearances (2) as it is also a driver for convective volume in postdilution hemodiafiltration.

Blood flow is related to the functionality of the vascular access, and when it is an arteriovenous fistula (AVF), is associated with longer survival (3,4). However, AVF is not free of complications, such as inadequate maturation, cannulation difficulties (5,6), and subsequent needle infiltration. According to a study by Lee et al. (7), 26% of the infiltrations, more common in older patients, were associated with subsequent fistula thrombosis. Currently, the dialysis population in most countries is mainly elderly patients, with several comorbidities associated, in particular cardiovascular diseases (8). Not surprisingly, these patients have often vascular access problems, with earlier failure (9) and with the need for temporary or permanent catheters. In an attempt to decrease AVF complications at the start of the hemodialysis treatment, a study using single-needle dialysis for new patients for the first 3 months to prolong maturation, resulted in fewer central venous catheter placements and need for vascular access investigations (10).

In 1979, 8% in Europe (11) and 60% of the hemodialysis patients in Belgium (12) were treated with the single-needle technique for several reasons: to decrease the risk of an early AVF failure (13), to facilitate cannulation for nurses, and to reduce the burden of pain for the patient. However, the single-needle dialysis approach was mainly limited by inadequacy of the treatment due to lower blood flow, higher recirculation and shortened treatment time (caused by the biphasic circulation) (14) with a suboptimal amount of cleared blood volume and low  $Kt/V$  (15), respectively. Moving from double to single-needle dialysis, the increase of treatment time by about 30 min as demonstrated by Trakarnvanich et al. (16) is the only valid option to maintain the adequacy. However, in the current factory-like hemodialysis environment (17), this is often not economically sustainable. Therefore, a new technical solution for single-needle hemodialysis technique able to improve the volume of processed blood is highly needed.

Various techniques have been developed. One approach is based on two blood pumps with an expansion chamber before the dialyzer. In a two-phase process, at first the arterial pump is active pumping blood to the expansion chamber until the planned phase volume is achieved or earlier, in

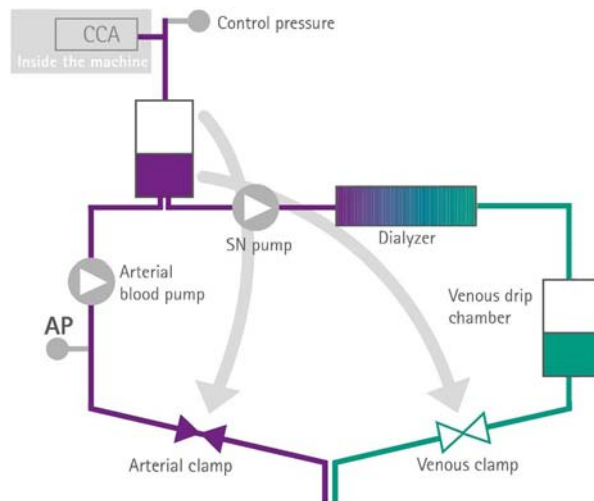


FIG. 1. Single needle set-up for FMC 5008.

case the pressure threshold is reached. This second occurrence may happen in the conditions when the planned phase volume cannot be achieved for an excessive increase of the negative arterial pressure due to stenosis, needle dislodgement, etc. At the end of the first phase, the arterial pump stops and the venous pump is activated to return a defined phase volume of blood to the patient after flowing into the dialyzer. Two clamps, arterial and venous, act as additional safety features. In a variation of this model (Fig. 1), both pumps are positioned before the dialyzer (FMC 5008 approach).

Alternatively, the single-needle crossover procedure with two blood pumps allows a continuous flow through the dialyzer. During a single-needle crossover procedure, the pressure and pulsation conditions within the dialyzer are roughly the same as in double-needle dialysis. The arterial expansion chamber is filled with fresh blood due to the negative pressure in the chamber. With the arterial line clamp open and the venous line clamp closed, the blood pumps move at a constant rate blood from the arterial expansion chamber, through the dialyzer to the venous expansion chamber. The blood level in the venous chamber rises. The pressure in the venous chamber is monitored via the venous pressure sensor. Once the set positive venous switchover pressure (also named venous/arterial control pressure) has been reached, the arterial clamp closes. Shortly afterwards the venous clamp opens. The blood from the venous chamber is returned to the patient because of the positive pressure. The blood pumps operate simultaneously and pump blood from the arterial chamber through the

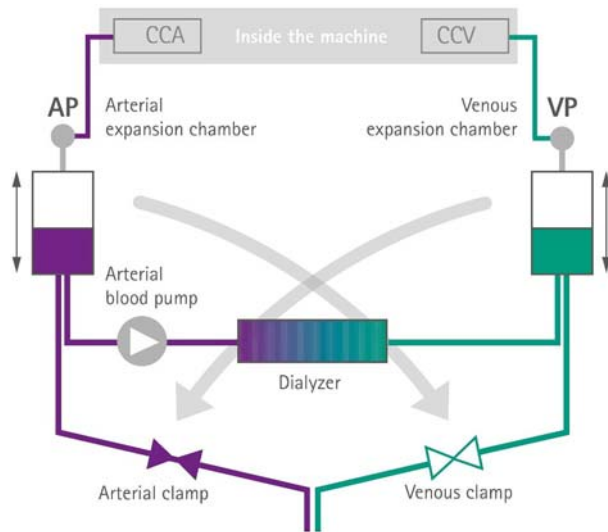


FIG. 2. Single needle set-up for B. Braun Dialog iQ.

dialyzer into the venous chamber. The pressure in the arterial chamber is monitored via the arterial pressure sensor. Once the set negative arterial switchover pressure has been reached, the venous tube clamp closes and the arterial tube clamp opens. Blood flows again into the arterial chamber and the process starts again with the withdrawal of blood from the patient.

Recently, a new, more effective procedure for single-needle dialysis which allows an easier application of the therapy has been developed by B. Braun, using only one blood pump to perform the therapy (Fig. 2). Compared to single-needle crossover with two pumps, in the single pump version (B. Braun Dialog iQ) internal expansion chambers (arterial and venous) were introduced and the external chambers (arterial and venous) have been reduced in size. Additionally, the system provides an auto-mode for single-needle dialysis. Only the phase volume has to be set, and the blood flow will be regulated automatically. The advantages of this system are the decrease of standstill periods with increased total treated blood volume and, from the user's perspective, the automatic adjustment of the optimal blood flow without user interaction at the machine. Last but not least, the procedure of assembling the bloodlines is simpler because of the absence of the second blood pump, saving precious nursing time (17). The description of the different phases of the single-needle cycle in B. Braun Dialog iQ and in FMC 5008 is reported in Table 1.

To prove the effectiveness of the newly developed single-needle system, this study was planned

to compare dialysis efficiency parameters of the new single-pump single-needle hemodialysis system (B. Braun Dialog iQ) with the standard double-pump system (FMC 5008). In addition, a laboratory test was set up to test and confirm the technical features impacting the clinical findings estimated in the clinical study.

## PATIENTS AND METHODS

### Clinical study

In this two-armed crossover study, patients were randomized into two sequences A/B or B/A of different single-needle HD techniques (A: B. Braun Dialog iQ, single blood pump crossover and B: FMC 5008, double pump single-needle). Study period was 2 weeks (6 HD sessions) for each SN HD system. Both B. Braun and FMC dialysis machines were operated in the single-needle auto mode whereas effective blood flow rate was optimized manually for FMC dialysis machines, as the automatic setting approach is not available in those machines. For B. Braun machines, it was optimized automatically using the auto-mode functionality. Phase volume, treatment time, needle type and size, and dialyzer type and size were kept constant per patient throughout the study. In defining the phase volume, fixed for all patients and treatments, we consider that Polaschegg et al. (18), analyzing the efficiency of pulsatile flow in respect to continuous flow in single-needle hemodialysis, found that the phase volume should be less than half of the volume of the dialyzer blood compartment. As blood flow in single-needle hemodialysis is normally low, we considered a dialyzer surface of 1.2–1.3 m<sup>2</sup> to be adequate and an internal blood compartment volume in the range of 60–70 mL. Therefore, a phase volume of 25 mL was considered optimal for the standard operative condition requiring this modality of treatment. Cumulative blood volume per session was assessed. Online  $Kt/V$  could be evaluated for all sessions conducted with B. Braun Dialog iQ by using the spent dialysate monitoring system Adimea (19), but not with the Fresenius Medical Care 5008 dialysis machine because the on-line clearance ionic monitoring (20) is not functioning in case of single-needle dialysis in the FMC 5008 machine.

Adverse events were collected.

### Study approval and patient consent

Trial registration was not compulsory because of the observational nature of the study. The protocol was submitted and approved by the

**TABLE 1.** Summary of the single-needle phases of a cycle in the equipment studied

Cycle phases	Cycle description	B. Braun Dialog iQ	FMC 5008
0	Start of the cycle	Arterial and venous clamp closed, blood pump running	Arterial and venous clamp closed, blood and single-needle pumps not running
1	Arterial phase	Arterial clamp opens	Arterial clamp opens, blood pump activated
2		Due to high negative pressure in the arterial chamber, blood flows from the patient into the arterial chamber. As the absolute value of pressure is progressively decreasing, blood flow rate into the arterial chamber decreases during arterial phase, up to the completion of the restitution of the phase volume. At the same time, because of the continuously working blood pump, blood flows from the arterial chamber via the dialyzer to the venous chamber, until the increasing pressure in the venous chamber reaches the venous control pressure. Blood pump control mechanisms match the set phase volume with venous control pressure.	Blood flows, driven by the blood pump, from the patient into the arterial chamber until phase volume is achieved. Pressure increases in arterial chamber.
3	Venous phase	The arterial clamp closes and the venous clamp opens, blood pump continues running	The arterial clamp closes, the blood pump stops, the single-needle pump is activated and the venous clamps open.
4		Due to high positive pressure in the venous chamber, blood flows from the venous chamber back to the patient. As the absolute value of pressure is progressively decreasing, the blood flow rate back to the patient decreases during venous phase, up to the completion of the restitution of the phase volume. At the same time, because of the continuously working blood pump, blood flows from the arterial chamber via the dialyzer to the venous chamber until the decreasing pressure in the arterial chamber reaches the arterial control pressure. Blood pump control mechanisms match the set phase volume with arterial control pressure.	Blood flows, driven by the single-needle pump, from the arterial chamber into the dialyzer at a constant flow and then to the venous drip chamber, to the venous line and finally to the vascular access until the reinfusion of the phase volume is completed.
5	end of the cycle	The venous clamp closes, blood pump continues running	The single-needle pump stops and the venous clamp closes

German College of Physicians (vote nr. 195/15, issued on Oct. 20, 2015 by the ethics committee of the “Ärztchamber des Saarlandes”, Germany). All participating patients signed a written informed consent.

### Sample size

The definition of the sample size able to detect a difference between FMC 5008 and B. Braun iQ working with single-needle hemodialysis in term accumulated blood volume was based on the following assumptions: (i) type 1 error ( $\alpha$ ) = 0.05, (ii) type 2 error ( $\beta$ ) = 0.20, that is power  $(1 - \beta) = 0.80$ . The relevant difference was stated around 5–10% of the mean accumulated blood flow. In consideration of the plan for six treatments per method and per patient as well as expected possible dropouts (8.3%), 12 patients were recruited.

### Statistical analysis

Continuous variables are described using means and standard deviations; percentages were used for categorical variables. The adequacy of the crossover design has been proven by a standard *t*-test, checking the assumption of a negligible carry-over effect, following the procedure described by Wellek et al (21). The null hypothesis for this test was the absence of a carry-over effect, and the statistical test checked if it can or cannot be rejected.

After having verified the absence of a significant period effect of the crossover analysis (no period effect) for cumulated blood flow as well as for other secondary outcome variables, data related to the FMC 5008 and B. Braun iQ phases of the two sequence AB and BA were merged and analyzed according to paired *t*-test.

The significance level was set to 0.05. Results are presented as per-protocol analysis.

### Laboratory test

To estimate dead times occurring with FMC 5008 single-needle cycle, the following study model has been created. The arterial and venous termination of the bloodline were set separately without using the Y connector. The two ends of the bloodline were then connected with two canisters, placing them on a level lower or higher than the dialysis machine to simulate the usual negative arterial and positive venous pressure, respectively. This model did not interfere with the actions of the clamps and pumps performing a standard single-needle therapy, as if working with the usual Y connector. To replicate the physical properties of blood, in particular viscosity, a solution of the plasma expander hydroxyethyl starch (Venofundin, molecular weight 130 Da, B. Braun Melsungen AG, Melsungen, Germany) at a concentration of 6% was used as the test solution. The measuring of the time required to open and close the clamps was performed by filming the operation of the clamps with a high speed capacity camera (Casio EX-F1) with a rate of 300 frames per second. The camera was positioned in a way to record the clamp of interest, the end of the vascular access and an added LED that turns on when the clamp receives the electrical command to change position. As the operation of the clamp was filmed, using a video editor or player, the number of frames necessary for the clamp to completely open and close can be counted and the time in seconds can be calculated. Additionally, the time between the electrical signal, the movement of the clamp and the reaction on the flow can all be calculated by counting the frames between events in the video.

A similar method was used to characterize the dead time of the FMC 5008 pumps during the switching of phases. The blood pumps were filmed by the video camera. The number of frames were counted between the end of one phase and the start of the next phase. Finally, the time required for the pumps to reach their target flow rate is the time during which the instantaneous flow is either increasing or decreasing, in any case different from the target rate. Therefore, every time there is a change of phase, the mean flow is reduced. To measure the flow in this phase a high-speed flow sensor was used directly before the arterial pump and after the single needle pump during a normal single needle hemodialysis session.

## RESULTS

### Clinical study

The main characteristics of the enrolled patients are summarized in Table 2. Twelve HD patients

**TABLE 2.** Main characteristics of the enrolled patients

Patients (N)	12
Males (n)	5
Age (years)	75.5 ± 8.8
Dry body weight (kg)	78.6 ± 15.8
Height (cm)	165.2 ± 8.4
BMI (kg/m <sup>2</sup> )	28.7 ± 4.4
Primary renal disease (n)	
Glomerulonephritis	3
Congenital renal disease	1
Nephro-vascular disease	5
Secondary glomerular disease/systemic disease	4
Unknown	1
Comorbidities (n)	
Diabetes	7
Peripheral vascular disease	1
Coronary heart disease	5
Cardiac failure	2
Chronic pulmonary disease	1
Cerebrovascular disease	2
Vascular access (n)	
AV-Fistula	11
Catheter	1
Dialysis vintage (years)	5.0 ± 3.9

(5 male/7 female, mean age 75.5 ± 8.8 years, median time on dialysis 3.61 years (25–75 percentile: 1.94–7.34 years) on a three times a week schedule were randomized to be treated on single-needle dialysis at first with the B. Braun Dialog iQ and then with FMC 5008 or vice-versa. Table 3 shows the baseline main lab results and the dialysis dose of the enrolled patients. The main characteristics of the prescribed treatment (treatment frequency and time, dialyzer membrane, type and surface, etc.), maintained for the full study, are reported in Table 4.

Out of the planned 144 treatments, 5 were not conducted on 3 patients, with 3 sessions lost because a patient was hospitalized during the study. Seven other treatments were not considered in the per protocol analysis because of deviations in respect to the baseline prescribed treatment in five patients, with six sessions excluded because of the use of an erroneous dialyzer, one because of different dialysis time (Fig. 3). As a result, the total number of per protocol treatments performed was 132 (65 B. Braun Dialog iQ, 67 FMC 5008). The assumption that carry-over

**TABLE 3.** Baseline laboratory and dialysis dose values

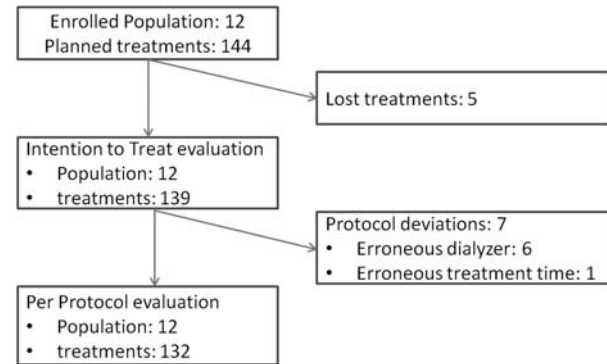
Variable, unit	Mean, SD
Potassium (mMol/L)	5.3 ± 0.9
Calcium (mMol/L)	2.20 ± 0.16
Phosphate (mg/dL)	5.2 ± 1.0
iPTH (pg/mL)	440 ± 287
Creatinine (mg/dL)	6.40 ± 1.82
Kt/V	1.38 ± 0.32
Hemoglobin (g/dL)	11.84 ± 0.98
Ferritin (µg/L)	268 ± 107

**TABLE 4.** Dialysis prescription

		Patients/dose
Treatment frequency (sessions/week)	3	12
Prescribed treatment time (min/session)	240	8
	270	3
	300	1
Dialyzer surface (m <sup>2</sup> )	1.8	7
	2.3	5
Dialyzer type	High flux	12
Dialyzer membrane	Polysulfone-based synthetic membrane (Amembris)	12
Needle size (Gauge)	14	3
	15	9
Unfractionated Heparin	Initial dose (IU)	2500
	Continuous Dose (IU/h)	1258 ± 406
rHu-Erythropoietin	Absent (n)	5
	Present (U/week)	8393 ± 5446
IV Iron	Absent (n)	6
	Present (n)	6

effect was negligible was not rejected ( $P = 0.6106$ ), allowing the two periods of each arm of the study to be merged together. The main results of the per protocol evaluation are reported in Table 5, whereas the intention to treat analysis, based on 139 sessions and providing very similar results is not shown. The mean dialysis time was  $253 \pm 20$  min/session when treated on B. Braun Dialog iQ,  $252 \pm 19$  min when on FMC 5008 (0.6054). The mean phase volume was  $25.1 \pm 0.2$  mL and  $25.4 \pm 3.1$  mL ( $P = \text{NS}$ ) for the B. Braun Dialog iQ and the FMC 5008, respectively. However, the mean cumulated blood volume (CBV) was for the B. Braun Dialog iQ  $55.0 \pm 5.5$  L and for the FMC 5008 only  $40.5 \pm 5.9$  L ( $P < 0.0001$ ). This benefit of the B. Braun Dialog iQ was distributed to all patients (Fig. 4). The mean blood flow ( $Q_b$ ) was  $217.8 \pm 12.9$  mL/min and  $178.6 \pm 14.9$  mL/min (effective  $Q_b$ ) by using B. Braun Dialog iQ or FMC 5008, respectively ( $P < 0.0001$ ), which corresponds to a difference of 39.3 mL/min (22.0%) in favor of the single pump-single needle equipment. Higher  $Q_b$  has an influence on the CBV.

To evaluate the impact of the blood pump standstill time of the reference double pump in respect to the single pump crossover system on the

**FIG. 3.** Patient Flow: all presented analyses were based on intention to treat.

performance, the effective treatment time based on the rate between CBV by  $Q_b$  was calculated, resulting in  $252.2 \pm 19.4$  min for sessions delivered by B. Braun Dialog iQ and  $226.8 \pm 27.6$  min for those on FMC 5008, ( $P < 0.0001$ ).

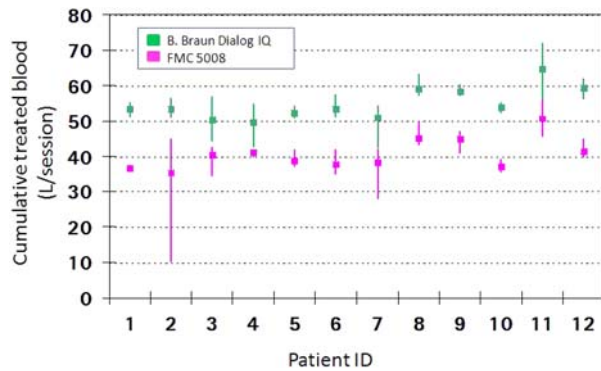
Therefore, the 35.7% higher cumulative blood volume achieved by B. Braun Dialog iQ is composed by the algebraic sum of 22.0% due to higher blood flow and 13.7% due to the increased effective treatment time. In addition, the coefficient of variation of CBV for those sessions on B. Braun Dialog iQ was 5.28%, for those sessions performed with single-needle FMC 5008 8.51%. Median online  $Kt/V$  value estimated during the sessions on B. Braun Dialog iQ of 1.24 (25–75 percentiles: 1.15–1.40) and the proportion of session with  $Kt/V \geq 1.20$  was 60.3%.

### Laboratory test

To support the in vivo data we measured the dead time on the clamps and pumps of the FMC 5008. The total dead time for opening/closure of the clamps after the signal has been issued was of about 364 milliseconds. Over a 240 min dialysis session, with a blood flow rate of 250 mL/min and a phase volume of 25 mL, the accumulated dead time was therefore estimated to be 14.56 min, which is 6.1% of the total session time. Similarly, it was estimated that the dead time of the pumps during

**TABLE 5.** Description main results by study phase (per protocol population)

Variable, unit	B. Braun Dialog iQ	FMC 5008	<i>P</i> value
Planned and actual dialysis time (min)	253 ± 20	252 ± 19	0.6054
Cumulated blood volume (L)	54.95 ± 5.45	40.46 ± 5.91	<0.001
Blood flow (mL/min)	217.8 ± 12.9	178.6 ± 14.9	<0.001
Ratio cumulated blood volume/blood flow (min)	252 ± 19	227 ± 28	<0.001
Phase volume (mL)	25.1 ± 0.2	25.4 ± 3.1	0.4017



**FIG. 4.** Mean, minimum and maximum cumulative blood volume achieved in 12 study patients in the two sequences of single needle dialysis sessions.

240 min dialysis session is 4.7 min, that is 1.9% of the session time.

## DISCUSSION

In summary, this study showed that the novel technology for single-needle hemodialysis ensures a significant 36% increase of cumulative blood volume in respect to a pressure controlled double pump system, and that the reproducibility of the performance is very high, with a coefficient of variation of 5.3% in respect to the 8.5% of the standard method. The improved performance of 38.4% is due to the gain in effective treatment time, increased from an average of 227 to 252 min. From the comparison of the descriptions of the single-needle cycle as implemented in the FMC 5008 and in the B. Braun Dialog iQ (Table 1), it is clear that:

1. Both equipment have dead time due to the open/close activity of the clamps. This is compensated for in the B. Braun Dialog iQ by the initial higher gradient of pressure, but not in the FMC 5008.
2. Only the FMC 5008 has dead time in the activation/deactivation of the two pumps, as the pump of the B. Braun Dialog iQ blood pump is constantly running.
3. Blood flow in the B. Braun Dialog iQ is automatically optimized according to arterial and venous pressure whereas in the FMC 5008 it has to be manually set.

Therefore, possible reasons for the difference in the cumulated blood volume showed by our study

may be related to the characteristics of the FMC single-needle cycle, with:

1. Dead time of the clamps
2. Dead time of blood and single-needle pumps
3. Manual setting of blood flow

To understand what causes this difference, we have to break up the difference in cumulated treated blood into the three components. However, as it was difficult to create a model to analyze the dynamics of the increased blood flow, we estimate the magnitude of this component from the difference between the total and the components related to dead times, which is actually easier to measure. According to the test performed in the lab, the accumulated dead time of the clamps and of the pumps can be estimated in the range of 6.1 and 1.9% of the session time, respectively. Therefore, the lost time is due to clamps and double pumps, in the FMC 5008 double pumps single-needle is about 8%, very close to the 10% evaluated by the in vivo results of the clinical study. This 10% difference is the delta between the rate of cumulated blood volume with blood flow, that is the time effectively used (227 min), in respect of the delivered treatment time (252 min). The similar results between the lost time with the model set in the research lab and the in vivo data derived by the study increases the confidence in our results.

If about 8–10% of cumulated treated blood is lost because of clamps and pumps, it means that the rest of the difference observed in this study should be due to a better management of the blood flow. This is the largest part of the advantage of the single-needle hemodialysis based on the single pump crossover approach (+22%), coming from an increase in blood flow from a mean of 179 to 218 mL/min. In the double-pump system of FMC 5008, blood flow has to be set manually. During the treatment, arterial and venous pressure change and the risk of annoying alarms increase. Therefore, it is an obvious consequence that users tend to set the blood flow on a lower level to decrease the risk of alarms. Nurses involved in the study had 8 years of experience working with the FMC 5008, whereas the experience with the new B. Braun Dialog iQ was in the range of some months. In the B. Braun Dialog iQ single-needle system, blood flow is continuously optimized by an algorithm based on the pressure profile of the arterial and venous blood chambers, which is related to the pressure in the vascular access. As the pressure in the vascular access may change during the treatment, a dynamic

system following these changes is an obvious advantage for the B. Braun Dialog iQ. This advantage is not available in the FMC equipment.

Another important point to consider is the transmembrane pressure during the treatment. With the two-pump method, transmembrane pressure is influenced by the stops of the blood flow in the dialyzer. Therefore, not only back filtration of dialysate can easily occur but also an activation of the coagulation cascade can be triggered by the rheological changes induced by the intermittent flow. In the past, concerns regarding the higher risk for hemolytic episodes has been reported (22). In fact, mechanical fragmentation of erythrocytes can also occur due to the higher stress imposed by the double-pump approach (23).

These issues have been definitively solved by the novel single-needle crossover method, where the constant blood pump rate avoids the increment-decrement pulsing blood flows of the double pumps system following pressure or phase volume control.

The efficiency of the single-needle system is dependent on the mean blood flow and the amount of recirculation. As stated by Vanholder et al., a recirculation rate of 14% reduces dialyzer urea clearance by 8.2% (24). By applying single-needle hemodialysis, recirculation is caused by three main factors (25): (i) a low blood flow in the AV-fistula, often present in poorly matured vascular access, which is one of the indications for the single needle technique, (ii) a significant dead space in the needle and up to the Y connection of the bloodline, and (iii) the compliance of the bloodlines between the needle and the blood pump. For the last point, the quality of the bloodline is of critical importance.

Some factors were maintained constant between the two phases of the study. We can assume that because of randomization, AV-fistula recirculation was not different. The dead space between needle and the Y connection was the same. Bloodlines were obviously different but applying the original bloodlines of the dialysis machine manufacturers we can assume to limit the issue related to bloodline compliance. Therefore, the technical differences of the dialysis machines described above had a major impact on treatment efficiency.

A limit of the study is related to the evaluation of the blood flow and of the cumulated blood volume. The estimation of these two parameters is performed by the equipment produced by the two companies, based on the number of rotations of the blood pump and the negative pressure generated when sucking the blood from the AV-fistula. In the past, some concerns were raised from the observation that not

all software managing dialysis equipment considered the negative pressure in the estimation of blood flow (26), but nowadays significant overestimation by the equipment used in the study can be excluded. Even in the presence of marginal nonsignificant differences in measuring blood flow between the used equipment, the results of this study showed a magnitude of difference of cumulated blood volume beyond possible described impact.

The absence of dialysis dose assessment for treatments performed with the FMC single needle equipment is a further limit of the study, not allowing additional confirmation of the expected superior dialysis adequacy with the new approach. The dialyzer surfaces used during the study reflected real world practice due to standardization of disposables. Most importantly, surfaces were not changed during the study.

Adequacy of dialysis dose is the pivotal feature to be ensured (27). In the past, this was judged as the Achilles heel of single-needle techniques. In this study, we maintained the same treatment time in both phases of the study and it was still possible to achieve a median  $Kt/V$  of 1.24 during the phase with the single pump crossover technique, with 60.3% of the sessions achieving the level of adequacy.

The last evaluation before study initiation, based on lab urea determinations, was with a median  $Kt/V$  of 1.41 (25–75 percentile: 1.12–1.72) and 73% of the patients, all on double needle dialysis, had a  $Kt/V \geq 1.20$ . These data confirm the comparable good results of 6 patients moved from double needle to single-needle dialysis (crossover) obtained by Ervo et al. (28). It needs to be stressed that in evaluating  $Kt/V$  of the single-needle technique, special attention should be in place to avoid underestimation of the end dialysis urea level. For this reason, it is generally recommended to take the final sample 20 min after the end of the session, instead of the stop flow method (3 min at a blood flow of 50 mL/min) generally recommended for double needle hemodialysis. For this study it was planned to evaluate  $Kt/V$  by using the proprietary online methods of the involved equipment, based on on-line ionic clearance (FMC) (20) and on the optical method analyzing online the absorbance changes in the spent dialysate (B. Braun) (19), so avoiding additional blood samplings. These options are particularly useful if the patient shifted from double needle to single-needle technique, allowing the maintenance of adequacy simply by monitoring  $Kt/V$  on the screen and terminating the session only when the target is achieved. This is possible with the B. Braun Dialog iQ but



unfortunately it is not possible with the FMC 5008 machine, as the online ionic clearance option (OCM) is not working with the pulse flow of the double pump single needle technique.

Therefore, this new single-needle single-pump method by increasing the amount of treated blood may be a valid alternative to double lumen catheters for elderly fragile patients. Double lumen catheters are today the most common dialysis access in patients older than 75 years (29). This implies a probable marginal prolongation of the treatment time, but this can be an additional advantage, as according to Saran et al. (30), targeting a gentler dialysis treatment with lower net ultrafiltration rate is associated with lower mortality risk.

In addition, allowing protective maturation of the AV fistula and treatment in part of the patient population with AV fistula acute problems awaiting interventions, the single needle single-pump method may also represent a valid temporary approach. According to Peterson et al. (31), in elderly patients, significant disparities in fistula maturation may persist even after the use of routine preoperative vascular mapping. Efficient single needle treatment with the B. Braun single pump system can bridge this vulnerable period of access maturation impacting access patency. Vanholder et al. (24) reported 76 patients in their hospital programs that were routinely treated using a commercially available twin-pump head single-needle system. Five-year fistula survival rate was 74%, a value higher than reported by other investigators on double needle dialysis patients: that is, Ravani et al. (32) in 2002 reported 36-month primary and secondary patency of the first AVF of 58 and 62%, respectively. This result is specifically relevant considering today's dialysis population of elderly, comorbid patients, whose vascular access is a very sensitive point related to their survival. Another option may be the prescription of an efficient single needle hemodialysis in the daily scheduling, as the FHN trial (33) showed increased incidence of access complications with double needle hemodialysis. Lower stress to vascular access will result, ensuring in the meantime the adequate level of dialysis dose and prolonging AV fistula patency.

### CONCLUSION

With this novel technique the efficiency of single-needle hemodialysis can be maximized, targeting higher blood flow and cumulative blood volume, respectively. In addition, considering this approach with an online method for *Kt/V*

monitoring, it is possible to ensure dialysis adequacy prolonging the session if necessary, just to the time required. As the cumulative blood volume per unit of treatment time is higher than in the FMC system, applying the new single needle single pump system means a shorter extension of treatment time is possible.

In short, in case single needle is the only practical option for a patient, the advantages of the new single-pump single needle system—namely the proven higher cumulative blood volume, the alarm-free auto-regulation of the blood flow and the easier handling for the nursing staff—ensure higher treatment efficiency than conventional double-pump single needle systems.

Further studies have to be planned to verify this hypothesis.

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