

Technique Article

In Vitro Evaluation of the Fresenius Kabi CATSmart Autotransfusion System

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Abstract: Use of autotransfusion systems to collect, wash, and concentrate shed blood during surgical procedures is a widely used method for reducing postoperative anemia and the need for blood transfusions. The aim of this study was to evaluate the CATSmart Continuous Autotransfusion System wash program performance with small (200 or 700 mL) and large volumes (1,000 mL) of shed blood and to determine non-inferiority of the CATSmart to the C.A.T.S.^{plus} system. Human whole blood was collected in citrate phosphate dextrose, diluted, and divided into two aliquots to be processed as a pair using the C.A.T.S.^{plus} and CATSmart systems with their corresponding wash programs: low-volume, high quality/smart, or emergency wash. Final packed red cell product was analyzed for red blood cell (RBC), white blood cell, and platelet counts; hemoglobin; hemolysis; RBC recovery

rates; and elimination of albumin, total protein, and potassium. The mean hematocrit (HCT) after processing with CATSmart and C.A.T.S.^{plus} systems were 59.63% and 57.71%, respectively. The calculated overall RBC recovery rates on the CATSmart and C.A.T.S.^{plus} systems were 85.41% and 84.99%, respectively. Elimination of albumin (97.5%, 98.0%), total proteins (97.1%, 97.5%), and potassium (92.1%, 91.9%) were also calculated for the CATSmart and C.A.T.S.^{plus} systems. The CATSmart and C.A.T.S.^{plus} systems both provided a high-quality product in terms of HCT, protein elimination, and hemolysis rates across the range of tested shed blood volumes and all wash programs. The study was able to confirm the CATSmart is non-inferior to the C.A.T.S.^{plus} system. **Keywords:** cell salvage, autotransfusion, blood conservation. *J Extra Corpor Technol. 2017;49:107–111*

Surgical procedures such as cardiac, orthopedic, vascular, trauma, and obstetrics can be associated with anticipated blood loss greater than 20% of a patient's estimated blood volume (1,2). Several methods of blood conservation have been established in an effort to reduce or avoid transfusion of allogenic blood during these procedures. Autotransfusion, also known as cell salvage, is one of those methods and involves recycling the patients shed blood from the surgical field (3). The blood is anticoagulated, collected into a reservoir, washed, and concentrated into a transfusable

packed red cell (PRC) unit. Cell salvage has become a valuable resource in the operating arena as it may minimize or eliminate the need for allogenic blood transfusion and its associated risks (4).

First-generation cell salvage systems use a Latham bowl for centrifugation of shed blood and operate discontinuously. The Food and Drug Administration (FDA) cleared the first Continuous Autotransfusion System (CATS) (Fresenius Kabi, Lake Zurich, IL) in 1996. This type of device is used during surgical procedures in which shed whole blood is collected from the surgical field, anticoagulated, and collected in a sterile reservoir. This blood is concentrated and washed into a PRC unit for reinfusion. Reported advantages of the CATS continuous system over discontinuous Latham bowl-type systems include the ability to remove lipids from the shed blood and the ability to obtain a consistently higher concentrated PRC product (5). During the washing process, shed blood is suspended with

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isotonic saline in the centrifuge and contaminants, along with fat, albumin, and plasma, are removed into a waste bag. The washed blood is concentrated to a final hematocrit (HCT) >50% and transferred into a reinfusion bag (6).

The C.A.T.S.^{plus} system was released in 2004 and uses similar blood and saline sensors, but this model also included data management and transfer capabilities. It is currently in use today and is the comparison device for their newest device in the product line—CATSmart system. The CATSmart system uses a higher resolution camera that monitors the red blood cell (RBC)-plasma interface and automatically adjusts blood and saline flow rates into the device, which optimizes product separation and washing. It also has the capacity to monitor shed blood and PRC HCT through an in-line sensor. There are three wash options similar to the C.A.T.S.^{plus} device: a low-volume wash, a smart wash, which is similar to the high-quality wash of the C.A.T.S.^{plus} device, and an emergency wash. To improve functionality of the device, the overall footprint is smaller and has a height-adjustable centrifuge body. User-friendly options have also been added including a touch screen interface and an auto start processing feature.

The primary objective of this study was to evaluate whether the CATSmart system is non-inferior to the C.A.T.S.^{plus} system, in being able to produce a mean PRC HCT within a 15% margin of the C.A.T.S.^{plus} system and whether the final PRC product had an HCT >50%.

Secondary objectives included the evaluation of washing and concentrating of RBC to produce a product within certain parameters. Low-volume (200 and 700 mL) wash parameters included >40% RBC recovery rate, >92% total protein and albumin elimination rates, and <1% hemolysis after 24 hours of storage. Smart wash parameters included >80% RBC recovery rate, >92% total protein and albumin elimination rates and, <1% hemolysis after 24 hours of storage. Emergency wash parameters included >80% RBC recovery rate, >50% total protein and albumin elimination rates, and <1% hemolysis after 24 hours of storage. These secondary objective parameters are based on the performance of the predicate device using studies associated with the 510K application for the CATS and C.A.T.S.^{plus} devices. They are consistent with the design specifications of the device and user requirements defined during product development. The FDA requires manufacturers of RBC products to demonstrate <1% hemolysis at the end of storage as part of the product approval process. This is also a measure of cell viability at the end of storage.

METHODS

Whole blood was collected from healthy human donors and stored in citrate phosphate dextrose solution at 1–6°C. Whole blood was purchased from Interstate Blood Bank,

who consented the donors. The study was granted an Institutional Review Board exemption and was conducted in a laboratory without any patient contact or collection of protected health information. ABO-compatible whole blood was pooled together and then diluted to an HCT of approximately 20% with isotonic saline to mimic shed blood that is routinely collected intra- or post-operatively. The pooled blood was divided into two aliquots and processed as a pair using the C.A.T.S.^{plus} and CATSmart systems with their corresponding wash programs: low-volume, high quality/smart, or emergency wash. To characterize the final PRC product, laboratory measurements were taken before and after processing the shed blood on each system. Additional testing was conducted at hours 6 and 24 to measure hemolysis during storage. Spun HCTs were tested using manual methods. Complete blood counts were conducted using the KX-2ln Hematology Analyzer (Sysmex, Lincolnshire, IL) at Duke University and Fresenius Kabi, and the XN Hematology Analyzer (Sysmex) at Maine Medical Center. Clinical chemistry testing was centralized using the AU400e (Olympus, Tokyo, Japan).

The data from previous validation studies performed showed a mean HCT of 56.8% for the CATSmart system and a mean HCT of 57.0% for the C.A.T.S.^{plus} system, with a maximum SD of 7.1. The one-sided 95% chi-squared confidence limit on this SD is 13.6. On the basis of these data, a minimum of 24 sample pairs were needed to provide sufficient power to find the CATSmart system non-inferior to the C.A.T.S.^{plus} system at a margin of 15%. A total of 27 sample pairs were used for an equal distribution among wash programs. Furthermore, to evaluate the performance of the device and quality of product when minimal shed blood is processed, nine sample pairs were added to evaluate the 200-mL low-volume wash program. This brought the total number of needed paired tests to 36 for the study.

Standard summary statistics (*N*, mean, SD, median, minimum, and maximum) are reported for all measures. Non-inferiority testing was carried out evaluating the new sample against a 15% decrease in the primary outcome, spun HCT using a *t* test only. A Bland–Altman plot was created for the primary outcome, spun HCT, and to assess agreement across all assay values. Paired 2-sample *t* tests were performed for all secondary outcomes assuming an alpha = .05. Summary and non-inferiority calculations were performed using BASE SAS 9.4 Procedure Guide: Statistical Procedures (SAS Institute, Cary, NC). Paired 2-sample *t* tests and the Bland–Altman plot were performed and constructed using Stata SE 14.1 (Statacorp, College Station, TX).

RESULTS

Thirty-eight paired tests were attempted on the CATSmart and C.A.T.S.^{plus} systems at three separate centers

(Fresenius Kabi, Duke University Hospital, and Maine Medical Center Research Institute) between October 14, 2015 and January 15, 2016. One pair was not evaluable after a PRC sensor error, meaning 37 paired tests were processed completely and available for review. The one non-evaluable procedure occurred on the CATSmart device due to an instrument failure, caused by a PRC failure alarm. This was likely due to a misaligned label on the disposable, which is a known issue and has been corrected.

All Wash Combined Results

Table 1 displays the data regarding spun HCT (%) after processing with mean (SD) spun HCT values for CATSmart and C.A.T.S^{plus} systems being 59.6% (6.4) and 57.7% (4.3), respectively. The Bland-Altman Plot (Figure 1) for spun HCT values for the two systems shows relative agreement across the spectrum of values. Table 2 demonstrates the non-inferiority of the CATSmart system at 15% margin when compared to the C.A.T.S^{plus} system with a resulting *p* value < .0001. For results in Tables 3 and 4, all washes are evaluated on the secondary efficacy blood analysis parameters, along with RBC recovery and elimination rates. Hemolysis values are found in Table 5. Differences in secondary outcomes between the two systems showed generally small clinically irrelevant, but statistically significant, differences in volume (*p* = .0007), WBC count (*p* = .0005), RBC count (*p* = .03), platelet (PLT) count (*p* = .0004), spun HCT (*p* = .046), WBC elimination (*p* < .0001), and PLT elimination (*p* = .001).

Low-Volume Wash

Ten paired tests were evaluated using a starting volume of 200 mL and an HCT of 20%. The mean (SD) HCT difference between the CATSmart and C.A.T.S^{plus} systems, respectively, were 55.8% (8.0) and 56.2% (5.9), with a mean RBC recovery rate of 71.0% (10.6) and 69.3% (8.7). The mean albumin and total protein elimination rates were 98.9% (.5) and 98.3% (.6) and 98.4% (.5) and 97.8% (.7), respectively. The mean hemolysis was .09% (.03) and .12% (.06) after 24 hours of storage.

Nine paired tests were evaluated using a starting volume of 700 mL and an HCT of 20%. The mean (SD) HCT difference between the CATSmart and C.A.T.S^{plus} systems, respectively, were 62.5% (5.8) and 58.3% (3.1), with a mean RBC recovery rate of 90.3% (14.1) and 90.5%

Table 1. Spun HCT values after processing, combining all wash programs.

	<i>N</i>	Mean (SD)	Median	Minimum, Maximum
CATSmart	37	59.6 (6.4)	59.5	39, 72
C.A.T.S ^{plus}	37	57.7 (4.3)	58	47, 66
CATSmart - C.A.T.S ^{plus}	37	1.9 (5.7)	2	-18, 14

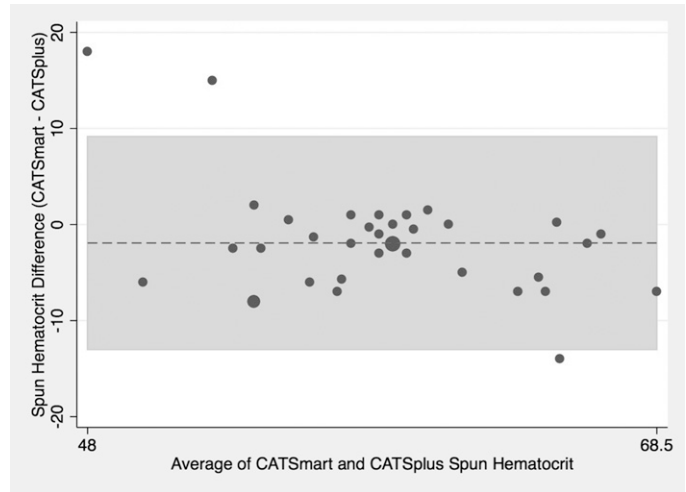


Figure 1. Spun HCT (Bland-Altman test).

(12.7). The mean albumin and total protein elimination rates were 97.1% (4.8) and 98.7% (.4) and 96.8% (4.7) and 98.5% (.5), respectively. The mean hemolysis was .07% (.07) and .05% (.01) after 24 hours of storage.

Smart Wash

Nine paired tests were evaluated using a starting volume of 1,000 mL and an HCT of 20%. The mean (SD) HCT difference between the CATSmart and C.A.T.S^{plus} systems, respectively, were 63.9% (4.0) and 60.3% (3.7), with a mean RBC recovery rate 91.1% (4.6) and 89.7% (5.6). The mean albumin and total protein elimination rates were 99.1% (.3) and 98.9% (.3) and 98.8% (.3) and 98.7% (.3), respectively. The mean hemolysis was .05% (.01) and .08% (.09) after 24 hours of storage.

Emergency Wash

Nine paired tests were evaluated using a starting volume of 1,000 mL and an HCT of 20%. The mean (SD) HCT difference between the CATSmart and C.A.T.S^{plus} systems, respectively, were 56.8% (2.3) and 56.2% (2.6), with a mean RBC recovery rate 90.8% (9.1) and 92.2% (8.6). The mean albumin and total protein elimination rates were 95.1% (.8) and 96.1% (.7) and 94.4% (1.2) and 95.2%

Table 2. Non-inferiority analysis results.

	Paired Difference (CATSmart - .85 × C.A.T.S ^{plus})		
	Mean (SD)	Lower Confidence Limit*	<i>p</i> Value
CATSmart - C.A.T.S ^{plus}	10.6 (5.2)	8.2	<.0001

*A lower confidence limit > 0 indicating non-inferiority at a 15% margin is met.

Table 3. Summary of blood analysis parameters after processing, combining all wash programs.

Parameter	Mean (SD)	Median	Minimum, Maximum	2-Sided Paired <i>t</i> Test, <i>p</i> Value
Volume (mL)				.0007
C.A.T.S ^{plus}	213.9 (112.0)	252.0	41.3, 368.2	
CATSmart	206.0 (107.2)	234.1	37.5, 363.3	
WBC count ($\times 10^3/\mu\text{L}$)				.0005
C.A.T.S ^{plus}	8.3 (2.8)	8.1	3.3, 15.2	
CATSmart	6.6 (2.2)	6.6	2.2, 11.7	
RBC count ($\times 10^6/\mu\text{L}$)				.03
C.A.T.S ^{plus}	6.1 (.4)	6.1	4.7, 7.4	
CATSmart	6.3 (.6)	6.4	4.2, 7.2	
PLT count ($\times 10^3/\mu\text{L}$)				.0004
C.A.T.S ^{plus}	68.0 (23.1)	63.0	29, 123	
CATSmart	56.3 (24.5)	54.0	14, 143	
Total hemoglobin (g/dL)				.4695
C.A.T.S ^{plus}	17.5 (1.8)	17.6	12.5, 22.5	
CATSmart	17.8 (3.3)	18.2	3.6, 23.1	
Spun HCT (%)				.046
C.A.T.S ^{plus}	57.7 (4.3)	58.0	47.0, 66.0	
CATSmart	59.6 (6.4)	59.5	39.0, 72.0	

(1.4), respectively. The mean hemolysis was .03% (.01) and .05% (.04) after 24 hours of storage.

DISCUSSION

The salvage of shed blood during surgical procedures has been recognized as an important component to hospital blood conservation programs (7). However, it has been well recognized that the quality of processed salvaged blood is quite variable (2,5). The RBC recovery rate and washing efficiency may be influenced by the type of centrifugal device used, rate of blood processing, or

Table 4. Recovery and elimination rates after processing, combining all wash programs.

Parameter (%)*	Mean (SD)	Median	Minimum, Maximum	2-Sided Paired <i>t</i> Test, <i>p</i> Value
RBC recovery				.7404
C.A.T.S ^{plus}	85.0 (13.2)	86.5	59.7, 113.0	
CATSmart	85.4 (13.2)	86.7	56.7, 123.2	
WBC elimination				<.0001
C.A.T.S ^{plus}	18.8 (14.6)	18.9	-12.6, 71.6	
CATSmart	34.7 (18.4)	34.4	1.9, 87.8	
PLT elimination				.0124
C.A.T.S ^{plus}	72.1 (21.2)	77.9	-9.8, 89.9	
CATSmart	78.0 (18.1)	83.5	-2.8, 96.1	
Albumin elimination				.2912
C.A.T.S ^{plus}	98.0 (1.2)	98.6	94.8, 99.4	
CATSmart	97.6 (2.8)	98.8	84.4, 99.3	
Total protein elimination				.3132
C.A.T.S ^{plus}	97.5 (1.6)	98.2	93.4, 99.2	
CATSmart	97.1 (2.9)	98.3	84.4, 99.1	
Potassium elimination				.6089
C.A.T.S ^{plus}	91.9 (2.1)	92.0	86.8, 95.8	
CATSmart	92.1 (3.0)	92.8	84.4, 96.5	

*Calculated parameters.

Table 5. Summary of hemolysis* after processing, combining all wash programs.

	C.A.T.S ^{plus} Mean (SD)	CATSmart Mean (SD)	2-Sided Paired <i>t</i> Test, <i>p</i> Value
Immediately AP	.06 (.05)	.07 (.14)	.6322
At 6 hours	.06 (.05)	.06 (.05)	.8862
At 24 hours	.07 (.06)	.06 (.04)	.1944

*Calculated parameters.

the volume of blood available for processing. Shulman examined the efficiency of RBC recovery rates and plasma washout rates of three different cell saver devices using various flow and wash rate protocols. He reported that continuous flow devices had superior performance in terms of processed blood HCT levels and plasma albumin elimination when compared to discontinuous flow devices (2).

The aim of this study was to determine if the CATSmart system was non-inferior to the C.A.T.S^{plus} system. We examined the HCT of the processed blood, the RBC recovery rate, the elimination of total protein and albumin, and RBC viability as measured by hemolysis. The performance was tested when three different processing programs were used on small and large aliquots of shed blood.

All objectives, primary and secondary, were met. The paired procedures conducted for evaluation of the CATSmart, as well as C.A.T.S^{plus} systems demonstrated reliable operation and function of RBC recovery, concentration, and washing. The evaluations used the lower end of acceptable blood volume for operation and expected use of the device.

The RBC recovery and concentration functions were measured by final HCT of PRC product. A mean RBC recovery rate of 85.4% and a mean HCT of 59.6% were identified across all wash programs evaluated. Of all wash programs evaluated, the smart wash revealed the highest RBC recovery rate of 91.1% and mean HCT of 63.9%. Conversely, the wash with the lowest mean rate of RBC recovery and HCT was the low-volume wash (200 mL) with 71.0% and 55.8%, respectively. Under this wash program, two procedures resulted in HCT <50%. The low-volume wash (200 mL) with 20% HCT represents 40 mL of RBCs, which approaches the minimal RBC volume the device can efficiently process and still produce a PRC >50%. However, a median HCT >50% was still achieved during the testing of 10 paired washes, demonstrating that even with low volumes, a sufficient product can be recovered (8). Likewise, with the emergency wash achieved an impressive end product mean HCT >50%.

The results demonstrate an efficient elimination of plasma constituents and soluble contaminants with all washes. This is important in the operating room, as irrigation fluids, anticoagulant, and other chemicals or debris may be aspirated into the reservoir during surgery. The

device removes such contaminants based on density. As the centrifuge spins, soluble blood components are separated from formed cellular bodies (RBC, WBC, PLTs) and removed (9). Overall potassium, PLT and WBC elimination data were also obtained and found to be 92.1%, 78.0%, and 34.7%, respectively. The WBC elimination was determined to be 34.7% and under special conditions in which it would be clinically advantageous to leuko reduce the RBC product, a leukocyte reducing filter may be used.

RBC washing functionality with the CATSmart system was measured by elimination of plasma constituents. Total protein and albumin elimination rates were excellent and measured 97.1% and 97.6%, respectively. The smart wash, as expected, demonstrated the highest elimination rates of protein and albumin of 98.9% and 99.1%, respectively, whereas the emergency wash had a slightly lower elimination rate of total protein and albumin of 94.4% and 95.1%, respectively. This finding is important as the product from an emergency wash is still excellent, while the processing time is far less than that of the smart wash, 9.3 minutes to 16 minutes, respectively.

Viability of the RBC collected over time is also important. Overall, very low levels of hemolysis were identified immediately after processing (.07%), at 6 hours (.06%), and at 24 hours (.06%). Maximum reported hemolysis was .27%, which met the secondary objective of <1% hemolysis after storage. Hemolysis testing was conducted at hours 6 and 24 because the device can be used for both intra- and post-operative shed blood collections. American Association of Blood Banks standard 5.1.8A states intra-operative shed blood stored at room temperature should be transfused within 4 hours of processing or if refrigerated at 1–6°C, within 24 hours. Post-operative shed blood can be stored for up to 6 hours after processing (10). Therefore, to assess product acceptability for both intra- and post-operative conditions, hemolysis at those specific time points was assessed.

There are a number of improved functionalities in the CATSmart. It has a quieter motor, the height-adjustable body and overall smaller footprint allows the CATSmart device to better fit in smaller spaces and is ergonomically friendly. The touch screen display, which can be used with gloved hands, has a quick start option which is helpful when rapid processing of shed blood is necessary. In addition, the autostart processing feature allows the operator

to focus on the patient, not the device, generating a safety benefit with the device.

Regardless of the wash program used, cells are efficiently recovered, washed, and concentrated, and produce a quality PRC product that is appropriate for autologous transfusion. Both the CATSmart and C.A.T.S^{plus} systems were able to consistently produce PRC with a HCT >50%. The study also confirmed the CATSmart system is non-inferior to the C.A.T.S^{plus} system in mean PRC HCT within a 15% margin. All secondary objectives—RBC recovery rate, plasma and total protein elimination, and hemolysis after 24 hours—were also achieved. This study demonstrated that the CATSmart and C.A.T.S^{plus} systems produce a high-quality PRC product, even when volumes as small as 200 mL are processed using the low-volume wash program. Overall, the enhancements to the CATSmart system, along with the study results, make it a viable addition to any institution using blood conservation and cell salvage.

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