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Use of clinical data and acceleration profiles to validate pneumatic transportation systems

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Abstract

Background: Modern pneumatic transportation systems (PTSs) are widely used in hospitals for rapid blood sample transportation. The use of PTS may affect sample integrity. Impact on sample integrity in relation to hemolysis and platelet assays was investigated and also, we wish to outline a process-based and outcome-based validation model for this preanalytical component.

Methods: The effect of PTS was evaluated by drawing duplicate blood samples from healthy volunteers, one sent by PTS and the other transported manually to the core laboratory. Markers of hemolysis (potassium, lactate dehydrogenase [LD] and hemolysis index [HI]) and platelet function and activation were assessed. Historic laboratory test results of hemolysis markers measured before and after implementation of PTS were compared. Furthermore, acceleration profiles during PTS and manual transportation were obtained from a mini g logger in a sample tube.

Results: Hand-carried samples experienced a maximum peak acceleration of 5 g, while peaks at almost 15 g were observed for PTS. No differences were detected in results of potassium, LD, platelet function and activation between PTS and manual transport. Using past laboratory data, differences in potassium and LD significantly differed before and after PTS installation for all three lines

evaluated. However, these estimated differences were not clinically significant.

Conclusions: In this study, we found no evidence of PTS-induced hemolysis or impact on platelet function or activation assays. Further, we did not find any clinically significant changes indicating an acceleration-dependent impact on blood sample quality. Quality assurance of PTS can be performed by surveilling outcome markers such as HI, potassium and LD.

Keywords: acceleration; blood sample quality; pneumatic transportation system; preanalytical; quality control; validation system; vibration.

Introduction

All phases of laboratory testing can theoretically affect blood sample quality and thereby measured clinical parameters. After three decades of improvement and standardization of the analytical phase, focus and interest have now turned to the pre-analytical phase of laboratory testing, and standardization and harmonization of each sub-portion of the pre-analytical phase is a high-priority topic. Transportation of samples is a major component of this process and is a future focus area [1].

Modern pneumatic transportation systems (PTS) are widely used in hospitals for rapid and effective blood sample transportation. As transportation time plays a major role in the overall efficiency and turnaround time (TAT) of the total laboratory analysis process, PTS can improve the cost-benefit efficiency of patient care. The use of PTS provides not only a significant reduction in TAT, but may also affect blood sample quality, primarily due to *in vitro* hemolysis by physical stress [2–4] and cell activation [4]. Features of PTS contributing to physical stress of the blood samples have been investigated and include time (samples spend approximately 30–60 s within the transportation system), transportation speed, distance, acceleration, deceleration, vibration of blood samples and lack of cushioning at sample arrival [3, 5–7].

Several papers describe how PTS may increase the risk of *in vitro* hemolysis [2, 8–10]. Clinical chemistry analyses are most often discussed in this context; however, blood gas, hematology and coagulation analyses have

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also been subject to evaluation when assessing the effects of PTS on specimen integrity [4, 11, 12]. Impact on platelet function has also been investigated, and as a possible consequence of physical stress and increased interaction between neighboring cells and the surface of the sample tube, reduced platelet activation has been shown [4, 12]. PTS transport has also shown significantly decreased response on impedance platelet aggregometry [13].

Previously, acceleration during pneumatic transportation of blood samples has been suggested to affect laboratory results [5, 7, 14, 15]. The combined three-axis effect of accelerations, expressed as area under the curve (AUC), has been found to correlate with PTS speed and to exhibit a direct relation to the degree of hemolysis [5]. Further, increase in lactate dehydrogenase (LD) and hemolysis index (HI) has been demonstrated to correlate with the number of accelerations with g-forces above 3 g [7]. Recently, two different accelerometers were tested in multiple PTS lines to define parameters for the evaluation and validation of PTS in hospitals [14].

In this study, we evaluated the impact of sample transportation by PTS with a focus on hemolysis. Further, we aimed to investigate the impact on platelet function assays, where TAT can be crucial for critically bleeding patients. Also, we sought to outline a process-based and outcome-based model for validation of this preanalytical component. To achieve this, various hemolysis measures (potassium, LD and HI), as well as platelet function and activation, were compared with acceleration measurements from a miniaturized data logger that traveled through the same PTS lines, and existing data for pre- and post-PTS transit clinical results were compared.

Materials and methods

Ethical considerations

The study was approved by the Danish Data Protection Board (journal number: 18/43639) and by The Regional Committees on Health Research Ethics for Southern Denmark (journal number: 18/47772). According to the requirements of The Regional Committees on Health Research Ethics for Southern Denmark, all participants provided signed informed consent.

Pneumatic transportation system

The PTS evaluated was Tempus600® (TIMEDICO A/S, Bording, Denmark), where samples are sent one by one without any additional packaging. Approximately 30 s after the samples arrive at the core

laboratory, they are handled by an automatic sorting system (GLP Systems, Sysmex, Denmark) connected directly to the laboratory automation system for further processing (i.e. centrifugation, analysis and archiving).

Populations and laboratory data

Use of past laboratory data: In order to evaluate differences between patients (due to disease-associated differences in cell fragility), historic laboratory data including results from laboratory analyses on samples sent before and after implementation of the Tempus system were compared for three different departments: Department of Hematology, Department of Nephrology and Department of Cardiology (abbreviations for the departments: A, B, C). From these departments, all laboratory results for potassium and LD were extracted from our laboratory information system (BCC, CGI, Kolding, Denmark) for the same (random) month of a year before (April 2016) and after Tempus installation (April 2017). Samples were in both periods measured on an Architect c16000 analyzer (Abbott, IL, USA). In total, the number of samples in this part of the study was: $n = 7027$ for potassium and $n = 3638$ for LD.

The speed of the PTS from the Oncology Ward was reduced from 10.9 to 9.7 m/s in September 2018. To investigate if the speed reduction had had any effect on potassium and LD results, we extracted data from April 2018 and October 2018 to represent data before and after speed reduction, respectively. Analyses were in both periods performed on a Cobas 8000 analyzer (Roche Diagnostics, Mannheim, Germany).

Prospective study

We collected four blood samples (two containing lithium heparin [Li-Hep] and two containing citrate) (Becton Dickinson, Franklin Lakes, NJ, USA) from 20 healthy volunteers aged between 18 and 70 years in our Phlebotomy Ward (D) over a period of 2 weeks. Duplicate blood samples were drawn from the antecubital vein by the same experienced phlebotomist following the local standard operating procedure using a 21-gauge vacutainer needle or push button (Becton Dickinson). The participants were not allowed to take any medication known to affect platelets within 14 days prior to blood sampling. For all participants, one tube of each kind (Li-Hep and citrate) was sent by PTS, while the remaining two were hand-carried to the laboratory. The Tempus line used in this case was placed at the Phlebotomy Ward (D).

Chemistry analyzers and analysis principles

Potassium, LD and HI were measured either on Architect c16000 or on Cobas 8000 in Li-Hep plasma. Potassium was measured using an ion-selective electrode method [16], while LD was measured by absorption photometry [17]. Calculation of HI was based on spectrophotometric readings: Sample and saline were pipetted into a cuvette and read at different wavelengths, and HI was then calculated by a formula using the absorbance readings [18, 19].

Methods for measuring platelet function

Platelet function and activation analyses were performed on whole blood from citrate tubes. Platelet aggregation was measured using a Multiplate analyzer (Roche Diagnostics, Mannheim, Germany), which uses whole blood impedance aggregometry. The change in impedance is transformed to arbitrary aggregation units and plotted against time, where area under the aggregation curve expresses the overall platelet activity [20]. The agonists used were adenosine diphosphate (ADP) (6.4 μM), arachidonic acid (AA) (0.5 μM) and thrombin activator receptor peptide-6 (TRAP) (32 μM). ADP was obtained from Sigma Aldrich (St. Louis, MO, USA), while AA and TRAP were from Roche Diagnostics (Mannheim, Germany).

Platelet p-selectin (CD62p) was measured as a marker of platelet activation by flow cytometry on FACS Canto II flow cytometer (Becton Dickinson, NJ, USA). For this analysis, 1 μL anti-CD62p antibody was mixed with 8.3 μL anti-CD42b antibody (eBioscience, San Diego, CA, USA). The antibody mixture was then mixed with 2.5 μL whole blood. Samples were incubated for 15 min at room temperature in the dark and then fixed with 0.5% formaldehyde diluted in phosphate-buffered saline. Samples were analyzed immediately after incubation. The flow cytometer was set to count 5000 events determined by platelet light-scattering properties on a forward-site scattered plot. The results were reported as percentage of platelets staining positively for CD62p (representing activated platelets), normalized to platelets at rest (no transportation) [21].

Data logger and data analysis of acceleration data

A miniaturized data logger (VitalTag VT0; Motryx Inc., Halifax, Canada) embedded in gel in a 10-mL plastic tube from Becton Dickinson (NJ, USA) was used to log acceleration data. The weight of the tube with the data logger was 25.50 g, whereas the weight of a blood-filled tube was 19.44 g. The logger was transported in the Tempus lines and by hand from Departments A, B, C and D to the laboratory.

The data logger consists of a three-axis accelerometer (x , y and z acceleration components), a gyroscope and a thermometer. In this study, only the accelerometer data were used. Acceleration data were processed following the procedure outlined in Streichert et al. [5]. First, the absolute vector sum from the x , y and z acceleration components for each PTS and hand-carried evaluation was calculated. Acceleration peaks were detected using Marcos Duarte's detect peak algorithm [22] and histogram distributions of the number of peaks at any given acceleration were calculated using 256 bins as outlined in Streichert et al. [5]. These distributions were then used to calculate the AUC with an upper threshold of 2 g. This procedure was repeated for each test and the average AUC and standard deviations (SDs) for each department and Tempus line were calculated. The between-day variability (coefficient of variation [CV]) of AUC in the four lines was calculated based on four tests over 4 separate days. AUC parameters were tested as a function of length of each system and the speed of each system. AUC was tested as a function of tube length and system velocity to determine whether these factors contribute to the AUC parameter, which describes overall vibration.

Statistical analyses

Data from blood parameters were tested for normality using the Shapiro-Wilk test and verified by visual inspection of histograms and quantile-quantile plots. Statistical significance was tested at a 95% confidence level and $p < 0.05$ was considered significant.

For the analyses on historic laboratory data, the laboratory results measured before and after Tempus implementation were compared by an unpaired t-test (data normally distributed) and the Mann-Whitney test (data non-normally distributed). In addition, the relative median biases (data non-normally distributed, data of median biases not shown) for potassium and LD were calculated and tested as a function of AUC of the Tempus line in question and compared with hand-carried samples. AUC was plotted with box plots illustrating medians, 25th and 75th percentiles.

In the prospective part of the study, blood parameters measured after manual transport or by PTS were compared with an unpaired t-test (data normally distributed) and the Wilcoxon signed-rank test (data non-normally distributed).

Clinical significance (in both the retrospective and prospective parts of the study) was estimated analyte-specific by established mean differences larger than analytical acceptable difference. The variance (SD^2) of this difference is expressed by equation [23]

$$\text{SD}_{\text{diff}}^2 = \text{SD}_{a1}^2 + \text{SD}_{a2}^2 = 2 \times \text{SD}_a^2 \rightarrow \text{SD}_{\text{diff}} = \sqrt{2 \times \text{SD}_a^2} = \sqrt{2} \times \text{SD}_a$$

where $a1$ and $a2$ indicate the two analyses (in this case the same). If Tempus does not increase variation or cause a systematic bias, we assume that the difference in results is normally distributed with a mean of 0. This means that the lower quantile (0.025) is 1.96 and the limits for combined uncertainty of 95% are [23]:

$$\text{Acceptable difference} \leq 1.96 \times \sqrt{2} \times \text{SD}_a$$

We used the SD for normal values over the measured range obtained from our own verification studies of all the analyses, including the verification of HI.

Results

Characterization of PTS

All hand-carried samples showed a significantly lower acceleration amplitude than those sent through the PTS (demonstrated by time series of vector norm in Figure 1). Hand-carried samples experienced a maximum peak acceleration of 5 g, while in the PTS peaks at almost 15 g were observed. There was no clear relationship between system velocity and AUC, while the relationship between AUC and system length was evident with increasing AUC for the longer tube line (Supplementary material, Figures 1 and 2). The technical specifications and AUCs of each Tempus line and the between-day variability of

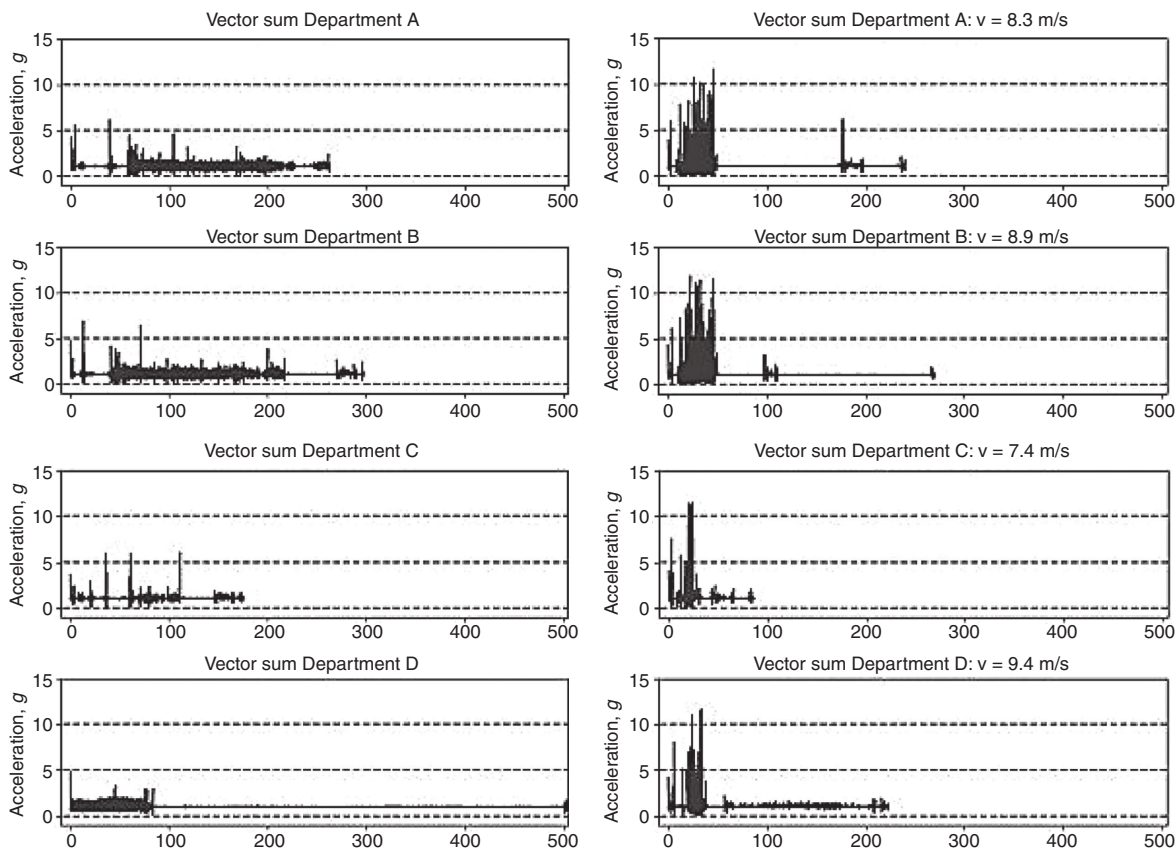


Figure 1: An example of acceleration time series for all four evaluated Tempus systems (A–D).

Graphs on the left are for hand-carried samples, and graphs on the right are for PTS samples. G-forces are plotted on the Y-axis and time in seconds on the X-axis. Each horizontal line (two graphs) represents one of the four experiments (for each department and for each transport form) carried out with the data logger. v , velocity.

cumulative accelerations in four lines of the hospital are shown in Supplementary Table 1. The between-day CV of cumulative accelerations ranged from 2% to 17%. The largest CV was found for Department C with the shortest pipe length, lowest speed, lowest number of connections and lowest AUC. In contrary, the lowest CV of 2% was found from Department B with the longest pipe length and highest AUC.

Laboratory results of the prospective study

The results of population means and SD and differences thereof, as well as SD for the analyses at Odense University Hospital (Cobas analyzer), are shown in Table 1 for the two transportation forms (PTS and hand-carried). The observed differences between those were not statistically significant and did not vary more than expected from the analytical variation. Representative scatter diagrams for the p-selectin analysis between the two transportation forms are shown in Figure 2.

Laboratory results of the retrospective study

The results of patient means and SD and the differences thereof, as well as the SD for the analyses at Odense University Hospital (Architect analyzer), are shown in Table 2. For all three Tempus lines, the differences between potassium and LD before and after Tempus installation were significant. For potassium, use of PTS did not result in more variation than expected from the analytical variation. For LD, PTS caused differences larger than could be expected from analytical variation for all three departments.

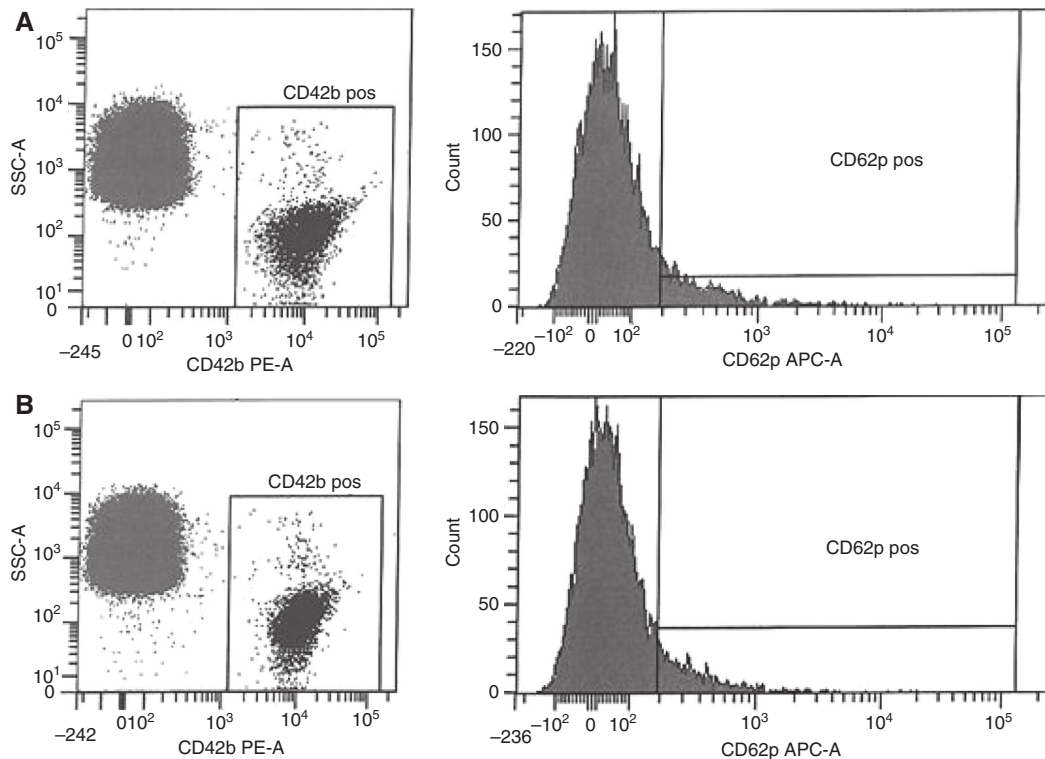
The relative median changes of potassium and LD as a function of AUC are shown in Figure 3. Changes in potassium and LD increased with increasing AUC (Figure 3) with the exception of Department C, where no change in potassium was observed and Department B and Department C where LD decreased. The frequency of results automatically replaced by the comment “Hemolysis” did not show any trend.

The results of potassium and LD before and after speed reduction of one Tempus line (Department E) are

Table 1: Prospective comparison of PTS with manual transport on potassium, LD, HI and platelet function and activation assays.

Analyte	Units	n	Mean (SD)		(PTS – manual)		p-Value	SD-OUH	Acceptable difference
			Manual transport	PTS	Mean _{difference}	SD _{difference}			
Potassium	mmol/L	20	4.07 (0.28)	3.99 (0.28)	-0.08	0.00	0.3856	0.05	+
LD	U/L	20	174 (32)	179 (31)	5.0	1.0	0.4819	3.9	+
HI	g/L	20	7.5 (3.0)	7.0 (2.6)	-0.5	-0.4	0.6261	0.2	+
Platelet									
Aggregation with multiplate									
TRAP 32, μM	AU/min	20	1090 (193)	1099 (173)	9	20	0.8711	4.3	+
AA 0.5, μM	AU/min	20	685 (188)	673 (177)	-12	-11	0.9246	0.1	+
ADP 12.8, μM	AU/min	20	732 (163)	715 (168)	-17	5	0.7600	1.4	+
Activation									
Platelet P-selectin	% Positive platelets	20	7.3 (3.6)	7.4 (3.9)	0.1	0.3	0.8498	0.9	+

PTS, pneumatic transportation system; SD, standard deviation, OUH, Odense University Hospital.

**Figure 2:** Whole blood flow cytometry analysis of p-selectin.

Representative scatter diagrams of two blood samples from the same test person: one sample transported manually (A) and one sample sent by Tempus (B). Platelets (CD42b positive) were identified by their characteristic light scatter properties in the left panel. The right panel reflects the fraction of activated platelets (CD62p positive). The gate was set using resting platelets according to the laboratory protocol.

shown in Table 3. The speed reduction did not result in a statistically significant difference between patient means of potassium or LD results before and after. The concentrations of LD differed more than expected from analytical variation, the lowest values obtained

at the faster speed. The frequency of LD results with the comment “Hemolysis” decreased from 264 (16.4%) to 222 (12.9%) with speed reduction. Also, a slight decrease in hemolyzed potassium results was observed (0.1%).

Table 2: Retrospective comparison of PTS with manual transport on potassium and LD.

Departments	Units	Results with comment "Hemolysis"		Mean (SD)		(After – before)		p-Value	SD-OUH	Acceptable difference
		Before PTS, n (%)	After PTS, n (%)	Before PTS	After PTS	Mean _{difference}	SD _{difference}			
Department A										
Potassium	mmol/L	2 (0.2)	3 (0.5)	3.78 (0.48)	3.65 (0.47)	-0.13	-0.01	0.001	0.08	+
LD	U/L	12 (3.4)	11 (4.5)	263 (160)	348 (355)	85	-195	0.001	3.7	-
Department B										
Potassium	mmol/L	1 (0.2)	2 (0.4)	4.26 (0.69)	4.42 (0.73)	0.16	0.06	0.000	0.08	+
LD	U/L	3 (3.0)	2 (2.0)	233 (82)	227 (63)	-6	-19	0.000	3.7	-
Department C										
Potassium	mmol/L	2 (0.5)	1 (0.2)	3.98 (0.48)	3.98 (0.54)	0.000	0.06	-	0.08	+
LD	U/L	0 (0)	1 (5.6)	291 (76)	282 (64)	-9	-12	0.000	3.7	-

PTS, pneumatic transportation system; SD, standard deviation; OUH, Odense University Hospital.

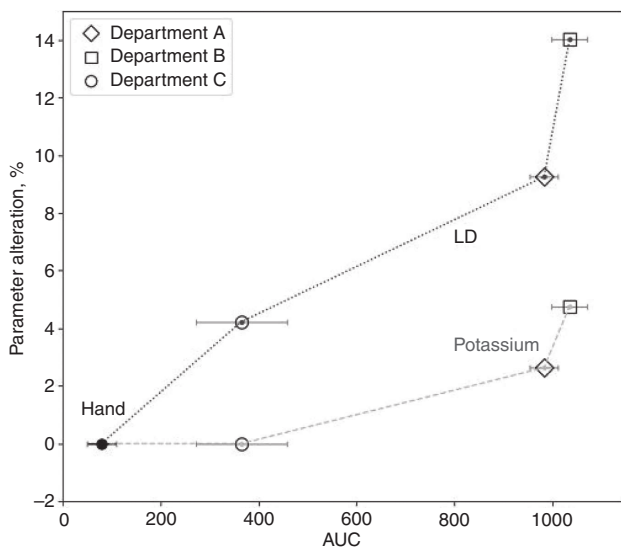


Figure 3: Percent changes in potassium and LD results (Y-axis) as a function of AUC (X-axis) in the evaluation of hematology (A), nephrology (B) and cardiology (C) departments from samples sent with Tempus.

AUC: area under curve assessed with a threshold of 2 g represents cumulative accelerations and the average AUC of four tests performed on 4 different days from each department. The variability of AUC is included in the figure as interquartile ranges. Number of analyses included (samples sent with Tempus represented by the non-filled symbols): A: potassium: n = 565, LD: n = 235; B: potassium: n = 534, LD: n = 100; C: potassium: n = 416, LD: n = 17. The filled symbol represents the average AUC from four hand-carried samples with the variability included as interquartile ranges.

Discussion

Investigation of PTS at our hospital using a three-axis accelerometer and blood sample parameters indicative of hemolysis and markers of affected platelets showed a

relationship between AUC and system length, but no correlation between AUC and system velocity. However, speed reduction in one PTS reduced the frequency of withheld LD results by 3.5%. Peak accelerations expressed in gravitational forces were 3 times higher for PTS than manual transport. Changes in potassium and LD increased with increasing AUC and compared with hand-carried samples with the exception of Department C, where no changes in potassium were observed and LD decreased and Department B where LD also decreased. Using past laboratory data, mean differences of LD between manual and PTS transport for all three departments (A, B and C) were larger than could be expected from the analytical variation. Surprisingly, the differences in LD concentrations from Departments B and C were negative when the samples were sent via PTS (Table 2). It seems that the correlation between outcome data and AUC for g-forces is not straightforward. Confounding factors could be differences in the gold standard of transporting samples by cart and courier which is difficult to standardize, quality in sampling depending on the type of patients and diseases, distances to the departments, time for transport and temperatures. So, in some instances, Tempus transport is actually gentler than transport by courier. Although acceptable analytical limits were exceeded for Department A when samples were sent via PTS, the variation was clinically acceptable for monitoring hematological patients, judged by hospital hematologists.

We did not find any relevant changes in potassium, LD and HI results in our prospective evaluation of duplicate blood samples transported by PTS or manually. For platelets, no impact on activation and function could be demonstrated when samples were sent via PTS compared to hand-carried samples.

Table 3: Retrospective comparison of PTS with a speed of 10.9 m/s vs. 9.7 m/s on potassium and LD.

Department	Units	Results with comment “Hemolysis”		Mean (SD)		(After – before)		p-Value	SD-OUH	Acceptable difference
		PTS 10.9 m/s n (%)	PTS 9.7 m/s n (%)	PTS 10.9 m/s	PTS 9.7 m/s	Mean _{difference}	SD _{difference}			
Department E										
Potassium	μmol/L	8 (0.4)	6 (0.3)	4.00 (0.39)	4.13 (0.39)	0.13	0.00	–	0.08	+
LD	U/L	264 (16.4)	222 (12.9)	233 (115)	235 (130)	2	15	0.3612	3.7	–

PTS, pneumatic transportation system; SD, standard deviation; OUH, Odense University Hospital.

The effect of transportation by PTS on platelets has previously been investigated. Using impedance platelet aggregometry TRAP and aspirin tests, significant influences were demonstrated in 50 patients scheduled for coronary artery bypass surgery under oral therapy with 100 mg/day acetylsalicylic acid by PTS [13]. On the contrary, no altered platelet aggregation induced by ADP stimulation was observed in patients scheduled for coronary angiography [24]. Increased collagen-induced aggregation but decreased epinephrine response by light transmission aggregometry was found in 10 healthy people [25]. Studies of effects of PTS on platelet flow cytometry assays in healthy people are also non-conclusive [4, 25]. Our results contribute to the better understanding of acceleration forces of PTS and impact on platelet aggregation and activation assays for the Tempus system, which has not been evaluated before. The above-mentioned studies related to the effect of PTS on platelet assays [4, 13, 24, 25] were performed on transportation systems which use containers containing several blood tubes, whereas the Tempus system transports tubes individually.

Comparable to our results, Streichert et al. [5] found the highest peak accelerations (expressed in gravitational force) in their PTS (installed by Sumetzberger) of 15 g for the system with the highest speed (2.5 m/s) compared to hand-carried transport (9 g). The peak acceleration for hand-carried transport exceeded what we found in our study (5 g); however, the hand-carried transportation may not be entirely comparable in the two studies (transportation box and transportation wagon). Of note, we could not demonstrate a positive correlation between AUC and PTS speed compatible with the study by Streichert et al. Interestingly, we found lower AUC (median: 946) for higher speed (10.9 m/s) compared to their highest AUC (of approximately 1600) at a lower speed (2.5 m/s) in their study, despite using the same discrimination cut-off for the cumulative effect of the forces between PTS and hand-carried transport. Further, Streichert et al. found clinically significant changes for potassium and LD (relative changes exceeding the allowed relative deviation of quality control

– 4.5% for potassium and 9% for LD) and these changes decreased with speed reductions and decreasing AUC. In our study, we observed similar increased changes in potassium and LD (between departments and PTS) to correlate with increasing AUC for Department A. We suppose that this could be due to increased cell lysis with increasing acceleration vector sums from hematological patients with unstable blood components.

A difference in the PTS systems must be noted. Streichert et al. evaluated a conventional system with the use of carriers for the blood samples opposite to the Tempus system which does not use carriers. In 2017, Suchsland et al. [26] demonstrated that the acceleration forces in one Tempus line did not compromise sample quality in 36 analytes and the median AUC for acceleration forces was below the previously reported limit (500) for noticeable hemolysis [5]. Yet, this study was limited to evaluation of only one Tempus line without any connections. Extended to all Tempus lines at our hospital (with different lengths, different speeds and different number of connections), we neither found any impact of the sample in terms of hemolysis related to the acceleration forces. We did, however, find median AUC exceeding the previously reported limit of 500 for noticeable hemolysis [5] in four of five lines tested. Without evaluating acceleration forces, Brandslund et al. [23] also investigated the safety of one Tempus line in relation to 90% of the most frequently ordered laboratory tests. For the majority of analytes, whether transported by courier or the tube system, no difference was observed for population means and distribution width. Oxygen saturation, oxyhemoglobin and pO₂ showed unacceptable deviation from a clinical point of view, whereas differences in pCO₂ were unacceptable from an analytical quality point of view but clinically acceptable in patients with obstructive lung disease.

No well-defined international recommendation of continuous quality assessment of transportation with PTS has been proposed. As a part of regular quality control for our Tempus system, the speed and pressure are continuously monitored and is checked every 6 months by an

electrical technician. Recently, Nybo et al. [27] reviewed the results of studies investigating the effects of PTS on laboratory results. They concluded that local validation of the PTS is mandatory to ensure the quality of this preanalytical component as each installation of PTS is unique in architecture and technical specifications.

Inspired by recent recommendations, we tested the usefulness of measuring acceleration forces with data loggers to predict sample integrity in terms of hemolysis and platelet testing [5, 14, 27]. Based on experiences from previous studies [5, 26], we decided to evaluate all PTS at our hospital. The investigated PTSs in our study differ in length (73–297 m), speed (7.4–10.9 m/s) and numbers of connections [2–4], which makes our study representative for a PTS installation designed to transport samples without the use of a carrier. Farnsworth et al. [14] found an inverse relationship between the number of blood tubes in a carrier and the magnitude of *g*-forces, which appears to be due to reduced mobility of the data logger. We therefore strived to simulate regular blood sample transportation by embedding the data logger in a sample tube normally used for blood samples, the only difference being the weight of +6.0 g. This study is, to the best of our knowledge, the first to document the safety of the Tempus system related to platelet function and activation assays.

Our study does have some limitations: In the retrospective evaluation, we used data from highly specialized departments with critically ill patients from whom blood components may be more unstable than in other patient populations or healthy persons. The prospective part of the study was performed on healthy individuals, but platelet activation and function testing are only used for patients susceptible to hemostasis-related disease; our findings must therefore still be confirmed in that patient population. We restricted the evaluation to hemolysis-sensitive analyses and platelet assays. Other laboratory parameters may be related to acceleration forces in different ways. Also, p-selectin is only one of many known markers for platelet activation and further analyses can be tested or even combined to demonstrate platelet activation more clearly [21].

The capability of individual PTS line investigation with a data logger and an interpretation of the impact hereof on sample integrity can be applied in different situations: (i) it can be used to simulate PTS installations prior to the actual installation; (ii) the PTS can be tested prior to clinical use.

In conclusion, validation of PTS can be performed by documenting the relationship between concentrations of hemolysis-sensitive analyses and cumulative accelerations/*g*-forces for PTS and hand-carried transport

registered by a data logger. If outcome parameters show that there is a problem with the change in component concentrations, the principle of testing the relationship of integrated total AUC of acceleration/vibration and the speed of the system will document if any reduction in speed will be relevant prior to clinical use. Regular quality control can be performed by monitoring outcome-based parameters of HI, potassium and LD. If any changes are observed in samples sent via PTS compared to hand-carried transport, the clinical importance of the changes can be judged against the acceptable analytical difference based on the analytical variation for the analysis in question.

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