Automation and Data Processing in Blood Banking Using the Ortho AutoVue® Innova System

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Key Words

Ortho AutoVue® Innova System · Blood bank automation · Blood bank workflow

Summary

Background: The use of automated techniques reduces the impact of human errors in blood banking and improves standardization and quality of achieved results. Work processes were analyzed to see where improvements could be made before installing an automated testing instrument. The suitability of automation and data processing in order to reduce the bulk of routine and emergency work was explored. **Methods:** The evaluation focused on blood group and subgroup typing, cross-matching, and antibody screening using the Ortho AutoVue Innova System compared to standard manual methods. **Results:** The redesigned layout of the workspace led to a reduction of the operator's working process time of the specimen by 6%, whereas process optimizations resulted in shortening of the operator's working process time by 53%. Using the manual DiaMed system and the automatic AutoVue system, corresponding results were achieved for blood group typing (100%), rhesus typing (100%), antibody screening (100%), and autocontrol (87%). For known antibodies from freeze samples this correspondence amounted to 82%. The turnaround time from receipt at blood bank to completion for standard cross-matching, blood typing, and antibody screening is decreased up to 17% using the automatic system due to the standardization and automation of testing. **Conclusion:** The Ortho AutoVue Innova System facilitates the automation of routine blood bank testing, enrolling blood typing, cross-matching, and antibody screening with high reliability, sensitivity and specificity compared to standard manual methods.

Schlüsselwörter

Ortho AutoVue® Innova System · Automation in der Blutbank · Arbeitsablauf in der Blutbank

Zusammenfassung

Hintergrund: Die Anwendung automatisierter Techniken verringert das Auftreten von Fehlern durch menschliches Versagen und optimiert die Qualität der erzielten Ergebnisse. Arbeitsprozesse in der Blutbank wurden retrospektiv analysiert, um im Vorfeld vor Einführung des automatischen Testsystems AutoVue Innova erforderliche Verbesserungen durchzuführen. Die Möglichkeiten der Blutbankautomation und Datenverarbeitung zur Unterstützung der anfallenden Routine- und Notfalldiagnostik wurden untersucht. **Methoden:** Die Evaluation konzentrierte sich auf die vergleichende Bestimmung von Blutgruppen und Blutuntergruppen sowie die Durchführung von Kreuzproben und Antikörpersuchtesten mittels des automatischen Ortho AutoVue Innova Systems sowie manueller Standardmethoden. **Ergebnisse:** Die Neuorganisation des Laborarbeitsplatzes führte zu einer Reduzierung der Prozessierungszeit der Probe durch die Laborantinnen von 6%, während die Verbesserung von Arbeitsabläufen zu einer Zeitersparnis von 53% führte. Für die durchgeführten blutgruppenserologischen Untersuchungen (AB0 und Rh) sowie für die Antikörpersuchtestungen wurden unter Verwendung des manuellen DiaMed-Systems und des automatischen AutoVue Systems übereinstimmende negative Ergebnisse (100%) erzielt. Bei bekannten Antikörpern aus eingefrorenen Proben war die Übereinstimmung 82%. Die Bearbeitungszeit der Probe, beginnend mit der Ankunft in der Blutbank bis zur Fertigstellung von Standardkreuzprobe, Blutgruppenbestimmung und Antikörpersuchtest, wird durch den Einsatz des AutoVue Innova Systems aufgrund der standardisierten und automatisierten Testung um bis zu 17% verkürzt. **Schlussfolgerung:** Im Vergleich mit manuellen Standardmethoden ermöglicht das Ortho AutoVue Innova System die Automatisierung von Blutbank-Routinetestungen wie die Bestimmung von Blutgruppen sowie die Durchführung von Kreuzproben und Antikörpersuchtesten mit hoher Reliabilität, Sensitivität und Spezifität.

Introduction

The implementation of good manufacturing practice (GMP) requires standardized methods of laboratory testing [1]. The use of automated techniques reduces the impact of human errors in the blood bank and improves standardization and quality of achieved results [2–4]. Human errors due to manual processing are a significant cause of fatal transfusion complications [2, 5, 6]. In order to optimize the GMP processes at the blood bank of the University of Regensburg, an automation of laboratory methods for blood testing was implemented. The clinic of the University of Regensburg is a large, level IV, university-based hospital. Its transfusion services (TS) laboratory provides patient testing and consulting services for in- and outpatients from area clinics and hospitals.

The TS performs approximately 39,000 cross-match analyses annually and transfuses nearly 18,000 units of red blood cells (RBCs). Nearly 20,000 Group and Screen tests are performed, with 20% of patient blood specimens being tested for additional RBC antigens such as C, c, E, e, C^w, K1.

This report summarizes the validation of the automation and data processing in the blood bank of the Institute for Clinical Chemistry and Laboratory Medicine at the University of Regensburg using the Ortho AutoVue Innova System and compares the results of routine blood bank testing by this fully automated system with those obtained by standard manual methods. In our opinion, validation has to be performed on all automated systems that are considered critical, e.g. if its use is directly linked to the decision made for blood or blood product manufacturing, testing, labelling, and release for transfusion. The comparative testing evaluates the performance of the system with regard to its effectiveness based on the intended purpose and establishes documented evidence, providing a high degree of assurance that a specific process will consistently generate a product meeting its predetermined specifications and quality attributes.

The Ortho AutoVue Innova System was developed to automate a number of critical immunohematology testings such as human blood group determinations, antibody screening and compatibility testing using Ortho BioVue[®] System cassettes.

Assessment Goals and Scope

With respect to the high volume of routine and other immunohematological tests, our laboratory was interested in exploring the suitability of automation in order to reduce the bulk of routine and emergency work. Before installing an automated testing instrument, we aimed to review our work processes to see where we could make improvements.

The medical and technical staff of the blood bank greatly assisted in the evaluation of this new technology. The evaluation focused on blood group and subgroup typing, cross-matching, antibody screening, and antibody titers concentrating on the following areas:

- workflow in terms of pre-analytical and analytical work processes in the transfusion services area which includes the manual testing primarily with ID-Gel (DiaMed, Cressier sur Morat, Switzerland) and Immucor test trays and DiaMed reagents,
- reviewing of laboratory layout for flow of raw material (patient specimens), operators, and supplies needed for daily work processes,
- collecting representative process data to develop current state value stream map,
- observing and interviewing supervisory and operator personnel,
- videotape capture of work processes and flow of blood specimens.

Materials and Methods

Specimen and Request Form

Samples and request forms are received directly in the TS. There is at least one request document coming with each patient sample, and often there are multiple documents that accompany the sample. Blood group, Rh typing and antibody screening were performed routinely from samples using the manual and the automated method. In addition to the routine samples, we used freeze samples with defined antibodies for prolonged antibody screening.

Monitoring of the Operators' Workflow Efficiency

To evaluate the activity of the operators, videotaping was performed for each of the above-named processes for at least 30 min concentrating on the operator's hands. The process of each operator was videotaped and analyzed separately. The time required was segmented into the following categories:

- value-added (VA) time: any time changing the adaptation, form or handling of the specimen,
- required non-VA (or waste) (RW) time: time spent with other activities not related to the specimen (considering waste as any element of the production that add no value to the product),
- non-VA time is further broken down into the amount of time spent to handling the raw material, doing manual operations, walking, inspecting and to activities of electronic data capture or documentation on forms,
- pure waste (PW) time: time in which operator is idle.

Ortho AutoVue Innova System

The Ortho AutoVue Innova System (Ortho-Clinical Diagnostics GmbH, Neckargemünd, Germany) is worldwide the first complete automated system for a number of critical immunohematology testings such as human blood typing, antibody screening and compatibility testing using Ortho BioVue System (Ortho-Clinical Diagnostics GmbH) cassettes technology and digital picture editing. This system provides automated test editing functions such as liquid pipetting, cassette handling, incubation, centrifugation, reaction grading and interpretation as well as data management. The AutoVue blood bank automation may be used as an independent system as well as connected to the customer laboratory information system (LIS) in terms of a bi-directional link with sample data passing from the LIS to the AutoVue and test results passing from the AutoVue to the LIS. It is vital that the information transfer between the AutoVue and LIS is reliable and accurate. The principle of measurement and grading is based on a camera with coupling charge device, which reads both front and back side of BioVue cassettes 25 times. Reaction interpretation is done using an

Table 1. Comparison of the manual DiaMed and the automatic AutoVue system for analysis of the ABO system, Rhesus factor, subgroup and antibody screening as well as cross-match analysis

Parameters	Expected correspondence, %	Accepted minimum, %	Accepted maximum, %	Validated correspondence, %
ABO system	99.5	99	100	100
Rhesus factor D	99	98	100	100
Rhesus subgroup	99.5	99	100	100
Antibody screening	98.5	97.5	100	100 ^a
Internal control	90	85	100	87 ^b
Cross-match	99.5	99	100	100

^aInvestigation was performed on routine samples without known antibodies. All test samples were negative for antibodies against erythrocytes.

^bThe expected occurrences of positive internal controls in the automatic system are due to the high centrifugation of samples which is applicable in the manual system.

Table 2. Comparison of the results for analysis of antibody screening using freeze samples with defined antibodies against erythrocytes

Amount	Antibody	AutoVue System	DiaMed system	Annotations
20	anti-D	pos	pos	
1	anti-D	pos	questionably pos	only in enzyme detectable
1	anti-D	weakly pos	pos	only in papaine detectable
1	anti-D	pos	neg	
3	anti-C	pos	pos	
1	anti-C	neg	neg	only in enzyme detectable
4	anti-E	pos	pos	
1	anti-E	neg	neg	in enzyme strong positive reaction, in Coombs weak
1	anti-E	neg	pos	
1	anti-e	pos	pos	
1	anti-e	pos	neg	
1	anti-K	pos	pos	
6	anti-Fya	pos	pos	
	anti-Kpa	pos	neg	antigen not on DiaMed screening cell
1	anti-Le(a)	pos	neg	
1	anti-Le(b)	neg	neg	
1	anti-Lua	neg	neg	
2	anti-Jka	neg	neg	
1	anti-Jkb	pos	pos	
1	anti-Jkb	weakly pos	neg	
1	anti-M	pos	pos	
1	anti-P1	pos	neg	
2	anti-s	neg	neg	
1	cold autoantibody	pos	pos	
1	warm autoantibody	weakly pos	neg	
1	anti-Chido	pos	pos	
1	HLA suspect	pos	pos	

Neg = negative; pos = positive.

image processing system (IPS) software and a grading algorithm. The original picture of each cassette is saved in a JPG format on a hard disc and a DVD.

The test principle of the Ortho BioVue System is the column agglutination technique using columns containing reagents and glass spheres. By centrifugation of the cassettes agglutinated erythrocytes form a layer on top of the reagent-ball mix, whereas non-agglutinated erythrocytes sink to the bottom of the column. Ortho BioVue System cassettes consist of 6

columns which contain reagents in a buffered solution. One of the most important innovations of the AutoVue is the possibility to start emergency analysis during routine diagnostics. Using this random access modus, blood typing with antibody screening test and 6 cross-matches needs 25 min; if the blood group is known, this analysis time can be reduced to 22 min. Thus, it is no longer necessary to collect samples and to handle long analysis times as testing can be started for each sample individually.

Results

The analyzer produced consistent results in routine samples in comparison with our manual method (table 1). Discrepancies were observed in antibody screening, if we used freeze samples (table 2).

Activity of the Specimen

Samples and requested documentation are received just inside the TS. There is at least one form coming with each patient sample, and often there are multiple forms that accompany the sample. Approximately 2 min is required to inspect and handle the various forms and to input the information. Specimens generally are transported about 20 feet or 6 m, but can travel up to 40 feet or 12 m, depending on which work space is used for the testing.

The majority of total time is VA at 65% (fig. 1), which means that some activity is taking place. During 35% of the time, blood samples are waiting, being transported or being inspected. These waiting times are considered non-VA.

Operator's Work Processes upon Specimen Receipt

Table 3 shows the analysis of the VA and non-VA time analysis of the operator upon receipt of the specimen. The time in the column labelled 'Recommended process' reflects the estimated time based on making some minor changes to

Fig. 1. Product process flow analysis.

Table 3. Time analysis of work processes

Category measured	Current process, s	Percentage of total, %	Recommended process, s	Percentage of total, %	Improvement, %
VA time	0	0	0	0	
Non-VA time	1,214	100	1,114	100	
Material operations	379	31	379	33	
Manual operations	89	7	79	7	
Inspection	34	3	34	3	
Walking ^a	13	1	13	1	
Other	699	58	635	56	
Total operator time	1,214		1,140		6

^aDistance walked 120 feet (36.5 m).

Table 4. Activity of the operators

Category measured	Current process, s ^a	Percentage of total, %	Recommended process, s	Percentage of total, %	Improvement, %
Pure waste	842	42	0	0	
VA time	48	2	48	5	
Non-VA time	1,113	56	900	95	19
Total operator time	2,003		948		53

^aTotal process time 3,354 s.
Walk distance 356 feet (109 m).

Table 5. Optimization of the workflow

Process	Current process time, s	Improved process time, s	Reduction in time, %
General testing	2,775	2,237	19
Manual testing	1,489	955	36
Review of results	511	424	17

the current process. For the most part, this process is quite efficient, given the time constraints of the LIS itself. The primary opportunities for the 6% improvement result from a redesign of the physical layout of the workspace that includes:

- locating the specimen centrifuge closer to where samples come into the laboratory,
- installing a stationary barcode reader/scanner at the LIS terminal.

Activity of the Operators

Two different operators were videotaped performing blood group and subgroup typing as well as cross-match testing on patient samples. One of the analyses is shown in table 4. It represents testing of two patient samples for second typing, group and subgroup typing as well as cross-match of two units for one patient and one unit for the other.

Turnaround Time

Table 5 shows the optimization of the workflow in our blood bank. The turnaround time is expected to be 60 min from receipt at the blood bank to completion – whereas the current time for a standard cross-match, blood typing and antibody screening is 90 min. This is due to a decrease in incubation time from 30 min with the manual method to 15 min on AutoVue as well as to the standardization and automation of all other aspects of testing.

Errors

All investigated blood samples that are tested in the observed period of 18 months were correctly identified by the AutoVue System.

Discussion

In this study we report our experiences with the new automated system, AutoVue Innova and our improvements of work processes before installing an automated testing instrument. However, automation is of interest across all clinical laboratory fields. A variety of approaches have been used to optimize processes according to GMP and to reduce the risk of transfusion errors [7–9]. In the blood donation services, pressure for automation also derives from the greater number of blood borne infectious diseases [10]. In addition to a serologic test for *Treponema pallidum*, in Germany donor blood must be screened for the surface antigen of HBV as well as for antibodies to HBV core, HCV and HIV types 1 and 2 [11]. Also mandatory are molecular tests for HCV and HIV RNA. Antibodies to CMV may be sought in selected cases. These automated methods have led to a dramatic improvement in blood safety and to low risk of viral transmission [12]. However, automation provides additional value in the field of immunohematology in which any human errors

can have dramatic consequences for the patients [13–16]. Automation is now widely used in serological typing of blood groups, of irregular antibody screening and of compatibility testing. This study evaluated a fully automated device based on column agglutination technology: AutoVue Innova System. We compared the automatic Ortho AutoVue Innova System with the established standard manual DiaMed Typing System (gel centrifugation test) in terms of the detection of human blood typing, antibody screening and cross-match testing. It is generally accepted that gel technology is very sensitive and far superior to manual tube testing [17]. Therefore, combining gel technology with the automatic AutoVue Innova System takes testing in the field of immunohematology to a clearly higher level. Our results (tables 1, 2) indicate that the AutoVue Innova performs routine blood bank tests with an accuracy that is comparable to manual DiaMed standard methods. Observed discrepancies in the prolonged antibody screening using freeze samples may be due to different gel materials and centrifugation conditions of both methods. On the other hand, the poor quality of the freeze samples may negatively influence the achieved results compared to fresh samples.

A further advantage of the AutoVue Innova is its improved system and data security as a result of automated reading, positive sample reagent identification, positive cassette identification, reaction grading and interpretation, bi-directional interface, menu-driven computer screens, and password protection, allowing for an optimization of the pre-analytical and analytical work processes in the TS. Its safety is assured through a fully enclosed system with software-controlled access doors, minimal handling of patient samples, and automated cassette disposal.

Moreover, one of the most important innovations of the AutoVue Innova is the possibility to start emergency analysis during running routine diagnostics. In addition, it is no longer necessary to collect samples and to handle with long analysis times as testing can be started for each sample individually. On the other hand, no automated blood typing system is available that can match the speed of an experienced blood bank technologist performing a manual tube ABO and Rhesus D type screening, abbreviated antibody screening, or cross-match analysis. Consequently, we use the manual system to type ABO and Rhesus D in very urgent cases.

However, a large number of samples with complex testing profiles can be processed economically, allowing staff to perform other critical tasks. Since implementing the Ortho AutoVue Innova System, staff size has not changed, but an increasing and more complex workload is still manageable. Substantial reduction in labor costs are due to the fact that the entire procedure can be performed by 1 or 2 operators, whereas previously 2–4 staff members were required due to the labor-intensive nature of manual blood typing, antibody screening, and compatibility testing. This has produced savings in our blood bank as it allowed re-engineering job tasks

and use staff more efficiently. In addition, we have a testing system in place that is objective, reliable, and reduces the risk of clerical error.

Furthermore automation provides benefits beyond staff reduction. One of the impacts is to meet current GMP requirements. Quality controls, expiration date of reagents, charge number, incubation times, and other processing steps that needed to be documented manually before are now done by the AutoVue Innova System. If limits are exceeded, the system will cancel those results. In this way the automated data management eliminate manual compilation and data transfer, which has the potential for operator error. Moreover the process of automation offers specific sample identification throughout the process, producing a secure and completely audit traceable procedure. For quality control, the AutoVue performs electronic tracking of samples, keeps event logs and error messages, and produces proofs of correct processing of each sample.

The Ortho AutoVue Innova System has now been implemented in our routine TS for about 18 months, and the everyday experience confirms the results of this study.

Conclusion

The Ortho AutoVue Innova System automates routine blood bank testing, enrolling blood typing, cross-matching, and antibody screening with high reliability, sensitivity, and specificity. The Ortho AutoVue Innova System improves the quality in terms of consistency and integrity of techniques and results, offering standardized pipetting, incubation, centrifugation, reading and interpretation of results by automatic readers.

Furthermore it shows decreased hands-on time with reduced possibility of operator error and reduced binding of personnel as well as the increased operational efficiency in terms of documentation of all compounds for analysis with ID number, charging number and expiration date, continuous monitoring of consumables, continuous feed modes, random access, and liquid level detection.

The total automation process produces an efficient, secure, and economical system for immunohematological diagnostics, enhancing the testing capacity of our laboratory.

However, no automated blood typing system has been developed that can match the speed of a manual tube ABO and Rhesus type screening.

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