Original Article

The possibility of automatic capillary blood testing in routine blood tests: an evaluation of the automatic mode of the Mindray BC-7500 CRP Auto Hematology Analyzer for capillary blood testing

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Background: Capillary blood is a common specimen type used for infant blood routine tests. Until now, this specimen type could only be tested with the manual mode in hematology analyzers. Manual sample mixing and loading increases the amount labor force and can be more easily affected by human factors. This study was designed to investigate the proficiency of the automatic mode of the Mindray BC-7500 CRP Auto Hematology Analyzer for capillary blood testing.

Methods: The complete blood count (CBC) results for capillary blood were compared between the automatic and manual modes. Special types of samples, including samples with high or low volume, thalassemia red cells, high fibrinogen, high hematocrit (HCT), or high triglyceride levels, were compared and evaluated. The intraclass correlation coefficient (ICC) was used to define the agreement between the 2 modes. The industry standard Analytical Quality Specifications for Routine Tests in Clinical Hematology (WS/T 406-2012), published by the National Health Commission of China, was used to evaluate the correlation between the results from the 2 modes.

Results: There was good correlation between the automatic and manual modes for every type of sample, and the ICCs were all higher than 0.9. Except for high HCT or high triglyceride samples, there were no differences found between the 2 modes based on the WS/T 406-2012 standard.

Conclusions: This new automatic mode utilized in the Mindray BC-7500 CRP Auto Hematology Analyzer for capillary blood yielded the same results as the manual mode except in the case of samples with high HCT or triglycerides. Capillary blood might be routinely tested automatically with hematology analyzers in the near future, which might reduce the labor required and improve standardization.

Keywords: Automated hematology analyzer; complete blood count (CBC); capillary blood

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Introduction

Capillary blood, a blood specimen composed of arteriole blood, venule blood and tissue fluid (1), is not the best choice for a routine blood test because of its higher likelihood of contamination with skin flora, the effect that peripheral circulation has on it, and its smaller total volume. The accuracy and repeatability in the assessment of capillary blood are inferior to those of venous blood (2). This is why almost all hematology analyzers with automatic loading modules on the market are only available for venous blood in standard 2- or 3-mL collection tubes. Capillary blood can only be mixed and loaded manually one by one, which is a time-consuming and labor-intensive process. However, for some special populations, such as newborns or hemodialysis patients, capillary blood is preferred over venous blood for the advantage of preventing iatrogenic anemia and protecting blood vessels (3). Therefore, for laboratories serving for these special populations, there is a pressing need for automatic capillary blood testing.

Mixing is the core process in routine blood testing. According to the requirement by College of American Pathologists (CAP) checklist of hematology (HEM) 22000, all blood specimens collected in anticoagulant for hematology testing need to be mixed thoroughly immediately before analysis. There was a questionnaire survey including 28 provinces and 410 medical institutions in laboratory departments in China suggested that the proportion of capillary blood specimens in routine blood tests was about 10%, and the factors affecting the results of routine blood tests with capillary blood specimens were dominated by the mixing method (86.6%) (4). Although automatic mixing and loading for capillary blood samples would help considerably in reducing the influences of subjective factors and saving time and labor costs, there is little data to ensure the effectiveness of capillary blood automatic mixing. For some characteristics of capillary blood specimens, such as a small volume and a narrow lumen, mixing capillary blood specimens by hand is harder than mixing venous blood specimens, which means that the automatic mixing module for capillary blood should not be a simple imitation of the venous method. As there is now a hematology analyzer that can automatically analyze capillary blood specimens, it is very important to evaluate this newly developed equipment.

This study was designed to evaluate the automatic mode of the Mindray BC-7500 CRP Auto Hematology Analyzer for capillary blood testing. We present this article in accordance with the GRRAS reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-23-84/rc).

Highlight box

Key findings

- Capillary blood could be tested automatically for complete blood count with the BC-7500 CRP Auto Hematology Analyzer in the vast majority of cases.

What is known and what is new?

- Capillary blood for complete blood count can only be mixed and loaded manually until now.
- Capillary blood for complete blood count could be tested automatically not only for normal samples but also for samples with high or low volume, thalassemia red cells, and high fibrinogen, but not for those with high hematocrit (HCT) or high triglyceride. This may reduce the amount of labor required and improve standardization.

What is the implication, and what should change now?

- We did not change the automatic mixing setting in this to study to determine whether adding a mixing or shaking process could optimize the comparability of samples from the high HCT and high triglyceride groups. This is also the direction we are considering for our future research.

Methods

Samples

This study is a clinical *in vitro* diagnostic evaluation. The samples studied were the remaining clinical specimens with EDTA-K2 (dipotassium ethylenediaminetetraacetic acid) anticoagulant for which test reports had been sent and did not involve the privacy and interests of patients. The study was approved by the Medical Ethics Committee of West China Second University Hospital, Sichuan University (No. 2021S160). The study was carried out in line with the Declaration of Helsinki (as revised in 2013). The obligation to collect signed informed consent from patients was waived due to the study's retrospective nature.

For the experimental samples, after the chosen remaining specimens were thoroughly remixed upside down 8 times, and a portion of the blood (200 μL) was immediately transferred to anticoagulant-free blood collection tubes designed specifically for capillary blood (*Figure 1*). After 20 minutes of standing, a complete blood count (CBC) was performed in the automatic and manual modes, which was repeated once, and the mean values were calculated.

Figure 1 The special blood collection tubes used in the experiments have the same height as normal venous blood collection tubes but are cleverly reduced in lumen volume to avoid the difficulties of mixing capillary blood for a small sample volume relative to the venous blood.

Table 1 Standard of relative deviations from WS/T 406-2012

Parameter	Relative deviations (%)
WBC	≤5.00
RBC	≤2.00
HGB	≤2.00
HCT	≤3.00
MCV	≤3.00
PLT	≤7.00

WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; PLT, platelet.

The manual mode was performed by mixing the specimens upside down 8 times and flicking the tube gently with fingers and was always performed by the same person.

All samples were "normal" samples with normal or abnormal levels, and those with abnormal histogram or scattergraph that might have affected the accuracy or precision of CBC testing were not included.

Instruments and reagents

The BC-7500 CRP analyzer and supporting calibrators, control materials, reagents and Intralipid used as an additive agent to generate samples with high triglycerides were all obtained from the Shenzhen Mindray Corporation (Shenzhen, China). The analyzer was effectively calibrated and well monitored by daily quality control, and all reagents were within their validity period.

Study methods

Specimens from healthy individuals

According to WS/T 406-2012, 5 samples from specimens of healthy individuals were tested in the automatic and manual modes separately, and each sample was tested twice. The relative deviations between the mean values of the results in the 2 modes were calculated separately, and the requirements of this standard (*Table 1*) were used to evaluate the comparability of the 2 modes.

Specimens with interference factors in the mixing process

Four groups of samples were obtained from specimens of the different kind groups to evaluate the influence of common interference factors that were susceptible to the mixing process, with 20 samples each from each group drawn in total. The 4 groups are described below.

In the thalassemia group, samples were obtained from patients with clinically diagnosed thalassemia and abnormal blood routine results for mean corpuscular volume (MCV) lower than 80 fL and mean corpuscular hemoglobin (MCH) lower than 26 pg. In the high fibrinogen group, samples were obtained from patients with fibrinogen concentrations greater than 600 mg/dL. In the high hematocrit (HCT) group, samples were obtained from patients with an HCT greater than 50%. In the high triglyceride group, samples were obtained from healthy individuals, and Intralipid was mixed into samples to generate triglyceride concentrations of greater than 4 mmol/L.

For each group, samples were tested in automatic and manual modes and repeated once to calculate the mean values respectively. The requirements of the standard listed in *Table 1* were used to evaluate the comparability of the 2 modes.

Specimens with different blood volumes

Five groups of samples obtained from the same healthy population but with different blood volumes (20 samples each) were used to evaluate the effect of the automatic mixing mode on the small- and large-volume samples. The five groups with different blood volumes were 80, 120, 200, 400, and 500 μL. In this part we used venous blood. According to the WS/T 406-2012 standard, same results were obtained

Table 2 Validation results for the different sampling modes

Parameter	Relative deviations %						Conclusion
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Standard	
WBC	1.4	−3.1	−0.8	−0.8	−2.5	≤5.00	Pass
RBC	−0.4	0.9	0.2	−1.8	−1.6	≤2.00	Pass
HGB	−1.5	0.0	0.0	−1.5	−1.6	≤2.00	Pass
HCT	−0.2	1.1	0.3	−0.8	−1.5	≤3.00	Pass
MCV	0.2	0.0	0.1	0.8	0.2	≤3.00	Pass
PLT	−0.7	−1.5	1.8	2.6	−0.4	≤7.00	Pass

WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; PLT, platelet.

between each group when tested in manual mode.

Statistical analysis

Relative deviation based on the manual mode was used to evaluate the comparability between these 2 methods. Intraclass correlation coefficient (ICC) analyses were performed using a single-measurement, absolute-agreement, 2-way random model, and Bland-Altman deviation plots were drawn.

Results

Specimens from healthy individuals

For normal samples, there was good consistency between the automatic and manual modes. The relative deviations between the results from these 2 modes were all within the requirements of WS/T 406-2012 (*Table 2*).

Specimens with interference factors in the mixing process

For samples with common interference factors, there was good consistency between the automatic and manual modes found in all items of the thalassemia group and high fibrinogen group. However, the compliance rates of the white blood cell (WBC) and platelet (PLT) items in the high triglyceride group and the WBC item in the high HCT group were less than 80%, which failed to meet the requirements of the WS/T 406-2012 standard. The comparisons for the high triglyceride group and the high HCT group were performed with Bland-Altman bias analyses, as shown in *Figures 2,3*.

The ICC values we calculated were all greater than 0.9, suggesting excellent agreement between the 2 mixing methods for capillary blood. In the 95% confidence interval of the ICC estimate, the lowest ICC value was also greater than 0.88, which indicated good agreement between the automatic mixing method and the manual mixing method (*Figure 4A*).

Specimens with different blood volumes

Different blood volumes (80–500 μL) did not influence the mixing effect. The comparisons of the relative deviations of the 2 mixing methods among the 5 subgroups with different blood volumes all met the WS/T 406-2012 standard (*Table 1*). The ICC values were all greater than 0.9, indicating excellent agreement between the 2 mixing methods. The lower boundary of the 95% confidence interval was overwhelmingly above 0.75, with only the slightly inferior parameter of MCV in the 80-μL group, whose interval ranged from 0.6 to 0.9, which also suggested consistency between the 2 mixing methods (*Figure 4B*).

Discussion

The preanalytical phase is an important component of laboratory quality, especially regarding the mixing of blood specimens, which is the key to ensuring the accuracy of the CBC (5,6). Manual mixing of specimens allows for the targeted slowing down or increasing in the number of times of mixing upside down due to the visual observation of the blood flow in the collection tube. Nevertheless, manual mixing is easily subject to individual differences in clinical application. The Mindray BC-7500 CRP employs fully automated bionic mixing technology and contains 4 techniques, including flexible acceleration and deceleration,

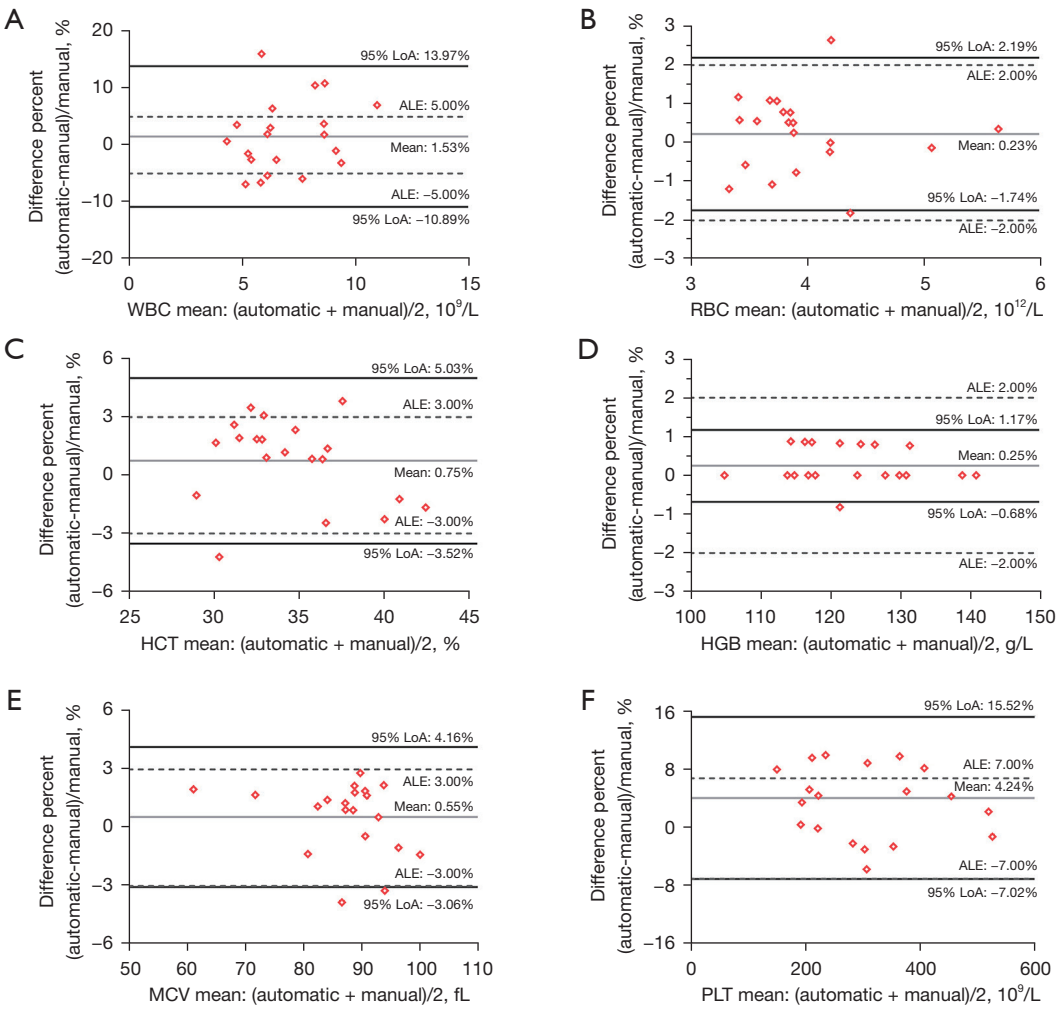

Figure 2 Graphical representation of the Bland-Altman deviation analysis for the high triglyceride group. The horizontal axis represents the mean value of test results of the 2 methods, and the vertical axis represents the relative deviations. The mean difference (light solid line), the ALE for each parameter (dotted lines), and the 95% limits of agreement (dark solid line) are shown. LoA, limits of agreement; ALE, allowable limits of error; WBC, white blood cell; RBC, red blood cell; HCT, hematocrit; HGB, hemoglobin; MCV, mean corpuscular volume; PLT, platelet.

reverse hedging, liquid level suppression, and micro force mixing, to prevent the splashing of trace samples and blood hanging on the wall (7). The program of mixing used in the automatic mode is constant, which is more conducive to the standardization of the clinical laboratory and avoids the risk of laboratory-acquired infections from opening the cap. A prior study has shown that the accuracy of the automatic mode was good in random specimens (8), which is consistent with our findings. For a more thorough evaluation of the automatic mode, especially in unusual conditions, several experimental groups were created.

The precision and accuracy of capillary blood have been found to be poorer than those of venous blood in routine blood testing (9). Except for the sample composition and the method for obtaining blood, CBC from capillary blood also has deficiencies in testing. In most cases, capillary blood testing is an open-cap experiment performed manually. This process might increase the risks for laboratory-associated infections and uncertainty resulting from manual numbering and mixing. Nevertheless, routine blood tests with capillary blood are still a better option for infants or other special situations, such as in patients with blood disorders who require routine blood tests monitoring frequently (10). Therefore, an automated hematology analyzer for capillary

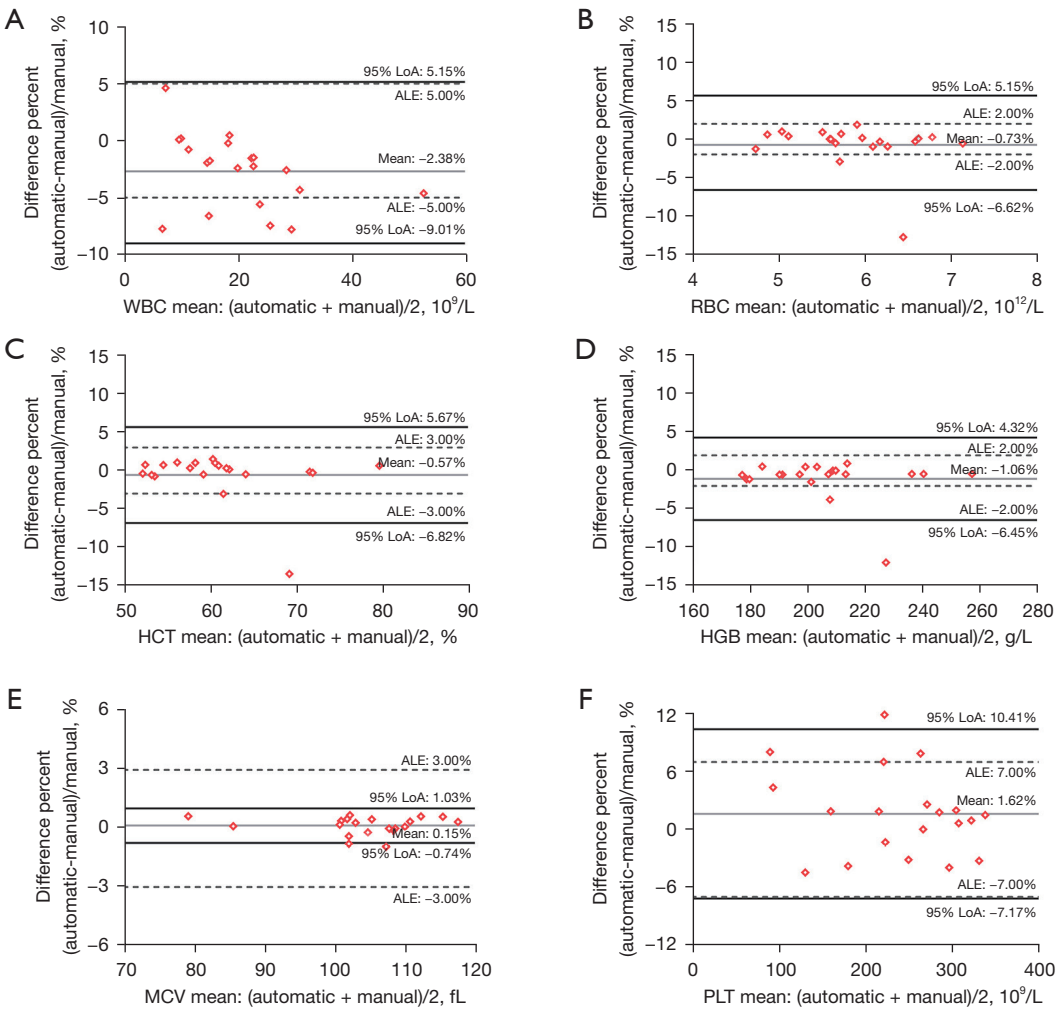

Figure 3 Graphical representation of the Bland-Altman deviation analysis for high hematocrit group. The horizontal axis represents the mean value of test results of the 2 methods, and the vertical axis represents the relative deviations. The mean differences (light solid line), the ALE for each parameter (dotted lines), and the 95% limits of agreement (dark solid line) are shown. LoA, limits of agreement; ALE, allowable limits of error; WBC, white blood cell; RBC, red blood cell; HCT, hematocrit; HGB, hemoglobin; MCV, mean corpuscular volume; PLT, platelet.

blood testing might be highly valuable for the efficient and standardized testing in the clinical laboratory. We thus aimed to evaluate this newly developed equipment for automated mixing and the loading of capillary blood.

The purpose of mixing is to keep the particles uniformly distributed in the blood sample. The higher the viscosity of the blood is, the more difficult the task. Blood is a 2-phase liquid, and the fluidity of the plasma and cellular phases, as well as the HCT of the cellular phase, dictate its fluidity (11). Thus, the level of whole blood viscosity is closely related to blood cells, mainly red blood cells (RBCs), and plasma proteins. The RBC volume (HCT), RBC features (size, rigidity, etc.), and plasma fibrinogen and lipoprotein concentrations are key elements determining viscosity (12-15). In our study, to evaluate the ability of automatic mixing function, we used 4 groups, including samples from a high HCT group and a thalassemia group to represent abnormal viscosity from blood cells and samples with high concentrations of fibrinogen and triglycerides to represent abnormal viscosity from plasma proteins, with manual mixing used as a control method. Additionally, we used ICC as the statistical analysis method, as the ICC reflects

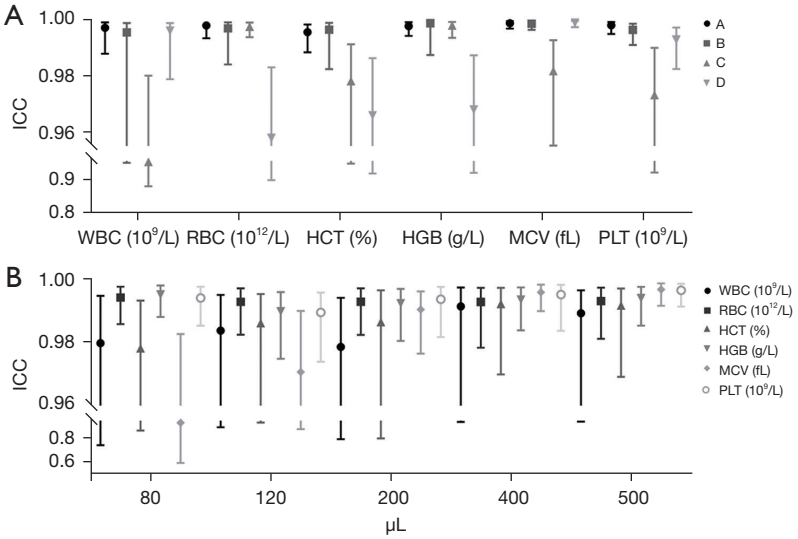

Figure 4 The distribution of the ICC 95% confident interval for the experimental groups. In (A), the letters A, B, C, D represent the thalassemia group, high fibrinogen group, high triglyceride group, and high HCT group, respectively. In (B), these represent the different blood volume groups in the various items of the routine blood test. ICC, intraclass coefficient; WBC, white blood cell; RBC, red blood cell; HCT, hematocrit; HGB, hemoglobin; MCV, mean corpuscular volume; PLT, platelet.

not only the degree of correlation but also the agreement between measurements (16). In the thalassemia group and high fibrinogen group, we obtained excellent agreement between the 2 mixing methods for capillary blood according to both the relative deviations and the ICC results. For the high HCT and high triglyceride groups, although the ICC results were all greater than 0.9, suggesting excellent agreement between the 2 mixing methods, the compliance rates of WBC in the high HCT group and those of WBC and PLT in the high triglyceride group all failed to pass the comparability standard of WST/406-2012 between the different sampling modes. When we enlarged the deviation standard to 1/2 allowable total error (TEa), all the items passed the comparability analysis, indicating that the bias between the 2 modes might not affect clinical judgment. In actual clinical use, except for newborns, few patients can achieve such high HCT. Finally, in clinical use, the operator can determine whether the sample needs to be reviewed manually by observing the HCT or the mean corpuscular hemoglobin concentration.

In addition to viscosity, blood volume is another main factor affecting mixing. The standard blood volume in the capillary tube is approximately 200 μL. However, compared with sampling from veins with negative pressure blood collection tubes, sampling from capillaries leads to far more difficulty in controlling the blood volume in the tubes. Too much or too little blood often requires special handling, such as shaking or increasing the number of times when mixing manually, and therefore it is very important for automatic mixing to have the ability to handle these situations. In our study, within the range between 80 and 500 μL, there was good correlation and comparability between all groups with different blood volumes, indicating that the blood volume in the tube was not a factor that affected the automatic mixing mode.

Our study suggested an excellent agreement between automatic and manual modes in CBC for capillary blood except in the case of samples with high HCT or triglycerides. This finding indicates that the automated hematology analyzer may not be perfect for capillary blood testing but is still a feasible solution.

Limitations

There were several limitations in our study. First, there was a small number of samples with extreme values. Second, this experiment used Intralipid mixed with whole blood to simulate specimens with high triglycerides, which might not fully represent the actual situation of lipidemia. Third, we did not change the automatic mixing setting to study whether adding a mixing or shaking process could optimize the comparability of samples from the high HCT and

high triglyceride groups. This is also the direction we are considering for our future research.

Conclusions

This was the first study to evaluate the automatic method for capillary blood. The results suggested an excellent agreement between the automatic and manual modes in CBC for capillary blood except in the case of samples with high HCT or triglycerides. This finding indicates that the automated hematology analyzer may not be perfect for capillary blood testing but is still a feasible solution.

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Footnote

Reporting Checklist: The authors have completed the GRRAS reporting checklist. Available at https://cdt.amegroups.com/article/view/10.21037/cdt-23-84/rc

Data Sharing Statement: Available at https://cdt.amegroups.com/article/view/10.21037/cdt-23-84/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-23-84/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by Medical Ethics Committee of West China Second University Hospital, Sichuan University (No. 2021S160). The study was carried out in line with the Declaration of Helsinki (as revised in 2013). The obligation to collect signed informed consent from patients was waived due to the study's retrospective nature.

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