Comparison of Automated Differential Blood Cell Counts From Abbott Sapphire, Siemens Advia 120, Beckman Coulter DxH 800, and Sysmex XE-2100 in Normal and Pathologic Samples

Lisa Meintker, MD, Jürgen Ringwald, MD, Manfred Rauh, PhD, and Stefan W. Krause, MD

Key Words: Automated blood cell count; Leukocyte differential count; Flag; Immature granulocytes; Blasts

DOI: 10.1309/AJCP7D8ECZRXGWCG

Abstract

Reliable automated blood cell characterization and quantification remain challenging in pathologic samples, whereas slide reviews due to unnecessary flagging should be avoided. We compared 4 modern hematology analyzers—Abbott Sapphire, Siemens Advia 120, Sysmex XE-2100, and Beckman Coulter DxH 800—regarding complete blood cell count (CBC), leukocyte differential count, and flagging efficacy in a total of 202 samples from hematology patients and normal controls. Manual differential count was used as reference. The analyzers exhibited very good correlation for CBC parameters. Neutrophils and eosinophils also showed very good correlations, whereas lymphocytes and monocytes correlated fairly. The Advia 120 displayed notably lower measurements for both parameters, which is attributable to classification of some events as large unstained cells. Basophil counts were unreliable with all analyzers. Flagging for blasts and immature granulocytes showed moderate sensitivity and specificity. Operators must not rely on blast flagging alone to detect leukemic samples with any analyzer.

Modern hematology analyzers combine multiple techniques such as absorption spectrometry, impedance, and conductivity measurement, as well as flow cytometry, for cell counting and differentiation. Together with improved analytical algorithms and pattern recognition, automated cell differentiation is a rapid and cost-efficient method for complete blood cell count (CBC) and leukocyte differential count (LDC). Previous reports indicate that CBC and LDC among analyzers generally have quite good but not perfect agreement. Nonetheless, in various situations, accurate automated measurement is difficult or not possible (eg, immature cells, platelet clumps), and microscopy is triggered by the respective “flags” in the laboratory results. Therefore, the objective of modern hematology laboratories is to optimize the number of samples for which further, putative expensive action (eg, microscopic smear review) is needed while minimizing the number of false-negative results.

We compared 4 modern analyzers, all top of the range from the respective manufacturers, regarding accordance of CBC and LDC among analyzers, compared with microscopic smear review and flagging efficiency in normal and pathologic samples.

Materials and Methods

We included in this study 202 EDTA-anticoagulated samples submitted to our hematology laboratory for routine testing of CBC. The samples were stored at room temperature no longer than 4 hours prior to testing. All samples were tested on the CELL-DYN Sapphire (Abbott Diagnostics, Santa Clara, CA) as the primary routine method in our laboratory. To ensure sufficient numbers of pathologic
as well as normal values and a representative effective range, we used the following sample selection: all samples with at least 1 flag indicating abnormal values in the LDC. A similar number of samples without any flag (ie, normal or close to normal differential) were included. Prior to further processing, all samples were anonymized and labeled with unique barcode identifiers. The local ethics committee approved this study without the need for individual patient consent because of complete anonymization of samples.

Interinstrument agreement was analyzed by serial processing of samples with the CELL-DYN Sapphire, Advia 120 (Siemens Healthcare Diagnostics, Eschborn, Germany), XE-2100 (Sysmex, Kobe, Japan), and UniCel DxH 800 (Beckman Coulter, Brea, CA). All analyzers were run in accordance with the standard operating procedures as routine instruments in 3 different laboratories at our institution and were checked with quality control samples twice daily. Automated CBC, LDC, and flagging of pathologic cells or other abnormalities were recorded for further evaluation.

Abbott Sapphire determines RBC count, platelet count, and cell volume of both cell types with impedance. In parallel, optical measurement of RBCs and platelets is performed by light scatter technology, and a flag indicates significant deviations between both methods. Optical platelet measurements and impedance RBC measurements are routinely reported as a final result and are also used in our study. Platelets can also be quantified by immunostaining. However, this method was not used in our study. Hemoglobin is measured after a dilution procedure with repetitive absorption spectrometry at a wavelength of 540 nm. For WBC count, LDC, reticulocytes, and nucleated RBCs (NRBCs), Sapphire operates with flow cytometry, 4 optical detectors, and 3 fluorescence detectors. NRBCs and nonviable leukocytes are stained by propidium iodide.

In the Siemens Advia 120, all measurements including RBCs and platelets are performed optically. WBCs are analyzed after erythrocyte lysis and measurement in a “peroxidase channel” and a “basophil channel.” WBC measurements from the basophil channel are used for the final report, and a flag indicates insufficient concordance with the peroxidase channel. Flow cytometry separates the 5 known clusters of the LDC using data from both channels and generates an additional cluster of large unstained cells (LUCs), which consist of activated lymphocytes, myeloid and lymphatic blasts, and plasma cells.

In the Beckman Coulter DxH 800, WBC, platelet, and RBC measurements are performed by impedance. For the LDC, the DxH 800 uses light scatter technology with a red laser and 5-angle light scatter to define cellular granularity and lobularity. Simultaneously, the system obtains information about the cell volume and inner cell structures with impedance and conductivity measurements. NRBCs are also determined using a lysis solution to maintain NRBCs, leukocytes, and platelets and are separated from other populations by means of distinct axial light loss characteristics using flow cytometry.

The Sysmex XE-2100 determines RBCs and platelets by impedance and is able to perform an additional optical platelet measurement in the reticulocyte channel. The optical
measurement is triggered by a switching algorithm in case of interferences regarding the impedance measurement. For the WBC and LDC counts, the XE-2100 uses flow cytometry with a red laser at 633 nm in 3 channels, including fluorescence detectors after different pretreatment procedures of the cells. WBC is reported from the “WBC/baso” channel, and control WBC data are generated from the independent “diff” channel. A dedicated channel for NRBCs is available but was not evaluated for this report.

Manual differential counts were performed on May-Grunwald-Giemsa–stained slides by experienced technicians at the hematology laboratory. One hundred leukocytes were discriminated into segmented and band neutrophils, lymphocytes, monocytes, eosinophils, basophils, metamyelocytes, myelocytes, promyelocytes, blast cells, atypical lymphocytes, plasma cells, and unclassifiable cells. If ambiguous cell types were present, cells were scored by 2 different technicians and/or a hematologist. If the automated differential of any analyzer indicated a blast flag, at least 200 cells were analyzed to not miss actual blasts by chance of Poisson statistics.

In the first part of the study, quantitative parameters were compared: hemoglobin, hematocrit, mean corpuscular volume (MCV), RBCs, WBCs, and platelets from the CBC as well as the percentage of neutrophils, eosinophils, basophils, lymphocytes, and monocytes from the 5-part LDC. Single measurements were compared with the mean of all 4 analyzers. To prevent distortion of the mean values by abnormal measurements of 1 analyzer, we excluded a few outliers showing marked disagreement with all other analyzers from the mean value calculation. The respective numbers of outliers excluded from the mean value calculation are given in Table 2. For the analysis of automated LDC, only samples with a maximum of 1% blasts in the microscopic count were included. Regarding lymphocytes and monocytes, the Advia 120 was excluded from the mean value calculation if the LUC population accounted for more than 5%. Microscopic counts were not included in the calculation of mean values of the LDC but were compared with these mean values for control purposes.

Interinstrument agreement was first assessed by analysis of the correlation and linear regression of single measurements from each analyzer against the mean of all 4 analyzers. Further calculations were performed as suggested by Bland and Altman with slight modifications. According to the results of the regression analyses, factors instead of constant differences are plausible to describe the systematic deviation of the measurements of single analyzers from the mean. This is also in accordance with the fact that operators can introduce constant correction factors into the CBC measurements during calibration. Therefore, the regression line was forced through zero, and the slope of this regression line (ie, proportional bias, equivalent of a correction factor) was used to quantify the systematic lack of agreement between the mean value and the individual analyzer with an optimal agreement at a slope of zero. Furthermore, the scatter of the residuals around this regression line was assessed with a distribution histogram. If the distribution of the residuals appeared roughly gaussian, the Bland-Altman analysis and the calculation of the standard deviation as a measurement for “scatter” were performed with the untransformed values. For some parameters, this distribution was strongly skewed due to a strong increase of the scatter with increasing absolute values so that measurements in the upper range would completely dominate the calculations. In these parameters, values were transformed before the Bland-Altman analysis. For WBCs, relative differences (transformed value = [single value – mean]/mean) led to reasonable results. For platelets, the calculation of relative differences led to a distribution of residuals skewed into the opposite direction with an inadequate effect of small absolute measurement values. A reasonable distribution for these parameters could be obtained by calculating the following: transformed value = (single value – mean)/sqrt (mean). Basophils showed a marked deviation of single measurements. For a reasonable assessment, we calculated the median instead of the mean value for further comparisons.

In the second part of the study, flagging efficiency was compared with the results of slide review. For this analysis, 186 samples with a WBC count greater than 500/µL were included. Samples were considered as containing blasts if there were more than 0% blasts. Samples with 1% or more of metamyelocytes, myelocytes, or promyelocytes were assessed as containing immature granulocytes (IGs). Samples with more than 5% band neutrophils or 1% or more of metamyelocytes, myelocytes, or promyelocytes were assessed as left shifted (LS). For IGs, the most sensitive flags provided by the Advia 120 and DxH 800 were used. For LS, flags with balanced sensitivity and specificity were used. For the Advia 120, either the presence of LUCs (LUCs >3%) or the blast flag was assessed as indicating blasts. Detection of immature
cells by analyzers vs slide review was depicted in contingency tables containing the 4 categories: blast, IG, LS, and no immature cells. In this comparison, only the most abnormal (immature) cell type detected was scored (ie, blast > IG > LS). Sensitivity and specificity were analyzed with contingency tables using a 2-tailed Fisher exact test.

Statistical analysis was performed using Excel (Microsoft, Redmond, WA) and GraphPad Prism (version 5.03, GraphPad Software, La Jolla, CA).

Results

Complete Blood Cell Count

Hemoglobin measurements of all instruments were in good accordance with each other ($r^2 > 0.98$). The Advia 120 failed to measure hemoglobin in 1 sample (discarded from further analysis). Scatter was higher with the Sapphire compared with the other instruments. Measurements resulted in the lowest values for the Advia 120 and the highest values for the Sapphire (Table 2) [Figure 1]. RBC also showed very good accordance ($r^2 > 0.99$) and very little scatter. For the MCV, overall agreement was good ($r^2 > 0.95$). Lowest values were measured with the Sapphire and highest values with the DxH 800. Scatter was in a similar range with all instruments. Measurements of the hematocrit were in good accordance as well ($r^2 > 0.97$). Values were highest with the XE-2100 and lowest with the Sapphire, with the latter also showing a larger scatter than its competitors.

For WBC count, we also found a good correlation among the different analyzers ($r^2 > 0.99$). Analysis of the absolute values resulted in a domination of the systematic deviation and the scatter by high absolute values. We therefore transformed the WBC values for the Bland-Altman analysis. Highest values were measured with the Sapphire and lowest values with the XE-2100. Scatter was in a similar range with all instruments. A Bland-Altman analysis of the hematocrit in 2 samples, a WBC count of zero was erroneously reported by the Advia 120.

Platelet counts also showed good correlations ($r^2 > 0.99$). For platelets, to obtain a gaussian distribution of the residuals, we used the following transformation: (single value – mean)/sqrt (mean). After this transformation, scatter of all analyzers was comparable. Platelet counts were above average from the Sapphire and Advia 120 and below average from the XE-2100 and DxH 800. Since determination of very low platelet values is of special interest regarding the indication for platelet transfusions, we performed an additional subgroup analysis on 32 samples with a mean platelet value below 25,000/µL. Because of a smaller range of these measurements, no transformation was necessary. In this analysis of thrombocytopenic samples, the interinstrument correlation was considerably lower ($r^2 > 0.87$). Sapphire measurements correlated best with the mean and showed the lowest scatter.

For the 5-part LDC, 2 samples were erroneously reported with a WBC count of 0 by the Advia 120. These samples were disregarded in the evaluation of the Advia 120 LDC measurements. Neutrophil measurements showed very good overall correlation with the analyzer mean ($r^2 > 0.94$). Scatter was slightly higher with the Advia 120, DxH 800, and microscopic count than with the Sapphire and XE-2100 [Table 3 and Figure 2].

Eosinophils also showed very good correlations among all analyzers ($r^2 > 0.98$), with little systematic deviation and very little scatter for all analyzers. Microscopic counts were lower than the values of all analyzers and showed higher scatter.

For the analysis of lymphocytes and monocytes, we excluded the Advia 120 from the mean value calculation for samples with a LUC population greater than 5%, as described earlier. Lymphocytes showed fair overall correlation ($r^2 > 0.93$). Systematic bias was minimal among the Sapphire, DxH 800, and XE-2100, whereas lower lymphocyte measurements were reported by the Advia 120 and higher values by microscopic examination. Scatter was moderate overall and highest with the microscopic count and the DxH 800.

Monocyte values had acceptable correlations with the analyzer mean ($r^2 > 0.87$), systematic deviation, and scatter except for the Advia 120, which had a considerably lower correlation with the analyzer mean ($r^2 = 0.67$). The Advia 120 counted lower monocyte numbers, which is partly accounted for by the LUC population displayed by this machine, whereas DxH 800 monocyte counts were slightly above average. Scatter was highest with the microscopic examination and lowest with the Sapphire. Interestingly, incorrectly high monocyte values were scored by the XE-2100, DxH 800, and Sapphire in 3 samples from leukemic lymphomas, whereas microscopic examination and the Advia 120 were in agreement in counting high lymphocyte values in these samples.

For basophil numbers, we found only very poor correlation among the different instruments [Table 4]. Since this was unsatisfactory, we analyzed if any 2 instruments showed good accordance with each other, which was not the case ($r^2 < 0.1$), and if any machine showed good correlation with the microscopic examination, which was also not the case ($r^2 < 0.25$). The XE-2100 and Advia 120 reported an especially high number of implausibly high values (8 samples >4% for the XE-2100, 4 for the Advia 120, 1 for the DxH 800, and 1 for the Sapphire). In a further evaluation, we excluded all basophil measurements flagged as “unreliable” by the respective analyzer. This led to somewhat improved correlations for the Advia 120 ($r^2 = 0.48$; 52 samples excluded).
**Figure 1** Interinstrument evaluation of CBC parameters: regression of individual measurements to the mean of all analyzers. 

- **A**, hemoglobin; **B**, RBC count; **C**, hematocrit; **D**, mean corpuscular volume; **E**, WBC count; **F**, platelet count.

**Table 3** Interinstrument Evaluation of Leukocyte Differential Count Parameters: Individual Measurements Compared With the Mean of All Analyzers

<table>
<thead>
<tr>
<th></th>
<th>Neutrophils</th>
<th>Lymphocytes</th>
<th>Monocytes</th>
<th>Eosinophils</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Slope, $\times 10^{-2}$/Scatter</td>
<td>$r^2$</td>
<td>Slope, $\times 10^{-2}$/Scatter</td>
<td>$r^2$</td>
</tr>
<tr>
<td>Sapphire</td>
<td>-0.55/7.89</td>
<td>0.9725</td>
<td>2.61/5.49</td>
<td>0.9797</td>
</tr>
<tr>
<td>Advia 120</td>
<td>1.82/9.52</td>
<td>0.9618</td>
<td>-7.32/5.26</td>
<td>0.9789</td>
</tr>
<tr>
<td>XE-2100</td>
<td>-1.58/8.10</td>
<td>0.9661</td>
<td>1.14/6.95</td>
<td>0.9686</td>
</tr>
<tr>
<td>DxH 800</td>
<td>0.33/10.66</td>
<td>0.9444</td>
<td>0.81/9.70</td>
<td>0.9458</td>
</tr>
<tr>
<td>Microscope</td>
<td>1.28/10.66</td>
<td>0.9456</td>
<td>5.54/11.16</td>
<td>0.9284</td>
</tr>
</tbody>
</table>

a Slope: proportional bias. Scatter: 2× SD of residuals after correcting for the slope.
and the DxH 800 ($\tau^2 = 0.27$; 4 samples excluded), minimal improvement for the XE-2100 ($\tau^2 = 0.05$; 53 samples excluded), and no change for the Sapphire ($\tau^2 = 0.30$; 3 samples excluded).

Flagging Sensitivity and Specificity

Detection of immature cells by analyzer flags vs manual counts is depicted in Table 5. In this contingency table, the most immature cell population as observed on the slides (blast > IG > LS) is plotted against the respective most abnormal flag of each of the 4 analyzers. Considering flagging with blast alert alone (including increased numbers of LUCs for the Advia 120), sensitivity was in the range of 65% to 94% and specificity between 67% and 86%, with the Sapphire being least sensitive and most specific, whereas the Advia 120 was least specific Table 6. Of the samples containing blasts, the
Sapphire gave an IG flag instead of a blast flag in 3 samples, and the DxH 800 showed this behavior in 2 samples. In the samples with IG in the microscope, both overscoring with blast flags and underscoring (no flag) were seen. Samples with normal manual counts were mainly scored correctly.

**Discussion**

In this study, we compared 4 modern hematology analyzers—Abbott Sapphire, Siemens Advia 120, Sysmex XE-2100, and Beckman Coulter DxH 800—regarding CBC, LDC, and flagging sensitivity and specificity for immature cells.

**Table 4**

Interinstrument Evaluation of Basophil Counts: Individual Measurements Compared With the Median of All Analyzers

<table>
<thead>
<tr>
<th>Basophils</th>
<th>Slope, $\times 10^{-1}$/Scatter</th>
<th>$r^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sapphire</td>
<td>$-1.49/0.78$</td>
<td>0.32</td>
</tr>
<tr>
<td>Advia 120</td>
<td>$7.25/4.98$</td>
<td>0.04</td>
</tr>
<tr>
<td>XE-2100</td>
<td>$9.48/6.71$</td>
<td>0.01</td>
</tr>
<tr>
<td>DxH 800</td>
<td>$2.78/1.39$</td>
<td>0.14</td>
</tr>
<tr>
<td>Microscope</td>
<td>$-2.16/1.24$</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*a Slope: Proportional bias. Scatter: $2\times$ SD of residuals after correcting for the slope.

**Table 5**

Detection of Immature Cells by Analyzer Flags: Contingency Table of Flags vs Microscopic Examination

<table>
<thead>
<tr>
<th>Microscope</th>
<th>Sapphire</th>
<th>Advia 120</th>
<th>XE-2100</th>
<th>DxH 800</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>17</td>
<td>11</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>IG</td>
<td>43</td>
<td>10</td>
<td>28</td>
<td>22</td>
</tr>
<tr>
<td>LS</td>
<td>29</td>
<td>5</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Ø</td>
<td>97</td>
<td>8</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>186</td>
<td>34</td>
<td>77</td>
<td>112</td>
</tr>
</tbody>
</table>

**Table 6**

Detection of Immature Cells by Analyzer Flags: Sensitivity and Specificity of Immature Cell Flagging

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sapphire</td>
<td>65</td>
<td>86</td>
<td>62</td>
<td>82</td>
<td>14</td>
<td>88</td>
</tr>
<tr>
<td>Advia 120</td>
<td>71</td>
<td>67</td>
<td>56</td>
<td>84</td>
<td>14</td>
<td>88</td>
</tr>
<tr>
<td>XE-2100</td>
<td>94</td>
<td>80</td>
<td>56</td>
<td>84</td>
<td>14</td>
<td>88</td>
</tr>
<tr>
<td>DxH 800</td>
<td>82</td>
<td>80</td>
<td>73</td>
<td>84</td>
<td>14</td>
<td>88</td>
</tr>
<tr>
<td>Microscopeb</td>
<td>17/186</td>
<td>43/186</td>
<td>72/186</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a Sensitivity and specificity of the respective flags using microscopic evaluation as reference.

*b Number of samples with the respective abnormality out of all samples evaluated.
is larger. The higher platelet counts generated by the Advia 120 are in line with previous studies by Sandhaus et al. and Müller et al., who also observed higher platelet counts with the Advia 120 when compared with the XE-2100, Beckman Coulter’s predecessor model (LH 750), and the Sapphire. Our subanalysis of samples with mean platelet counts below 25,000/μL showed favorable results for the Sapphire, which uses optical measurements and has correlated well with flow cytometry in previous studies and alternative CD61-immunoplatelet counting with the Sapphire. Up to now, conflicting data were published concerning the preferred method for platelet counting at very low counts and in a hemat-oncological setting, where putative interference with microcytes, schistocytes, leukocyte fragments, and chemical substances may occur. Others have found optical measurement to be more accurate at optical platelet counting at very low platelet counts in this situation using Sysmex machines. Others have found optical measurement to be more accurate at low platelet counts when compared with manual and immunoplatelet counting as reference. According to our results, precise measurements of low platelet may be achieved with either principle depending on the actual design of the analyzer.

The LDC is measured with optical methods (combined optical and electrical methods in the DxH 800) to classify the WBC count according to cell size, lobularity, granularity, and intracellular fluorescence by using slightly different techniques and dyes with all 4 analyzers. As for the CBC, we first computed the proportional bias (slope) and thereupon calculated the scatter according to Bland and Altman’s approach for nonuniform differences. We used the mean of the 4 machines as reference. Microscopic counts were used for control purposes but not as reference due to Poisson statistics of lower cell numbers analyzed raising the scatter of manual counts.

Neutrophils showed little systematic deviation (lowest counts in the XE-2100) and acceptable scatter (somewhat higher in the Advia 120) with all analyzers. Eosinophils showed very good accordance among all machines with very little systematic deviation and little scatter. Even though eosinophils are a small population, this might in part be explained by the bright autofluorescence and sideward scatter, making these cells easier to separate from others. Notably, microscopic eosinophil counts were systematically lower than the values determined by all analyzers. This may occur because some degranulated eosinophils may be erroneously counted as neutrophils under the microscope.

For the evaluation of monocytes and lymphocytes, we restricted the inclusion of values for mean value calculation to samples with LUCs of 5% or less by the Advia 120 to prevent distortion of the mean value for further comparisons. The LUC population of the Advia 120 analyzer adds 1 population to the classical 5 clusters of the 5-part differential. It consists of activated lymphocytes, myeloid and lymphatic blasts, and plasma cells. The classification of atypical cells into the LUC population instead of the closest similar, corresponding populations (eg, lymphocytes or monocytes) as in other analyzers therefore leads to systematically lower lymphocyte and/or monocyte numbers when atypical cells are present in the sample.

Lymphocyte measurements between different analyzers were in quite good agreement, with moderate scatter and without considerable systematic bias, except for the Advia 120, which counted fewer lymphocytes probably due to the extra LUC population described earlier. Monocyte counts were systematically and significantly lower with the Advia 120 and slightly above average with the DxH 800. Furthermore, higher percentages of lymphocytes and lower percentages of monocytes were counted by microscopic examination than by the analyzer average. An erroneous classification of immature, small monocytes leading to frequent outliers and underscoring of these cells by the analyzers was recently made accountable for this discrepancy by Tan et al. Monocyte counts by 2 different analyzers have been compared with flow cytometry of immunostained cells by Grimaldi et al. In this report, the Beckman Coulter LH 750 reported slightly higher monocyte counts and the Advia 120 considerably lower monocyte counts than the reference method, which may have underestimated monocyte numbers slightly, since only CD14 and not CD64 or CD33/sideward scatter was used for the detection of monocytes. In accordance with these results, in an accompanying study, we evaluated the CytoDiff strategy of Faucher et al. and monocyte counts as defined by CD45, CD36 and forward/sideward scatter correlate very well the Sapphire measurements (manuscript in preparation). Therefore, true monocyte numbers may be frequently underestimated by both microscopic examination and by the peroxidase staining used in the Advia 120. In contrast, in 3 lymphoma samples, atypical lymphocytes were misclassified as monocytes by the XE-2100, DxH 800, and Sapphire.

Basophils showed the least agreement among the analyzers. We tried to improve the comparison by using the median as the target for comparisons to reduce distortion by noncredibly high single measurements. Nevertheless, basophils still showed poor agreement with high systematic deviation and scatter. In particular, the Sysmex XE-2100 (and, to some degree, the Advia 120) showed a large systematic deviation, including implausibly high basophil numbers in some samples. Even if samples were excluded due to being flagged as “unreliable” (almost one-third of the samples in the XE-2100 and the Advia 120), instrument accordance remained poor. It has been previously reported that especially the Sysmex XE-2100 and the Advia 120 fail accurate basophil
counting in the presence of atypical lymphocytes or blast cells,\textsuperscript{18-20} whereas the Sapphire shows somewhat better correlation with immune-detected basophil counts.\textsuperscript{18} According to our data, basophil numbers from none of the analyzers can be used with confidence without consideration of the cytogram analysis or microscopic control.

None of the analyzers showed perfect flagging of atypical cells. This result was comparable to prior analysis by Kang et al.\textsuperscript{2} who showed superiority and equal sensitivity of the XE-2100 blast flagging when compared with the Sapphire, Advia 120, and Beckman Coulter predecessor LH 750, which is consistent with recent studies regarding the XE-2100\textsuperscript{21} and the newer DxH 800 analyzer.\textsuperscript{4,22,23} Nevertheless, our results showed a slightly lower sensitivity for blasts with the Sapphire (65%) than that formerly reported (77%-81%) by Kang et al\textsuperscript{2} and Müller et al,\textsuperscript{3} who partly used combined blast/IG flags, and clearly better results for the Advia 120 (71% vs 59%).\textsuperscript{2} These differences might be explained by the sample selection and furthermore by the addition of LUCs more than 3% as an indicator for blasts for the Advia 120 in our analysis. Our study also reconfirms the superiority of the Sapphire and DxH 800 for IG flagging, with the same high sensitivity for IG by the Sapphire compared with the competitors.\textsuperscript{2} However, to detect blast cells with sufficient sensitivity given the clinical consequences of false negatives, operators must not rely on blast flags but need to react to IG flags and gross abnormalities of the CBC. Otherwise, blast-containing samples can go undetected with any of the analyzers.

Taken together, capabilities of the 4 analyzers were comparable overall. The Siemens Advia 120 showed larger scatter for neutrophil measurements, failed with WBC measurements in 2 samples and hemoglobin measurement in 1 sample, measured lower monocyte counts, and showed a comparably low specificity of its blast flag. The Abbott Sapphire produced the largest hematocrit and MCV scatter but displayed reliable measurements in low platelet samples and in the LDC as well as the most specific blast flagging. The Beckman Coulter DxH 800 produced measurements close to the analyzer average with comparably low scatter in the CBC and comparably larger scatter in the LDC with monocyte numbers above average. The Sysmex XE-2100 showed low scatter overall except for the MCV. Basophil counts cannot be reliably used from any machine. XE-2100 and, to a lesser degree, the Advia 120 detected implausibly high counts in some samples. For the detection of leukemic blasts, operators cannot rely on the blast flag alone in any of the analyzers but have to take into account clinical information and CBC data.

\textit{From 1Medizinische Klinik 5, Hämatologische & Internistische Onkologie, 2Transfusionsmedizinische und Hämostaseologische Abteilung, and 3Kinder- und Jugendklinik, Universitätsträklinikum Erlangen, Erlangen, Germany.}

Address reprint requests to Dr Krause: Medizinische Klinik 5, Hämatologische & Internistische Onkologie, Ulmenweg 18, D-91054 Erlangen, Germany; e-mail: stefan.123.456@web.de.

Disclosure: S.W.K. was supported by Beckman Coulter for a different scientific project not directly linked to the analysis presented here.

Acknowledgments: We thank the technicians of all 3 laboratories involved for excellent support.

References


