

A Survey Study of Benefits and Limitations of using CellaVision™ DM96 for Peripheral Blood Differentials

SANDRA J VANVRANKEN, EMILY S PATTERSON, SALLY V RUDMANN, KATHY V WALLER

ABSTRACT

In most clinical laboratories, hematologists rely on the microscopic analysis of stained blood films to accurately classify cells, aiding in the diagnosis and monitoring of a variety of disorders and conditions. Use of the microscope, although considered the gold standard in performing white blood cell differentials, presents a variety of limitations. Digital image technology can facilitate a variety of essential job functions in clinical hematology such as: consulting with colleagues, improving training, referencing an abnormal cell, and utilizing archived images for quality assurance and competency assessment.

A questionnaire was developed to survey medical laboratory professionals about their perceptions regarding the benefits and limitations for using digital images in clinical hematology. The questionnaire was sent in March 2012 to an entire list of 81 current CellaVision™ DM96 (CellaVision AB, Sweden) consumers. A response rate of 46% was obtained.

Background information on participants, 5-point Likert scale averages, percentage agreement (strongly agree and agree), and disagreement (strongly disagree and disagree) were calculated and analyzed. The benefits of using the CellaVision™ DM96 rated the strongest by respondents included: decreased eyestrain, consistency among patient results and advantages in training personnel. Respondents reported notable limitations as being: restrictions with accurately estimating platelets and red cell morphology.

Digital image software is currently being utilized in pre-clinical and clinical hematology and offers potential benefits. With upgrades in slide scanning features and improved capabilities to view platelet and red cell morphology, a transition to digital image technology from the conventional method for performing peripheral blood cell differentials is possible.

ABBREVIATIONS: MLP - medical laboratory professionals; MLS - Medical Laboratory Science; FDA - Food and Drug Association; CLIA - Clinical Laboratory Improvement Acts; CAP - College of American Pathologists

INDEX TERMS: Image interpretation, computer-assisted; blood cells; hematology; informatics

Clin Lab Sci 2014;27(1):32

Sandra J VanVranken, MS, MT(ASCP)SH, Laboratory Compliance Director, Wexner Medical Center at The Ohio State University, Columbus, OH

Emily S. Patterson, PhD, Assistant Professor, School of Health and Rehabilitation Sciences, The Ohio State University, Columbus, OH

Sally V. Rudmann, PhD, MT(ASCP)SBB, Professor Emeritus, School of Health and Rehabilitation Sciences, The Ohio State University, Columbus, OH

Kathy V. Waller, PhD, MLS, Associate Professor, School of Health and Rehabilitation Sciences, The Ohio State University, Columbus, OH

Address for correspondence: Sandra J VanVranken, 339 Doan Hall, 410 W 10th Ave, Columbus, OH 43210, Vanvranken.3@osu.edu, 614-293-6258

INTRODUCTION

Many advances have been made in the field of digital imaging and virtual microscopy in a variety of medical disciplines. Radiology has successfully adopted digital images for routine clinical practice.¹ Several subdivisions in pathology have begun to capitalize on the rewards of using digital images, including histology, cytology and dermatopathology. These fields have also utilized digital images for use in research, education, and telepathology.²⁻⁸

Although use of the microscope has been the traditional gold standard for examining peripheral blood cells, it has a variety of limitations including: physical fatigue; lack of an ability to compare cells; possible inconsistencies among personnel; and an inability to review previous work.^{9,10,11} Limitations of the microscope also include missed malignancies and significant abnormalities, especially if the malignant cells occur in low numbers. Training and teaching are also hindered by the limitations of the microscope, often causing frustrating and incomplete training. In the educational setting, glass slides, often representing rare and unusual cases, can fade, be damaged or break over time.¹²

Digital images offer potential benefits to improve patient care, clinical accuracy, and educational opportunities.⁷⁻¹⁷ With new technology in differential reading and pre-classification software, such as the CellaVision™ DM96, (CellaVision AB, Sweden) it is possible that these obstacles can be overcome. The CellaVision™ DM96 offers quality images that can be zoomed, compared side-by-side, converted to a picture (.jpeg) format and viewed simultaneously by other medical personnel. The software pre-classifies white blood cells for an automatic differential count on peripheral blood or body fluid smears; pre-characterizes parts of the red morphology; and supports platelet estimation.

Benefits and limitations of digital images have been explored in other fields in pathology, but there is limited research in hematology.⁸ More clinical laboratories are investing in this instrumentation, but perceptions utilizing digital images in clinical hematology are not well documented in the literature. There have been some studies describing the accuracy of the instrument's pre-classification capabilities,^{10,11,13-15} but little known research encompassing the complete benefits and limitations of the technology. By studying the benefits and limitations of digital image software in clinical hematology, medical laboratory professionals (MLP) can offer insights for possibly transitioning from the traditional microscope to digital image technology and provide improvements for the future. Since MLP in clinical hematology are currently the only ones in pathology using digital images in a clinical setting, their perceptions are valuable. They can offer knowledge to the field of pathology, which is currently using digital

images primarily for educational, research and telepathology purposes.

MATERIAL AND METHODS

A questionnaire originally developed for pathologists about perceived benefits and limitations to digital images by a member of the research team¹ was significantly tailored for use in this study. The survey was redesigned to target practicing MLP who currently use CellaVision DM96 to conduct peripheral blood differentials. The population investigated included all known users of CellaVision™ instrumentation who have purchased instrumentation directly from CellaVision. Study participants were emailed with a request to participate in the study as well as a link to the online questionnaire (SurveyMonkey®). A pilot study was conducted with 10 individuals from the target population as a convenience sample of current CellaVision users. Minor revisions (three grammatical changes) were made to the survey to improve the clarity and dictation. The data gathered from these 10 individuals were included in the study.

In March 2012, the survey was sent to an additional 71 individuals, representing 55 medical facilities in the USA and Canada from a list provided by CellaVision. Two follow up non-respondent e-mails were sent approximately two weeks apart to increase the response rate. Responses were received from 37 of 81 individuals (46%), representing 23 of 55 (42%) medical facilities. The questionnaire was divided into three sections. The first area sought individual and facility demographic information for all respondents including: degree, years of experience, years performing differentials (total and with digital images), type of employing clinical institution, gender and current position. Each respondent then was asked to indicate if their laboratory currently used digital images for reading peripheral blood cell differentials. The non-users of digital images were directed to a pathway of two sections of questions: first, regarding possible transitioning to digital slides and then about perceived usefulness of digital images capabilities. Although some instructions were on the user client list, they classified themselves as non-users of the technology since they were still in the validation stage of the software. The users of digital image technology were directed to different sections of the questionnaire. These included comparison of the microscope to digital images; possible advantages using

digital images; perceived usefulness of digital images (the same set was used for non-users); possible limitations using digital images; and opinions regarding digital images in training and education. Questions examining perceptions used a five point Likert scale of strongly agree, agree, neither agree nor disagree, disagree, strongly disagree and do not know. The questionnaire received exempt IRB approval from The Ohio State University Office of Responsible Research Practices.

The data were analyzed by Microsoft Excel® to investigate the following two research objectives: 1) characterizing the demographics of respondents and 2) identifying the perceptions of benefits and limitations for digital image usage. Results for the first research objective were tabulated and reported. For the second research objective, responses were ranked by level of agreement with each question and total statements of agreement and disagreement were calculated.

RESULTS

Demographic Characteristics

Demographic characteristics of the entire group surveyed are summarized in Table 1. The majority (67.6%) of the participants possessed a 4-year degree in medical laboratory science (MLS). Medical Laboratory Science programs in Canada have an equivalent 3-year degree, which accounted for 8.1% of the respondents. Almost half of the participants (43.2%) had more than 20 years of experience in reading peripheral blood smears. Nearly 40% (38.9%) had between 1-3 years of experience using digital images for reading differential smears and 25.0% had worked between 4-6 years. The type of the facilities represented varied, with the highest sources being university hospital/teaching hospital (51.4%), cancer hospital (35.1%) and medium sized hospital (32.4%). Females comprised over 75% (78.4%) of the surveyed population. Most individuals completing the questionnaire held a higher position than a staff laboratory scientist: supervisor/manager (40.5%) and lead scientist/charge scientist (32.4%).

The questionnaire was divided into two different paths based on current use or non-use of digital images for reading peripheral blood cell differentials. The user group comprised 78.4% (n=29) while non-users represented 21.6% (n=8).

Perceived Benefits and Limitations

The rates of agreement and disagreement for all responses are listed in Table 2 of the user group. The pilot data were pooled with the rest of the data because there were no statistically significant differences on any of the items. The percentage of agreement with benefits ranged from 58.6% to 96.5% (median 79.2%), whereas the percentage of agreement with limitations ranged from 10.7% to 60.7% (median 32.1%). The benefits with the highest agreement were: 1) reduced eyestrain (97%), 2) more consistent results (93%), and 3) easier training for new employees (89%). The benefits with the lowest agreement were: 1) easier recognition of bacteria and white blood cell inclusions (14%) and 2) easier to concentrate using digital images than a microscope (6.9%).

The limitations with the highest agreement were: 1) less accurate platelet estimation (61%), 2) less accurate evaluation of red cell morphology (54%), and 3) less efficient use of microscope when exclusively trained on digital images (52%).

The limitations with the lowest agreement, meaning that the study participants disagreed with these statements, were: 1) overestimation of abnormal cells (61% disagreement), and 2) difficulty fixing the instrument if it stops working (64% disagreement).

Non-User Group

The non-user group was also surveyed with a different set of questions. After the respondents indicated that they do not currently use digital images for peripheral blood smears, they were provided with a separate set of questions. The sample size for this population was very small, with 8 respondents. On the open ended response question for factors impacting their laboratory's decision to continue microscopy the results included: cost (1 time), availability of instrument (2 times), difficulty of transition (3 times), low volume of patients (1 time), administrative problems (2 times) and concern for turnaround times (1 time). Interestingly, 100% believed that digital images would be useful in their laboratories and 100% agreed that digital images would offer new benefits in the training process for new employees.

Frequency of Use of Education and Training Functionality

Digital images can be utilized for a variety of uses beyond clinical diagnosis. With the CellaVision™ DM96, images can be easily saved as .jpg images that can be reviewed at a later time. Users were asked how frequently their laboratory used available functionality to have easy access to create reference material, perform competency testing, or use images for case studies. The most frequently used functionality was competency

testing (50.0% frequently, 32.1% occasionally), then case studies (46.4% frequently, 42.9% occasionally), and then reference material (35.7% frequently, 60.7% occasionally).

DISCUSSION

Discussion on Benefits of Digital Image Technology

The highest rated benefit of digital image technology

Table 1. Demographic Information of All Participants

Certification of respondents	
4 year laboratory degree - MT (Medical Technologist) or MLS (Medical Laboratory Scientist)	67.6%
2 year laboratory degree - MLT (Medical Laboratory Technician)	16.2%
Specialist certification - H (Hematology), C (chemistry)	8.1%
Other	8.1%
Length of time working as a MLP	
<1 year	2.7%
1 - 3 years ago	2.7%
4 - 6 years ago	13.5%
7 - 10 years ago	13.5%
11 - 20 years ago	18.9%
>20 years ago	48.6%
Total years of experience reading blood differential smears	
< 1 year	2.7%
1 - 3 years	2.7%
4 - 6 years	18.9%
7 - 10 years	16.2%
11 - 20 years	16.2%
>20 years	43.2%
Years of experience using digital images for differential smears	
no experience	5.6%
< 1 year	27.8%
1 - 3 years	38.9%
4 - 6 years	25.0%
> 7 years	2.8%
Type of facility	
Doctor's office	0.0%
Small hospital <300 beds	5.4%
Medium hospital 301 - 800 beds	32.4%
Large hospital >801 beds	24.3%
University hospital / teaching hospital	51.4%
Cancer hospital	35.1%
Non-hospital clinical laboratory	10.8%
Other	8.1%
Gender	
Male	21.6%
Female	78.4%
Current position in the laboratory	
Student	0.0%
Generalist / Bench Technologist	10.8%
Key Technologist	10.8%
Lead technologist / Charge Technologist	32.4%
Supervisor / Manager	40.5%
Director	0.0%
Pathologist	0.0%
Other	5.4%

Table 2. Percentage Agreement and Disagreement and 5-Point Likert Average with Perceived Benefits and Limitations of CellaVision™ DM96

	% of Responses		Likert
	SA + A	SD +D	Average
Perceived Benefits			
Eye strain is less severe with the use of digital images.	96.5	3.4	4.4
Digital images allow for more consistency for patient results among scientists.	93.1	0	4.3
Training new employees on abnormal and rare disorders is easier with digital images.	89.3	3.6	4.3
Side by side cell comparison allowable by digital images is useful for an accurate differential.	86.2	0	4.1
I am less dizzy and physical fatigued using digital images.	82.7	3.4	4.2
The use of digital images allows me to recognize more abnormal results with low levels of abnormal cells.	79.3	6.8	4.0
Recognizing and classifying abnormal cells is easier with digital images.	79.2	3.4	4.0
Training new employees in differentials is easier with digital images.	78.6	3.6	4.2
Digital images make it easier to differentiate reactive/benign cells versus malignant.	75.8	6.8	3.9
My turnaround times are faster using digital slides than the microscope.	69	3.4	4.0
It is easier to concentrate using digital images than a microscope.	68.9	6.9	3.8
Digital images are useful for generalist technologists who do not perform differentials on a daily basis.	68.9	6.8	3.8
It is easier to recognize bacteria and/or white blood cell inclusions using digital images.	58.6	13.7	3.5
Perceived Limitations			
Digital images have limitations with accurately estimating platelets.	60.7	32.1	3.3
Digital images have limitations with evaluating red cell morphology.	53.6	35.7	3.2
New employees are not able to use the microscope as efficiently if exclusively trained on digital images.	51.8	18.5	3.3
Digital imaging instruments are difficult to use with neonatal specimens.	35.7	42.9	2.9
Instrument pre-classification of cells could lead to inaccurate reporting of patient results.	32.1	42.9	2.9
It is difficult to adjust to the color of cells with digital images.	20.7	55.1	2.5
Using the digital image could enable me to falsely classify or overcall higher numbers of abnormal cells.	14.3	60.7	2.5
It is not clear what the return on investment is for purchasing digital image equipment.	13.8	55.2	2.0
I am concerned that I will not know how to fix the instrument if it stopped working.	10.7	64.3	2.1

SA=Strongly Agree, A=Agree, SD=Strongly Disagree, D=Disagree,

from this survey was reduction of eyestrain, with a Likert average of 4.4, and a percentage of strongly agrees and agrees of 96.5%. Eye fatigue has been noted in a previous publication resulting from continuous observation using a microscope.⁶ With regards to other personnel-related benefits, less dizziness and physical fatigue using digital images was the fourth highest rated benefit, with a Likert average of 4.2, percentage of agreement of 82.7%.

Increased consistency of patient results received the second highest Likert average (4.3), and accounted for a high agreement percentage of 93.1%. Medical laboratory professionals described this benefit as standardization, uniformity, and consistent results from day to day and among scientists. An advantage of using digital images for consistency has also been noted in pathology research.^{2,5,11}

Benefits in education and training using digital image technology have been documented in the literature in

pathology and hematology.^{2,12,18-21} This benefit also received high Likert averages and agreement percentages in this study. The statement, training new employees on abnormal and rare disorders is easier, resulted in an 89.3% agreement rate (4.3 Likert average) and training new employees is easier with digital images a 78.6% agreement rate (4.2 Likert average). Of the user respondent group, only a low percentage of laboratories reported never utilizing the instrument's ability to use digital images for further use in education training – reference material (3.6%), competency testing (17.9%) and case studies (10.7%).

Speed and efficiency improve with the CellaVision™ DM96 system and is in agreement with previous reports.^{10,11,14} Data show turnaround times being faster with digital images obtaining a Likert average of 4.0, and an agreement percentage of 69%. The disagreement range was only 3.4%, 24.1% of respondents who answered with neither agree nor disagree. On the contrary, time was noted as a limitation from studies

performed in surgical pathology.⁴ Time (actual minutes performing the differential) was noted to be quicker with the CellaVision™ DM96 technology.^{10,11,14} Workflow was also reported in 2005 – with no significant difference for the experienced MLP, but 25% improvement for the inexperienced MLP.¹⁰ Workflow studies also demonstrated actual sample handling less than 50% than that of manual method of performing a differential.¹⁴

Discussion of Limitations of Digital Image Technology

Limitations with accurately estimating platelets and evaluating red cell morphology were rated highest among users, with Likert averages (3.3 and 3.2) and percent agreement (60.7 and 53.6%). An earlier study utilizing CellaVision™ DM96 also noted that in 23% of the cases the scientists believed the images did not allow them to adequately evaluate RBC and platelet morphology.¹⁰ Five percent of cases in a study by Briggs et al. were deemed inadequate for morphological assessment of red cells.¹³

In this study, the only other perceived limitation to have higher agreement was new employees not being able to use the microscope as efficiently, if exclusively trained on digital images. This limitation can be overcome with a training program that utilizes both methods. From the literature, transition and dependency were also other limitations noted. This includes transitioning from the microscope to digital images, and dependency on one method. Pathology was noted to have difficulty transitioning to new techniques^{5,22} while studies in hematology noted MLP became dependent on the technology.^{10,14}

Quality of images was frequently mentioned in pathology research^{2,4,5} but did not appear to be a limitation in clinical hematology literature. Method of preparing and staining smears affects this limitation, as slides can be automatically generated with a hematology instrument, or by transitional methods. Semi-automated or automated slides decreased the number of cases with inadequate cells from poor image quality.¹⁰ This questionnaire did not ask specifically about image quality, but adjustment to color was calculated with a low Likert average (2.5), and a higher disagreement percent (55.1%) than agreement (20.7%).

Technical issues were noted in the literature^{2,5} which are applicable to CellaVision™ technology as well. In previous studies, no breakdowns of the instrument occurred during the three month evaluation period¹², but in another study, the instrument was down for 8 times for a total time of 12-20 minutes each downtime.¹⁰ Concern with fixing an instrument received a Likert average of 2.1 (second lowest). Ability to fix the instrument received the lowest agreement percentage (10.7%), and the highest disagreement percentage (64.3%).

Cellular pre-classification ability of the CellaVision™ DM96 software has been studied by a number of researchers.^{10,12,14} Although results have to be verified by a MLP before being released, this feature was not noted in the literature. It was not highly regarded as a limitation by this survey, receiving a Likert average of 2.9, a higher disagreement percent (42.9%) than agreement (32.1%).

Cost of the instrument was perceived as a major limitation. One research study showed the instrument provided reduced labor costs.¹⁰ Cost has different personal and organizational interpretations and most likely relates to initial setup of instrument and purchase price of software. Some respondents in this investigation may also not have decision-making responsibilities and may not have been involved in price negotiations.

Some of the limitations identified in the literature from pathology do not apply to this instrumentation. For example, standards and regulation guidelines are not an issue for digital image technology in hematology. The instrument was first FDA approved in February 2004 and each proposal undergoes a strict validation study according to CLIA and CAP standards. The ability to annotate is also possible with CellaVision™ DM96 technology with ability to save images and create a reference set. The ability of software to efficiently produce quality images was noted as a limitation in pathology.^{2,4,6,22}

CONCLUSION

Results of this study are generally consistent with other research on the benefits and limitations of digital images. For benefits, these include: less severe eye strain and fatigue; enhanced use in personnel training and education; consistency, comparability, and consensus

review amongst MLP; and time optimization.^{10,11,14} Limitations include difficulty with platelet and red cell morphology and some issues with the pre-classification capability from the software.

An interesting finding is the low agreement scores for perceived limitations. The literature suggests that the use of digital images presents some obstacles when they are used for clinical diagnosis. Of the possible limitations surveyed, only three of nine listed limitations had strongly agree/agree scores higher than disagree/strongly disagree, suggesting the users did not agree this was a limitation of the instrumentation. On the contrary, all benefits had much larger percentages for total agreement than total disagreement. Since clinical hematology is one field in pathology using digital images for diagnosing patients, the limitations have the potential of being minimized. The technology is FDA approved and has been updated and improved over the years.

Limitations with red cell morphology and estimation of platelets have been noted in the literature and supported by data presented here. In some routine laboratory practices, these cell types are evaluated on a variety of microscopic powers (40X and 100X) and while scanning the slides, which is not a capability of the CellaVision™ DM96 instrument. In the current laboratory environment, there is still a need for the microscope in scanning slides. With improved instrument technology and eventually a full slide-scanning feature in the future, use of microscopes could be diminished in the hematology laboratory.

The CellaVision™ DM96 instrument is able to produce high quality images of white blood cells that can be enlarged and compared. This technology is currently in clinical use, and suggests the benefits outweigh limitations. If MLP in the laboratory can overcome the obstacles associated with cost, software upgrades and staff transitions, and embrace all of the capabilities of the instrument, the advantages are considerable. Also, if the manufacturer continues to develop or modify instrumentation focused towards smaller volume laboratories with lower costs, the market for this instrument can increase.

Currently, this instrumentation can be effective in laboratories with a high workload. The comparison

feature is also a beneficial tool in laboratories with a high population of patients with malignant and pathological hematological conditions. Beyond the everyday efficiency and capacity for comparison, digital images can improve education and training programs. Teaching hospitals can utilize the digital images for building case studies and reference materials. Digital images viewed on the computer screen are also valuable for laboratories that instruct new employees, students and interns, allowing the trainer and trainee to view images simultaneously.

There were several limitations to this study. First, this questionnaire was only distributed to users who purchased a CellaVision™ instrument directly from one of three possible vendors, so it is not an exhaustive sample of all users in the United States and Canada. Second, since the targeted population chosen was current users of the technology, a positive bias could exist for the technology. This population was selected on the assumption that experienced users could provide unique insights that those who have not actively used the software could not. A future study could investigate similar perceptions from a random population of users and non-users of the instrument. Finally, the response rate for this survey and overall number of participants might result in response biases. Nevertheless, this is an emerging area where there is great interest in learning how early adopters view perceived benefits and limitations, and this is the largest known study of this target population.

These results provide more information on an emerging and important technology. Although the results demonstrate a strong basis for MLP appreciating the benefits and capitalizing on the capabilities of digital image technology, additional research is needed. Future studies conducted with current users of the technology, as well as a larger base of non-users would be beneficial to further identify common benefits and limitations. Accuracy could also be further analyzed with MLP performing differentials on slides with a variety of diseases and conditions with abnormal cells, especially cases with low levels of abnormal cells. These studies could help the manufacturer further improve the instrumentation. The feedback from MLP offers valuable information to help other potential users of this technology evaluate its efficacy and potential in their own laboratories.

REFERENCES

1. Patterson ES, Rayo M, Gill C, Gurcan MN. Barriers and facilitators to adoption of soft copy interpretation from the user perspective: Lessons learned from filmless radiology for slide less pathology. *J Pathol Inform* 2011;2(1)1-7.
2. Guzman M, Judkins AR. Digital pathology: a tool for 21st century neuropathology. *Brain Pathol* 2009;19:305-16.
3. Hedvat CV. Digital microscopy. past, present and future. *Arch Pathol Lab Med* 2010;134:1666-70.
4. Li X, Liu J, Xu H et al. A feasibility study of virtual slides in surgical pathology in China. *Human Pathology* 2007;38:1842-8.
5. Jukic D, Drogowski L, Martina J, Parwani A. Primary pathology diagnosis via digital slides. *Arch Pathol Lab Med* 2011;135:372-8.
6. Chen X, Zheng B, Liu H. Optical and digital microscopic imaging techniques and applications in pathology. *Anal Cell Pathol* 2011;34:5-18.
7. Pantanowitz L, Valenstein PN, Evans AJ et al. Review of the current state of whole slide imaging in pathology. *J Pathol Inform* 2011;2:36.
8. Pantanowitz L, Wiley CA, Demetris A et al. Experience with multimodality telepathology at the University of Pittsburgh Medical Center. *J Pathol Inform* 2012;3:45.
9. Lee, Szu-Hee. Virtual microscopy: application to hematology education and training. *Lab Hematol* 2005;11:38-45.
10. Kratz A, Bengtsson HI, Casey JE et al. Performance evaluation of the CellaVision DM96 system. *Am J Clin Pathol* 2005;124:770-81.
11. Cornet E, Perol JP, Troussard X. Performance evaluation and relevance of the CellaVision™ DM96 system in routine analysis and in patients with malignant hematological disease. *Int J Lab Hematol* 2008;30:536-42.
12. Brueggman M, Swinehart C, Yue MJ et al. Implementing virtual microscopy improves outcomes in a hematology morphology course. *Clin Lab Sci* 2012;25(3):149-55.
13. Briggs C, Longair L, Slavik M et al. Can automated blood film analysis replace the manual differential? An evaluation of the CellaVision DM96 automated image analysis system. *Int J Lab Hematol*. 2009;31:48-60.
14. Ceelie H, Dinkelaar RB, van Gelder W. Examination of peripheral blood films using automated microscopy of Diffmaster Octavia and CellaVision DM96. *J Clin Pathol* 2006;60:72-9.
15. Rollins-Raval MA, Raval JS, Contis L. Experience with CellaVision DM96 for peripheral blood differentials in a large multi-center academic hospital system. *J Pathol Inform* 2012;3:29.
16. Kreamer D, Reimer S, Hornlein A et al. Evaluation of a novel case-based training program (d3web.Train) in hematology. *Ann Hematol*. 2005;84:823-9.
17. Vives Corrons JL, Van Blerk M, Albarède S et al. Guidelines for setting up an external quality assessment scheme for blood smear interpretation, Part II: survey preparation, statistical evaluation and reporting. *Clin Chem Lab Me*. 2006;44:1039-43.
18. Brereton ML, De La Salle B, Burthem J et al. Review of the UK NEQAS (H) digital morphology pilot scheme for continuing professional development accessed via the internet. *Int J Lab Hematol* 2008;30:365-71.
19. Triola, MM, Holloway WJ. Enhanced virtual microscopy for collaborative education. *BMC Med Educ* 2011;11:4
20. Koch LN, Lamos JN, Delong LK et al. Randomized comparison of virtual microscopy and transitional glass microscopy in diagnostic accuracy among dermatology and pathology residents. *Hum Pathol* 2008;40:662-7.
21. Marchevsky AM, Relan A, Baillie S. Self-instructional "virtual pathology" laboratories using web-based technology enhance medical school teaching of pathology. *Hum Pathol* 2003;34(5):423-9.
22. Lundin M, Szymas J, Linder E et al. A European network for virtual microscopy – design, implementation and evaluation of performance. *Virchows Arch* 2009;454:421-9.