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Remote Digital Microscopy Improves Hematology Laboratory Workflow by Reducing Peripheral Blood Smear Analysis Turnaround Time

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Abstract

Background The demand for morphological diagnosis by peripheral blood smear (PBS) analysis with clearly defined turnaround times (TAT), coupled with a shortage of morphologists and increasing cost containment, is driving digitalization to the forefront of laboratory workflow. Labor-intensive manual PBS review affects weekend workflow with limited staff availability. The impact of remote analysis of PBS on the performance of hematology laboratories has not yet been assessed.

Objectives Following implementation of fully remote digital microscopy within our laboratory, we measured its impact on morphology workflow efficiency, TAT, and hours saved per month.

Methods A retrospective study of the effects of remote PBS analysis on the morphology workflow in a tertiary medical center using the Scopio Labs X100 Full-Field PBS system was conducted. 10,704 PBS samples were analyzed pre-and post -implementation, over a 5-month period. Overall PBS workload, and average TAT of PBS samples over weekends and the first two weekdays were collected and evaluated.

Results Remote weekend viewing resulted in a 15.8% reduction in the overall morphology TAT of the laboratory ($p < 0.03$) over a 5-month period, despite similar overall workload. PBS analysis TAT on Fridays was reduced by 41.4% ($p < 0.006$), and by 59.1% on the first weekday ($p < 0.02$). The additional hours incurred over the weekend were offset against a reduced need for double weekday shifts resulting in approximately 12.76 work hours saved per month. Internet links to clinically relevant cases are provided.

Conclusion The Scopio Labs Full-Field X100 PBS system with remote analysis capacity significantly reduced PBS TAT and improved the morphology workflow of the hematology laboratory. PBSs with significant clinical findings are now available for remote viewing by on-call clinicians located outside the medical center perimeter. Remote PBS viewing, coupled with the overall monthly cost savings, merit consideration for the implementation of full digitalization for remote PBS review.

Keywords
- digital
- efficiency
- hematology
- morphology
- peripheral blood smear
- remote
- workflow

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Background and Significance

Cell morphology is a cornerstone of hematological diagnosis.[1] Interpretation of peripheral blood smear (PBS) is a complex process involving cell recognition and classification, identification of abnormal cellular elements, weighing of those abnormalities relative to each finding and the overall interpretation of the finding, ultimately leading to the generation of a comprehensive report.[2] In the laboratory setting, the pressure on the morphologist to finalize their review and move to the next case can negatively influence the result of a PBS examination.[3] Due to increasing pressure for cost containment within the laboratory environment, it is important to improve the efficiency of clinical workflows.[4] Turnaround time (TAT) is one of the most common objective measurements of laboratory services used to quantify the time for laboratory tests.[5]

PBS examination by manual microscopy remains one of the most time consuming and labor-intensive procedures in the laboratory, requiring specialized staff, which negatively impacts TAT, particularly during weekends with limited staff availability.[2,3] The increased demand for hematological morphology tests such as the PBS with clearly defined TATs, the complexity of PBS analysis, and the speed of diagnosis to enable immediate clinical action, coupled with the shortage of skilled morphologists and increasing pressure for cost containment, is driving digitalization of microscopy and remote review to the forefront of laboratory workflow management.[2,4,6–8]

While current digital image analyzers such as CellaVision systems, are constantly improving, the main drawback of this field is that only limited fields of view from the PBS are available for review.[2] Many of the digitally analyzed samples, especially those containing cellular abnormalities, still require manual review under a microscope.[2] Hence, the presence of a qualified morphology expert, or a hematologist, may be required within the hospital perimeter during times when full routine morphology services are not available, e.g., during night or weekend shifts.

In October of 2020, the U.S. Food and Drugs Administration (FDA) cleared Scopio Labs' X100 Full-Field PBS system. A digital PBS morphological analyzer with full field specimen view, offers fully digital and remote option for PBSs evaluation, interpretation, and review.[6] As previously reported by Katz et al,[6] the Scopio Labs X100 Full-Field PBS system has demonstrated that, under clinical study settings where each examiner reported a 200-white blood cell (WBC) differential, complete red blood cell (RBC) morphology evaluation and platelet estimation, the median time for PBS review was 7:46 minutes, a 60% improvement of workflow efficiency, when compared with a manual PBS review of 20.0 minutes per case.[6] However, the impact of remote PBS analysis on TAT, workflow efficiency, and cost effectiveness of PBS morphology under real life hematology laboratory settings have not yet been demonstrated.

Objectives

Following implementation of the Scopio Labs X100 Full-Field PBS system with full remote capability within the hematology laboratory at Tel Aviv Sourasky Medical Center (TASMC), we measured the impact of this tool on morphology workflow efficiency, TAT, and man-hours saved per month.

Methods

Study Design and TAT Measurements

This was a retrospective data study conducted in the hematology laboratory at TASMC, a tertiary medical center. The study was approved by the TASMC Institutional Review Board. The average number of CBCs and PBSs conducted at TASMC per month is 38,577 and 973, respectively. Hence, the review rate is 2.5%. The reason for this relatively low review rate is that PBSs in the laboratory are not generated as automatic reflex tests, but are conducted after a manual review of most abnormal CBC results, including scatter plots, pre-analytical parameters, delta checks, and patient histories prior to the generation of a PBS. TAT, defined as the time interval between sample arrival to the laboratory to final report release to the Laboratory Information System (LIS) (in hours) was analyzed by the Business Intelligence (BI) unit at TASMC. Average TAT of PBS was compared for two time periods according to the implementation of remote weekend PBS review: from November 2020 to March 2021 (pre-implementation, ►**Supplementary Fig. S1, Arm A** [available in the online version]) and November 2021 to March 2022 (post-implementation, ►**Supplementary Fig. S1, Arm B** [available in the online version]). Comparison between October 2020 and October 2021 (both pre-implementation, ►**Supplementary Fig. S1**, available in the online version) served as control. Pre-implementation of only stat samples (e.g., looking for schistocytes in the PBS) was performed during the weekends and holidays by the regular laboratory technicians, with no full differentials. Post-implementation, one to two laboratory morphology experts performed PBS remote analysis during the weekend, outside the hospital's perimeter.

Average TATs for PBSs were measured individually for Friday and Saturday (weekend days) and Sunday and Monday (first working weekdays in Israel), as well as a comparative weekly average and overall PBSs workload. Statistical analysis was conducted by a two-sided Student's *t*-test for significance using Excel, and p-values <0.05 considered significant. Data concerning extra hours invested in the remote review were obtained from the Human Resources department of TASMC, and calculated as detailed in the Results section.

Operation of the Scopio Labs X100 System

Samples were routinely analyzed by the Scopio Labs X100 Full-Field PBS system. As previously described,[6] the system is based on a computational photography approach, where a series of low-resolution full field images of the specimen are acquired by low power/wide field objective, and reconstructed into a high-resolution full field image based on a physical model. The system includes WBCs pre-classification by artificial intelligence (AI)-based tools and automated platelet location and pre-estimation. Both WBCs and platelet pre-classification operate as a decision support system,

requiring the operator to review the pre-classified data generated by the system and approve or correct it. RBCs classification is performed by the operator, based on the acquired image.[6] Full field view of the PBS is available to the operator throughout the process. Non-experienced operators require 1 to 2-hour long training sessions to start using the system, and after a week of use, operators can use the system in a fluent manner. There are four laboratory morphological experts certified to sign morphology reports in the hematology laboratory at TASMC. On Sunday to Thursday a single expert performs PBS analyses during the morning shift. Prior to implementing the remote PBS review system, two experts were required during the busy Sunday morning shift, but after implementation, only one was required.

Remote PBS Review Using the Scopio Labs X100 System

Specimens are scanned in the laboratory by the Scopio Labs X100 Full-Field PBS system (►**Supplementary Fig. 2A, B**, available in the online version). Upon approval of the operator, the final report data are transmitted to the LIS (►**Supplementary Fig. 2C**, available in the online version). The internet link is automatically generated and appears in the LIS report (►**Supplementary Fig. 2D**, available in the online version), and can be immediately viewed in the laboratory or remotely by any licensed user (e.g., laboratory specialist, clinician on-call, etc.) (►**Supplementary Fig. 2E**, available in the online version). The remote connection must be established and approved by the local Information Technology authority of the medical center, due to communication safety concerns. Users licensed to view PBSs remotely include all hematologists in TASMC, including seniors and fellows.

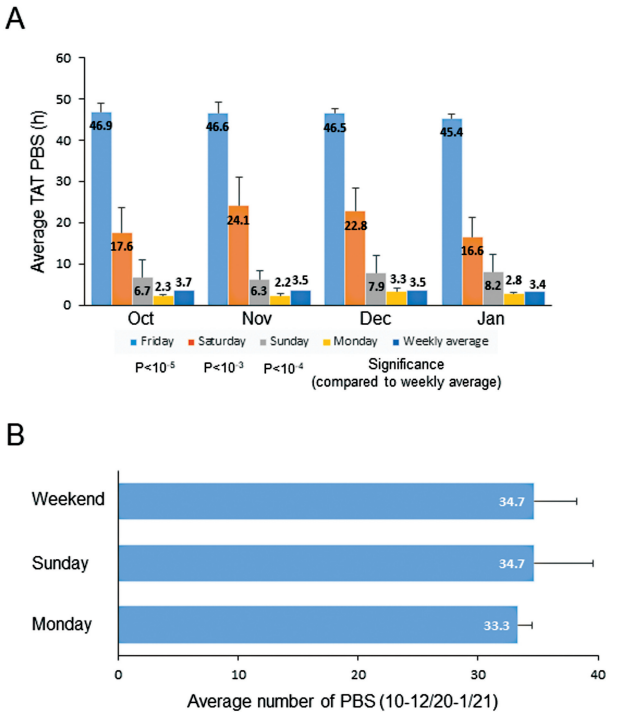


Fig. 1 Pre-implementation TAT and workload in the laboratory. (**A**) Average TAT of PBS (h) over weekdays and weekends pre-implementation. TAT was defined as the time interval between sample arrival to the laboratory, to the release of the final signed report to the Laboratory Information System. Statistical significance values (p, t-test) are presented (right). (**B**) The average numbers of PBSs performed in the laboratory during pre-implementation Weekends (Friday and Saturday), Sundays and Mondays and their SD during months October, November, December 2020 and January 2021 are presented. Average values (in hours) are presented within the bars. h, hour; PBS, peripheral blood smear; SD, standard deviation; TAT, turnaround time.

Results

Data from October 2020 to March 2021, and from October 2021 to March 2022 is presented. Our baseline results demonstrate the significantly prolonged PBS analysis TAT over the weekends (►**Fig. 1A**) as compared with weekdays. The average TAT for PBS analysis, from sample collection to report, on Fridays was 46.3 ± 0.7 hours, and 20.3 ± 3.7 hours for Saturdays (►**Fig. 1A**). The weekend workload also affected the first day of the workweek (Sunday), as shown by the TAT of 7.3 ± 0.9 hours when compared with the average TAT of 2.7 ± 0.5 hours on other weekdays (►**Fig. 1A**). The average number of samples processed on the first weekday was approximately 70, since both the weekend samples (average of 34.7 ± 3.5) and the samples sent on Sunday (34.7 ± 4.9) are processed on Sunday (the first weekday), compared with Monday's workload of 33.3 ± 1.2 samples (►**Fig. 1B**).

Remote weekend morphological analysis was initiated in the laboratory from November 2021, following a 1-month run-in period in October 2021, to train the staff on the digital PBS system. The comparison between October 2020 and October 2021, both pre-implementation of remote review, served as controls. The use of remote weekend morphology analysis during November 2021 till March 2022 resulted in a significant ($p < 0.006$) reduction of Friday TAT by an average of 41.4%, from 45.1 ± 3.1 hours to 26.4 ± 11.9 hours (►**Fig. 2A**). Saturday TAT for morphological analysis was also significantly ($p < 0.02$) reduced during this period by an average of 33.1%, from 21.3 ± 3.4 hours to 14.3 ± 3.3 hours (►**Fig. 2B**). The reduction of TAT during November 2021 till March 2022 was also evident on Sundays (the first weekday) with a significant ($p < 0.02$) reduction of an average of 59.1%, down from 7.9 ± 2.2 hours to 3.2 ± 0.8 hours (►**Fig. 3A**). The effects of remote PBS analysis during the weekends on the reduction of Monday's TAT, although much less pronounced (15.8%), were still statistically significant ($p < 0.03$) (►**Fig. 3B**).

The use of the Scopio Labs X100 Full-Field PBS system for remote weekend work resulted in a significant ($p < 0.03$) 15.8% average reduction in the overall morphology TAT of the laboratory (►**Fig. 4A**), despite similar overall workload during these two parallel periods (►**Fig. 4B**). Between October 2020 and March 2021, there were a total of 5,275 PBS samples with an average of 879.2 ± 85.0 samples each month, whereas between October 2021 and March 2022,

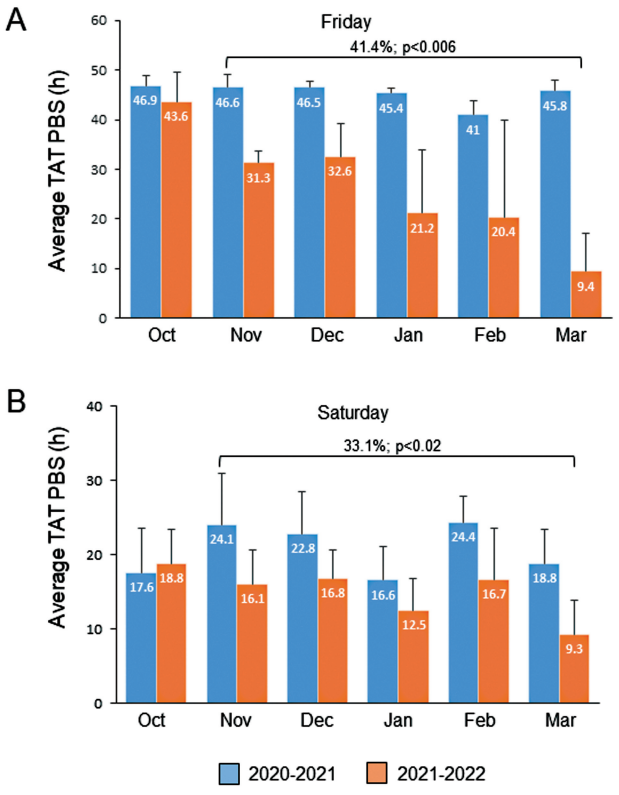


Fig. 2 Average TAT of PBS (h) on Fridays and Saturdays during pre and post-implementation. Average Friday (**A**) and Saturday (**B**) TAT and SD are presented for October to March, pre-implementation (*blue bars*) and post-implementation (*orange bars*) of the remote PBS solution. The average TAT reduction was 41.4% and significant ($p < 0.006$ in *t*-test) and 33.1% and significant ($p < 0.02$ in *t*-test) for Fridays and Saturdays, respectively. Average values (in hours) are presented within the bars. h, hour; PBS, peripheral blood smear; SD, standard deviation; TAT, turnaround time.

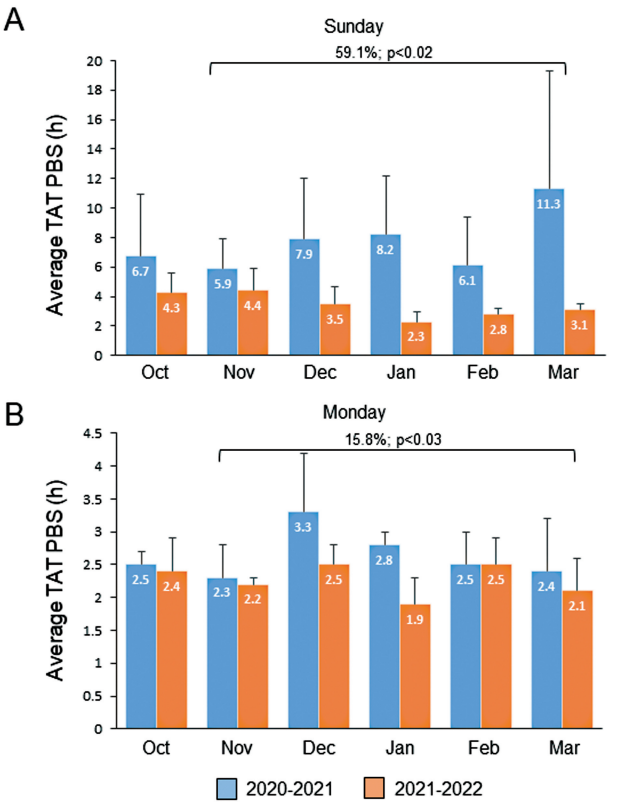


Fig. 3 Average TAT of PBS (h) on Sundays and Mondays during pre and post-implementation. Average Sunday (**A**) and Monday (**B**) TAT and SD are presented for October to March, pre-implementation (*blue bars*) and post-implementation (*orange bars*) of the remote PBS solution. The average TAT reduction was 59.1% and significant ($p < 0.02$ in *t*-test) and 15.8% and significant ($p < 0.03$ in *t*-test) for Sundays and Mondays. Average values (in hours) are presented within the bars. h, hour; PBS, peripheral blood smear; SD, standard deviation; TAT, turnaround time.

there were a total of 5,429 PBS samples with an average of 904.8 ± 36.0 samples each month.

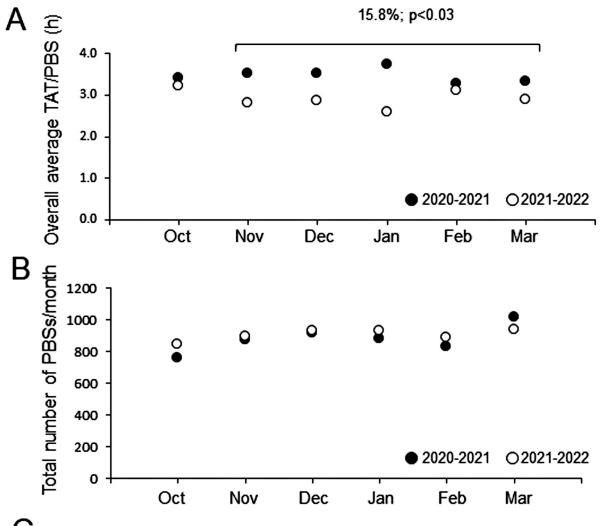
Operating the remote review of PBS samples over the weekend required an average of 16.6 ± 6.2 additional weekend hours worked during the month, corresponding to an additional average $9.4 \pm 1.5\%$ hours incurred by laboratory specialists (►Fig. 4C). However, by eliminating the need for an additional 8-hour Sunday shift every week to compensate for the backlog, this translated into an overall cost saving benefit for the laboratory, with approximately 36 work hours saved each month, following the first month of implementation of the remote PBS morphological analysis. Since the average hour value during a weekend is 140%, we evaluate the actual hours value of 16.6×1.4, which is 23.24. Hence, there was a net average of $36–23.24 = 12.76$ hours saved per month.

►Table 1 contains several cases that were analyzed remotely over the weekend, and demonstrate the value of remote PBS analysis during the weekend period when a full morphology service is unavailable. The presence of schistocytes in a PBS (case #1) can point to an ongoing microangiopathic hemolytic anemia. The correct identification of leukocyte morphology in the PBS may point to the accurate diagnosis of hematological malignancies such as lymphoma (case #2) or acute leukemia (case #3), and subsequently affect treatment.

Discussion

Digitalization and automation have the potential to improve both the quality and efficiency of PBS review, as well as providing economic benefits for laboratories.[4,6,9]

Digital morphology can have a major impact on clinical laboratory workflow through the elimination of geographical constraints embedded within the analytical process, thereby increasing the availability of qualified morphology experts, specifically outside of routine hours. Using manual microscopy, the necessary components of PBS analysis, the smear, the microscope, and the morphologist, are confined to the laboratory boundaries (►Fig. 5, top). Theoretically, current digital analyzers may allow the remote analysis of PBSs. However, common conditions such as pseudothrombocytopenia or the presence of malignant cells, may not be properly assessed due to the narrow scanned field of view and the presentation of limited snapshots of cells to the expert, thus further manual microscopic review is required



C

Month	Regular hours	Extra hours	Extra hours %
October	176	-	-
November	176	18	10.2
December	176	17	9.7
January	176	18	10.2
February	176	12	6.8
March	176	18	10.2
Average ± SD	176	16.6±6.2	9.4±1.5

Fig. 4 The effects of remote PBS review on laboratory performance. (**A**) Overall average TAT/PBS (h) over the two time periods. The difference in overall PBS TAT between pre-implementation (*black circles*) and post-implementation (*white circles*) of the remote PBS analysis was 15.8% and significant ($p < 0.03$ in *t*-test). (**B**) Total number of PBSs per month over the two time periods. No differences in total PBSs performed between pre-implementation (*black circles*) and post-implementation (*white circles*) of the remote PBS analysis were found. (**C**) Average number of hours worked per month and percentage additional hours during the months (November-March) following implementation of the remote PBS analysis. h, hour; PBS, peripheral blood smear; SD, standard deviation; TAT, turnaround time.

in such cases[3] (►**Fig. 5**, middle). Hence, the necessity to manually review some of the samples already processed by current automated digital analyzers limit their use as an ultimate remote morphological analysis solution (►**Fig. 5**, middle). The full-field PBS approach enables viewing of the whole PBS via a browser-based application, with full remote functionality[6] (►**Fig. 5**, bottom).

The Scopio X100 Full-Field PBS system provides a practical remote PBS analysis solution, especially in cases where the context of the slide is important in making a diagnosis, and in settings when a member of the hematology diagnostic team is not present on site and/or at a laboratory performing the test. Our study demonstrates that this solution significantly reduced the TAT for PBS reports on Fridays as these samples are now being analyzed and reported remotely from the morphology expert's residences. The clinical benefit of this approach may extend well beyond TAT improvement. As per the examples shown in ►**Table 1**, such reports may be critical for the time-sensitive diagnosis of severe clinical conditions. For example, identification and enumeration of schistocytes in PBSs are critical for a rapid diagnosis of microangiopathic hemolytic anemia, such as thrombotic thrombocytopenic purpura or hemolytic uremic syndrome, and prompt treatment initiation significantly improves clinical outcome.[10,11] As demonstrated in this study, the remote review of PBSs also significantly affects the TAT of the first workday of the week. Pre-implementation, the cumulative workload of the weekend was added to the samples sent on Sunday, resulting in a prolonged Sunday TAT, more than twice the average weekly TAT. This parameter improved significantly following the introduction of remote weekend PBS analysis. Minor improvement of Monday TAT was also observed.

Relatively few publications have assessed the cost-economic benefit of implementing digital processes into the hematology morphology workflow of the laboratory.[4] One reason for this lack of data could be the fact that implementation of technologies still lags behind that of digital pathology.[12] Hematology embraces the digital transformation but has to balance the upfront cost of such technologies and redesigning the workflow and staff, while demonstrating a cost-efficiency benefit. Successful digital transformations of pathology workflow within the laboratory setting have been published,[13–15] including the advantages of time-sparing workflows as well as reduced costs.[16,17] Hanna et al,[18] showed an increase in efficiency and operational utility with the implementation of digital pathology solutions which, among other parameters, measured the number of glass slide requests as whole slide images, decrease in

Table 1 Several cases demonstrating the value of full PBS analysis over the weekend

Case number	Indication	Main morphological finding	Clinical significance	Link
1	Normocytic, normochromic anemia, 8.0 g/dL hemoglobin	RBC fragments Poikilocytosis	Microangiopathic hemolytic anemia	https://demo.scopiolabs.com/#/view_scan/8aba7934-3af8-40d4-a853-864828005771
2	Pleural effusion, cough	Mature lymphocytes with cleaved nuclei	Lymphoma	https://demo.scopiolabs.com/#/view_scan/6fa6a233-067d-4b76-9b4e-fd9b3b5eba8c
3	Pancytopenia	Blasts	Leukemia	https://demo.scopiolabs.com/#/view_scan/2134e46f-e692-4a7e-a59f-8286437fd1ff

Note: Operation of links: internet addresses (right column) should be copied and pasted in a Google Chrome browser.

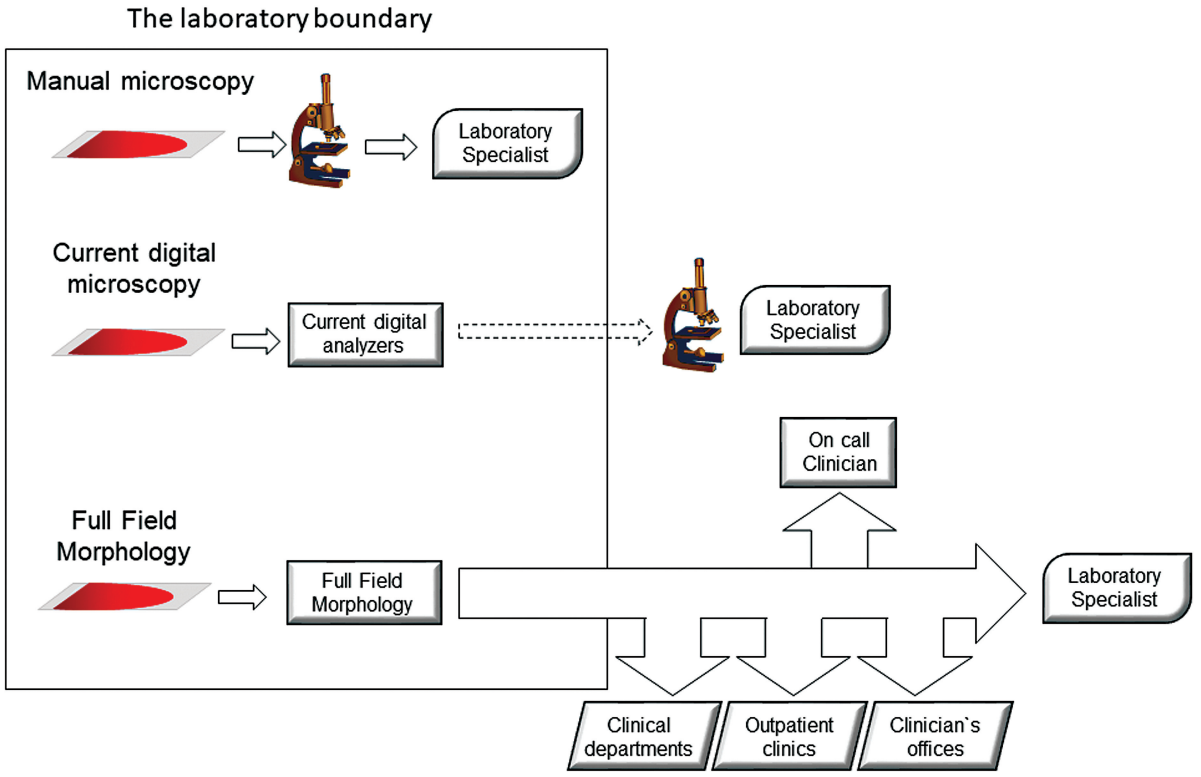


Fig. 5 The impact of remote digital morphology on the laboratory boundary and workflow. Manual microscopy requires the presence of the specimen, the microscope, and the morphologist in the same location, and hence it is confined to the laboratory (*top*). Current digital microscopy enables a limited view of cells and small regions of the specimen, and in many cases requires manual review of the slides. Hence, the remote capacity is limited (*middle*). Full field morphology enables full slide review, and hence the remote analysis of PBS is un-limited (*bottom*). PBS, peripheral blood smear.

confirmatory testing for patients with metastatic or recurrent disease, long-term decrease in off-site pathology asset costs, decrease in operational cost, and faster TAT for reporting cases.[18] It is reasonable therefore to assume that for fully digitized diagnosis and workflow in the morphology realm of hematology, one may expect similar benefits once fully suitable digital solutions are scaled up and available to all laboratories. To the best of our knowledge, our study is the first to assess the impact of a fully digital and fully remote PBSs review on laboratory TAT, workflow efficiency, and cost savings when reviewing cases after hours on the weekend, with limited on-site skilled staff availability. We clearly show a significant reduction of weekend and start of the week TATs, and improvement of overall PBSs TAT. Moreover, we show here that the overall cost of monthly hours invested in PBSs analysis have reduced since the introduction of the remote review. Importantly, remote PBSs analysis may address significant operational difficulties raised during the corona virus disease 2019 (COVID-19) pandemic. The continuous absence of medical care personnel due to quarantine and/or active disease, combined with increased workload, laid a heavy burden on attending medical care personnel, resulting in mental health difficulties among this population.[19] Worldwide, a surge in demand for telecommunication, remote work, and digital transformation was evident as possible solutions emerged for difficulties presented by the COVID-19 pandemic.[20] During the study period of October 2021 to March 2022, on several occasions per month, morphology experts in our laboratory were found positive for COVID-19, and could not physically be present at work. However, the X100 Full-Field PBS application enabled those personnel to continue providing their services, from home, without disrupting laboratory workflow.

In this study, we demonstrate that the ability to view and interpret cases fully remotely, without having to revert to manual microscopy review, combined with the convenience of being able to review these cases over the weekend, significantly and positively impacted the weekday workflow. This resulted in cost savings through the saving of additional weekday shifts to compensate for the weekend caseload backlog.

Limitations of our study: (1). Only one center was included. (2). The only parameters evaluated for cost-effectiveness were TAT and staff hours. Future directions: it is likely that in future multicenter settings, additional parameters such as reduction in confirmatory testing, and reduction in off-site hematologist costs will be included to ensure a more detailed and comprehensive cost-efficiency evaluation. Moreover, the long-term effects of rapid remote PBSs review on the outcome of specific clinical conditions should be assessed.

Conclusion

Implementation of the fully remote and digital PBS analysis significantly improved the efficiency of the morphology

workflow, resulting in a significantly reduced TAT per PBS, and increased monthly cost savings through the reduction of overtime weekday shifts. These benefits were complemented by the rapid delivery of critical medical information by the morphology experts and clinicians, outside the working hours. The findings of the advantages of the workflow efficiency and economic gains due to a remote AI-based decision support digital morphology system, may point to the opportunity to dissolve the physical boundaries of the laboratory in this discipline.

Clinical Relevance Statement

Implementation of the fully remote and digital PBS analysis significantly improves the efficiency of the morphology workflow, resulting in a significantly reduced TAT per PBS sample. Using a remote analysis approach resulted in monthly cost savings through the reduction of overtime weekday shifts. Remote digital PBS analysis enables the rapid delivery of critical medical information by morphology experts or clinicians, outside the working hours and beyond the medical center perimeter.

Multiple Choice Questions

1. Remote analysis of PBSs enables the morphology specialist outside the laboratory to:
   a. Communicate with the laboratory technicians to explain their findings.
   b. Come to the laboratory and use the manual microscope.
   c. Get pictures of slides by the cell phones of the laboratory technicians.
   d. Perform complete analysis of the PBS from a remote site.

   Correct Answer: The correct answer is option d. Up until now, the availability of morphology specialists to view and analyze PBS slides outside of working hours was limited to inappropriate approaches such as oral description of findings, or transmission of pictures via systems not incorporated into the hospital communication networks, such as personal cell phones. Hence, on call clinicians or morphology specialists had to physically arrive at the laboratory to perform morphological analysis. The full remote analysis approach abolishes the need for these illegal/not-safe/inappropriate methods of communication as well as the need to physically be in the laboratory.

2. Remote access to PBSs facilitates the work of:
   a. Hematologists on-call.
   b. Morphology specialists during outside work hours.
   c. Morphology experts in quarantine due to COVID-19.
   d. All of the above.

   Correct Answer: The correct answer is option d. The ability to perform remote analysis of PBS slides provides opportunities for on-call hematologists to review samples from their residence to reach medical decisions, and for morphology specialists to work outside the perimeter of the hospital outside working hours, or due to other reasons such as COVID-19 quarantine.

3. Remote analysis of PBSs
   a. Improves accuracy of PBSs analysis.
   b. Improves sensitivity of PBSs analysis.
   c. Improves the efficiency of the morphology workflow, with a significantly reduced average TAT per PBS.
   d. Improves specificity of PBSs analysis.

   Correct Answer: The correct answer is option c. So far, improvement of analytical performance (accuracy, sensitivity, and specificity) of PBSs morphological analysis over manual microscopy has not been demonstrated yet, but was shown to be non-inferior compared with manual microscopy. However, we clearly show in this manuscript that the morphology workflow in the laboratory is significantly improved by incorporating remote work, specifically by shortening the TAT.

Protection of Human and Animal Subjects

The study was performed in compliance with the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, and was approved by TASMC Institutional Review Board. Animal subjects were not included in the project.

Funding

None.

Conflict of Interest

B.-Z.K. and I.A. are consultants to Scopio Labs.

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