BMC Medical Education

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Development and assessment of a novel multimedia-based educational software for teaching peripheral blood smear morphology

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Abstract

Objectives This study has two aims: develop a simulated and interactive teaching software for highly skilled laboratory technicians, researchers, or practicing physicians in the departments of laboratory medicine, pathology, or hematology who are working on Peripheral Blood smear examination and evaluate the application and effectiveness of this educational software.

Methods For this research, a cohort of 26 laboratory professionals was enlisted. The teaching software enabled the examination of 12 distinct leukocyte morphologies. Participants were tested before the training and subsequently after the training (at 2 weeks and 4 weeks, respectively), once the cumulative study duration reached the predefined benchmark of 180 min bi-weekly. The accuracy rate and time expended were compared and analyzed. The participants' satisfaction with the learning experience provided by the multimedia software was evaluated by a questionnaire.

Results The employment of the multimedia-based educational software markedly enhanced the ability of medical laboratory professionals to recognize morphological features. Participants' feedback about this novel learning strategy was overwhelmingly positive.

Conclusion This interactive teaching software was implemented to accelerate and bolster the operational proficiency of medical laboratory professionals by enhancing their comprehension of peripheral blood cell morphology, and to invigorate their enthusiasm for learning. Findings from an initial evaluation of this software indicate that both goals were achieved. The clinical experience of laboratory professionals plays a crucial role in their learning outcomes; thus, educators should focus on fostering clinical practice skills alongside the integration of multimedia teaching strategies.

Keywords Clinical laboratory, Clinical practice, Medical education, Morphology, Peripheral blood smear, Teaching software

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Introduction

Laboratory medicine is a comprehensive subject that integrates both a theoretical basis and clinical practice [1]. The proficiency of laboratory professionals in making accurate diagnoses is intricately linked to the synthesis of knowledge concerning peripheral blood smear (PBS) morphology [2] and practical laboratory experiences. The morphological analysis of the PBS holds significant importance for the differential diagnosis of hematological diseases and other conditions [3]. Currently, the majority of the blood analysis processes have been automated. The widespread adoption and utilization of automated blood cell analyzers have enhanced the specificity and sensitivity of whole blood cell analysis, consequently providing laboratory professionals with greater convenience [4]. Nonetheless, trainees, individuals undergoing refresher courses, and primary laboratory professionals often face challenges in identifying morphological abnormalities in samples that necessitate manual reevaluation. This is primarily due to their lack of knowledge and experience with respect to the morphology of peripheral blood cells and bone marrow cells. Serious game educational methods refer to interactive games that are designed to promote learning or help players practice and refine their skills rather than just having entertainment [5]. There are relatively few multimedia-based serious game teaching methods in hematology. However, there is an interactive game that focuses on case-based learning and foundational knowledge exploration but does not provide training on identifying clinically significant yet easily confused hematological cells [5]. In response to these challenges, the Laboratory Department of Peking Union Medical College Hospital (PUMCH) integrated an innovative multimedia-based serious game teaching software into the existing standardized training programs for residents and individuals participating in refresher courses. The department evaluated the efficacy and practical application of the simulated and interactive teaching software, while concurrently developing an enhanced teaching model for peripheral blood cell morphology.

Historically, medical knowledge has been disseminated through lectures and textbooks. However, in recent years, numerous educators have adopted interactive learning strategies, such as problem-based learning [6] and flipped classroom [7, 8], to facilitate two-way communication. Recently, a growing number of articles have reported on the use of Artificial intelligence platforms in medical education [9]. The aforementioned methodologies aim to supplant the traditional one-way rote learning approach, motivating students to shift from passive receivers to active participants in their educational journey. Multimedia-based teaching, grounded in computer systems, leverages a diverse array of media formats—including text, symbols, numbers, images, videos, and animations—to bolster students' comprehension and memory retention by integrating technology into the classroom setting [10]. Currently, the education in laboratory medicine also employs a pedagogical model similar to Multimedia-based teaching [11]. Nevertheless, the instruction of blood cell morphology remains inadequate in developing the comprehensive skills of residents and individuals undergoing refresher courses. Lectures on cell morphology primarily concentrate on the conventional cell appearances found in clinically representative blood smear specimens [12]. Yet, in actual clinical scenarios, the complexity of PBS exceeds the scope of what has been taught. This gap in practical knowledge may lead to delays in identifying abnormal cells, subsequently hindering the provision of precise information for clinical diagnoses and potentially delaying patient treatment. Thus, the instruction of blood cell morphology should extend beyond merely teaching, guiding, and laboratory examination of typical PBSs; it should encompass a comprehensive understanding of various blood cell morphologies observable in blood smears, which could be an effective and beneficial complement to microscopy learning.

The Laboratory Department of PUMCH and Beijing XiaoYing Technology Co., Ltd. (XiaoYing) have collaborated to develop an innovative multimedia-based teaching software, referred to as "CEllink," aimed at enhancing learning experiences by providing detailed morphological information to facilitate a deeper comprehension of identified PBSs.

This study employs multimedia-based serious game instruction, personalized through human-computer interaction (HCI) as the core teaching methodology, with the "CELLink" teaching software serving as the medium. The objective is to ignite students' enthusiasm for learning and enhance the clinical operational proficiency of laboratory professionals. There is a pressing need to overhaul and enrich the prevailing instructional approach to blood cell morphology to nurture highly skilled medical laboratory professionals, facilitate the distribution and utilization of superior teaching resources, and elevate the overall standard of education. In this study, we integrated the instruction of peripheral blood cell morphology with HCI and assessed the educational outcomes of the students.

Materials and methods

Teaching software

The teaching software, a collaborative creation by PUMCH and XiaoYing, was incorporated into the multimedia teaching module as part of the HCI framework. This educational research necessitated only the use of a personal computer.

Design of the teaching software

The software's instructional design encompasses three distinct modes: practice, competition, and test (Fig. 1). Concurrently, the software integrates a teaching gallery, facilitating users' consolidation of their understanding of blood cell morphological characteristics by enabling a review of various blood cell images from their studies. Additionally, there are 30,000 annotated cells in the database available for teaching purposes. Each lesson (practice mode) includes 36 unique PBS single-cell images, organized into 18 pairs. Participants needed to accurately identify and select two identical cells from the non-repetitive cell map to eliminate the cells, while any incorrect pairing would leave the cells unchanged. The lesson chapter concludes successfully once all cells are accurately matched. A single practice session constitutes one lesson. For each correctly paired set of cells, the name of the cell type is displayed on the interface, thereby enhancing the user's morphological comprehension of the blood cell type. At the end of the course, the software automatically compiles and analyzes the user's learning outcomes. The practice mode is categorized into three tiers of difficulty: starter edition, advanced edition, and mastery edition, allowing users to choose their learning path based on their individual knowledge at baseline. The starter version encompasses seven clinically fundamental key cell types: band neutrophil, segmented neutrophil, eosinophil, basophil, monocyte, lymphocyte, and myeloblast (labeled as Blast No Lineage Spec in the software). The advanced version introduces an additional two cell types, specifically the lymphocyte variant form and metamyelocyte, building upon the starter version. Following this, the mastery version further incorporates three cell types: promyelocyte, myelocyte, and plasma cells, expanding upon the intermediate version's content.

Upon the computation of their scores by the computer system, participants receive immediate, thorough feedback on their performance. Following the conclusion of a lesson or assessment, the teaching software undertakes an automatic evaluation and synthesis of responses. This process supports students in identifying, comprehending, and mastering cell types that are either challenging or perplexing, urging them to deliberate on and elucidate the characteristics of such cells. This deliberation is facilitated by examining the accuracy rates in identifying various PBSs and the misidentifications of cell types that were ambiguous, considering the chosen exercise's level of difficulty. The software's summary page records alterations in the users' prior exercises, mirroring the students' learning trajectories. Moreover, it compiles tailored revision suggestions for the cell types that were puzzling during the response process, thereby enabling students to rectify and bridge their knowledge deficiencies.

Design of the multimedia teaching lesson within the HCI framework

The CELLink teaching software encompasses a learning mode, a competition mode, and a test mode, as

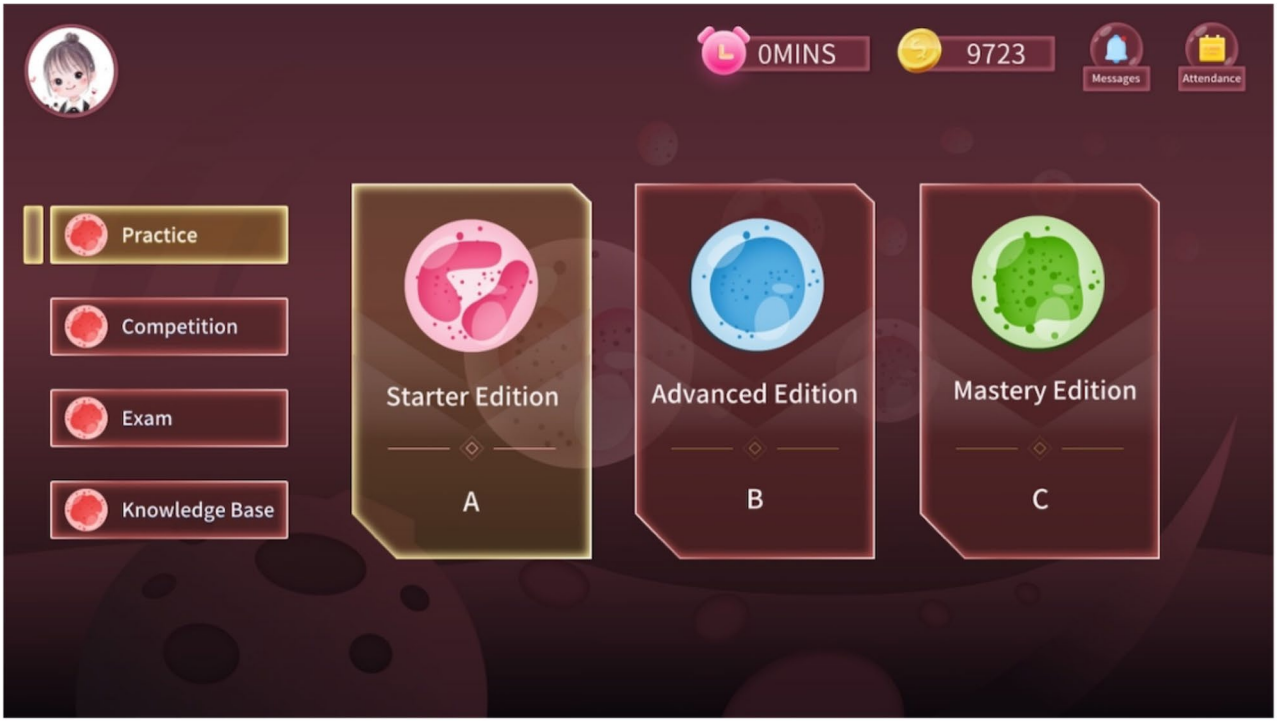

Fig. 1 User interface. Homepage of CELLink

illustrated in Fig. 1. It features a teaching gallery (Fig. 2), which facilitates users in reinforcing their grasp of the morphological characteristics of blood cells through the review of various blood cell images pertinent to their studies. Figure 3 illustrates the learning interface of CELLink designed.

Upon completion of the practice mode, the software automatically processes and compiles the responses. This functionality aids students in identifying, understanding, and mastering cell types they find challenging or perplexing. It prompts students to engage in reflective thinking and to articulate the characteristics of such cells by evaluating their accuracy in recognizing different blood cell types and their mistakes in selecting ambiguous cell types, in the context of the exercise's difficulty level. The summary page within the teaching software tracks modifications in users' prior practices and mirrors the students' learning progress (Appendix 1). Additionally, the software collates tailored review suggestions and furnishes students with a distinct compilation of incorrect pairings to scrutinize and bridge their knowledge gaps, thereby addressing the ambiguous cells encountered during the question-answering process (Fig. 4).

The competition mode within the CEllink teaching software utilizes a shared cell map among different users, enhancing interactivity and engagement (Fig. 5). The incorporation of a leaderboard, distinct from the practice mode, serves as an additional motivational tool by stimulating students' interest in learning through fostering a sense of competition.

In the assessment mode, a distinct cell image database is employed to ensure that identical cells do not recur, thereby preventing users from "memorizing" information as a means to enhance their test performance.

Peripheral blood smear libraries and data collection

All blood cell images utilized in the teaching software are sourced from the PUMCH laboratory. The collection encompasses both typical and atypical peripheral blood cells to closely replicate the real clinical setting. Importantly, personal information such as patients' names, genders, and diagnostic results are excluded from the dataset to ensure compliance with medical ethics. The data is exclusively used for the clinical laboratory education purposes of PUMCH.

The researchers photographed blood smears and assembled a database of PBSs, with the Sysmex SP-10 push-staining mechanism being utilized to prepare the PBSs. The preparation of blood smear materials, the smears themselves, and their staining were all conducted in accordance with production standards, as viewed under a low-power microscope. Furthermore, the "MarkServer" labeling system from XiaoYing Technology Co., Ltd. was employed for the manual screening and removal of blood cell images that were out of focus, exhibited

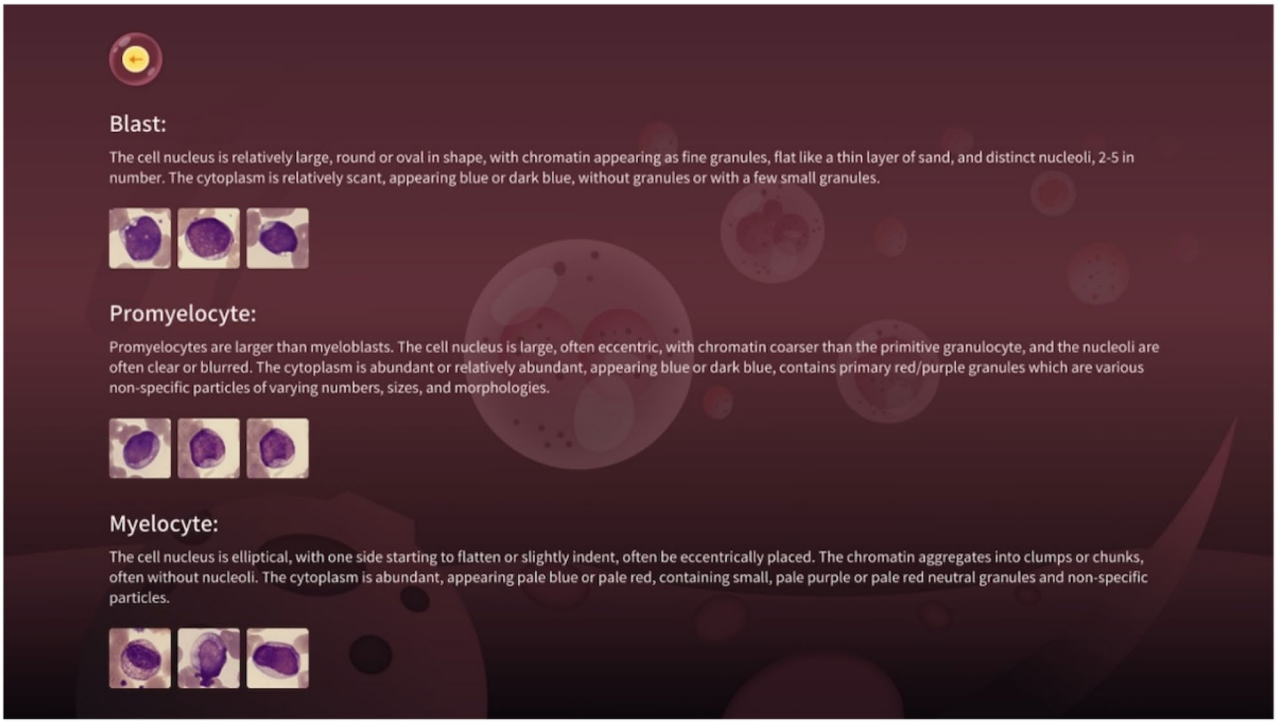

Fig. 2 Teaching Gallery

Fig. 3 Learning interface by CEllink. There are 18 pairs of need to be matched. When one pair is matched correctly, the selected images will disappear. The course/lesson is over until all the images on the interface are eliminated

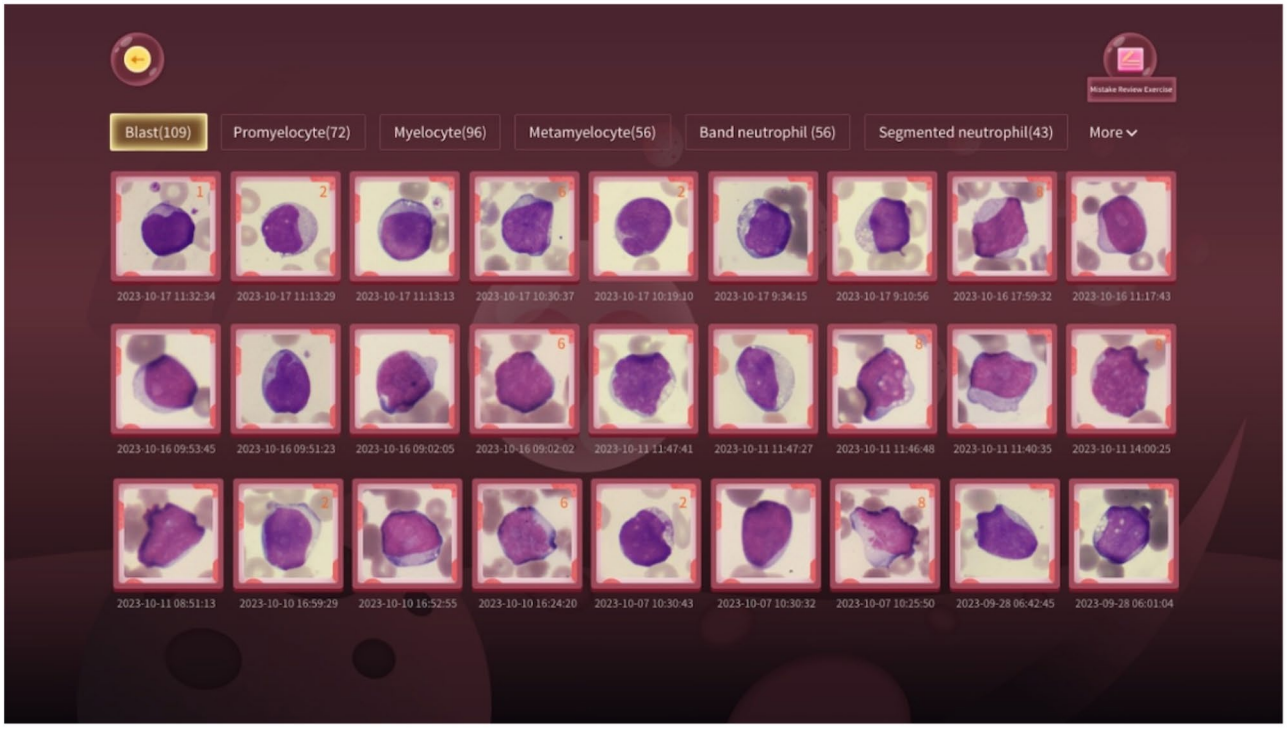

Fig. 4 Wrong-matched image bank. The buttons at the top of the picture categorize the blood cells, allowing users to review misidentified cells. The number in the upper right corner of each individual cell picture represents the number of incorrect matches that occurred during the study

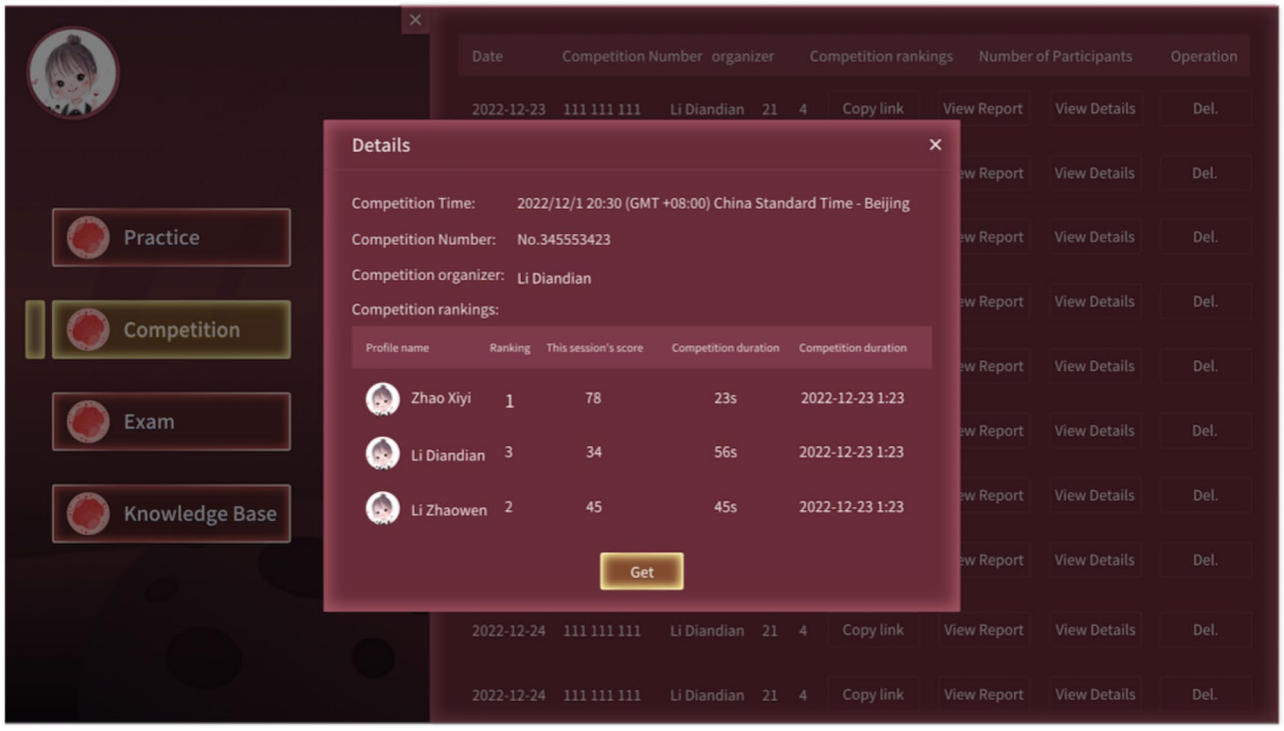

Fig. 5 Summary of the competition: The ranking list summarizes the results of the current class's PK competition

abnormal staining, or lacked effective cell information in the images.

Data annotation

The cell identification and labeling under the microscope were conducted by an expert group consisting of two senior laboratory professionals from the Laboratory Department of PUMCH. The procedures for labeling and the objectivity of the labeling outcomes were rigorously controlled. In instances of discrepancy in cell labeling by the expert group, a process of cross-labeling was initiated. In case of differing opinions on labeling a specific cell, acknowledged PBS diagnosis experts within the field were consulted to review, mediate, and deliberate with the expert team to achieve a consensus on the result.

Study design

Twenty-six laboratory professionals, aged between 22 and 41 years, including 11 junior and 15 senior laboratory professionals, were enlisted for this study from the clinical laboratory of PUMCH. Personnel working in the field of peripheral blood smear morphology for less than five years are classified as junior professionals, while those with five or more years of experience are considered senior professionals.

The study design required participants to complete three tests: a pre-training test, a during training test, and a post-training test, with each test separated by two weeks. The pre-training test served as the baseline assessment. Following the initial study plan, the on-training test was scheduled after participants engaged with the teaching software for a prescribed 180 min bi-weekly for self-directed learning. This on-training assessment occurred two weeks after the commencement of the study. The final examination, the post-training test, was administered after continuing the established learning regimen, which again involved using the software for 180 min every two weeks, allowing for a consistent study pace before undertaking the third test.

Upon completing the three examinations, the instructional phase was concluded, during which each participant's learning metrics—including usage data, accuracy rate, and temporal changes—were meticulously recorded and analyzed via computer. Subsequently, participants were asked to fill out an 11-item questionnaire aimed at gauging their user experience and evaluating any shifts in their self-efficacy. This questionnaire was designed to ascertain whether the teaching software adequately fulfilled the educational requirements it was intended to meet. Furthermore, it compiled insights on the software's application in teaching contexts, impacts on learning interest, assessments of capability enhancement, interface design, and overall user experience. Through the deployment of anonymous surveys, the feedback and outcomes related to the educational content were gathered and scrutinized to assess the effectiveness of the teaching software's utilization.

Statistical analysis

Prism 10 was employed for statistical analysis. The differences in responses to the "feedback questionnaire" before and after the training were analyzed using a paired t-test, comparing pre-training and post-training outcomes.

Results

All participants (100%) ($n=26$) reported an increase in self-efficacy following their use of the CEllink teaching software

In this study, changes in self-efficacy were assessed based on alterations in the participants' diagnostic capabilities, interest in learning, and execution speed (efficiency in examining PBS). Every participant reported in the questionnaire an enhancement in their self-efficacy subsequent to utilizing the teaching software as a learning instrument. A notable elevation in the accuracy rate across the three tests was observed (as depicted in Fig. 6A). Furthermore, significant differences were recorded in all three indices of change (diagnosability, learning interest, and execution speed) between the pre-training and post-training phases, with P values less than 0.05, as shown in Fig. 6B.

Participants' performance was enhanced after one month of learning

Figure 7A illustrates the enhancement in the accuracy of responses across all participants on the three examinations, accompanied by a considerable reduction in completion time. Furthermore, Fig. 7B depicts the shift in the average accuracy rate across the three tests. Subsequent analysis of specific cell types revealed a significant increase in accuracy rates. Notably, following a brief practice period, there was a marked improvement in the identification rates of promyelocytes, myelocytes, metamyelocytes, and myeloblasts, particularly evident in immature granulocytes.

Participants' scores were correlated to frequency of course attendance

As depicted in Fig. 8, there exists a positive correlation between the final scores attained by the participants and the frequency of their attendance in the course. The non-parametric Spearman's correlation coefficient (Rs) is calculated to be 0.7, with a significance level of $P<0.0001$, indicating a statistically significant relationship. This suggests that as the number of courses attended increases, there is a corresponding elevation in the grades achieved by the students.

Participants provided favorable feedback regarding the efficacy of the teaching software in facilitating their learning process

Based on the findings derived from the questionnaire survey (summarized in Table 1) and examination results (Fig. 7), it can be concluded that the implementation

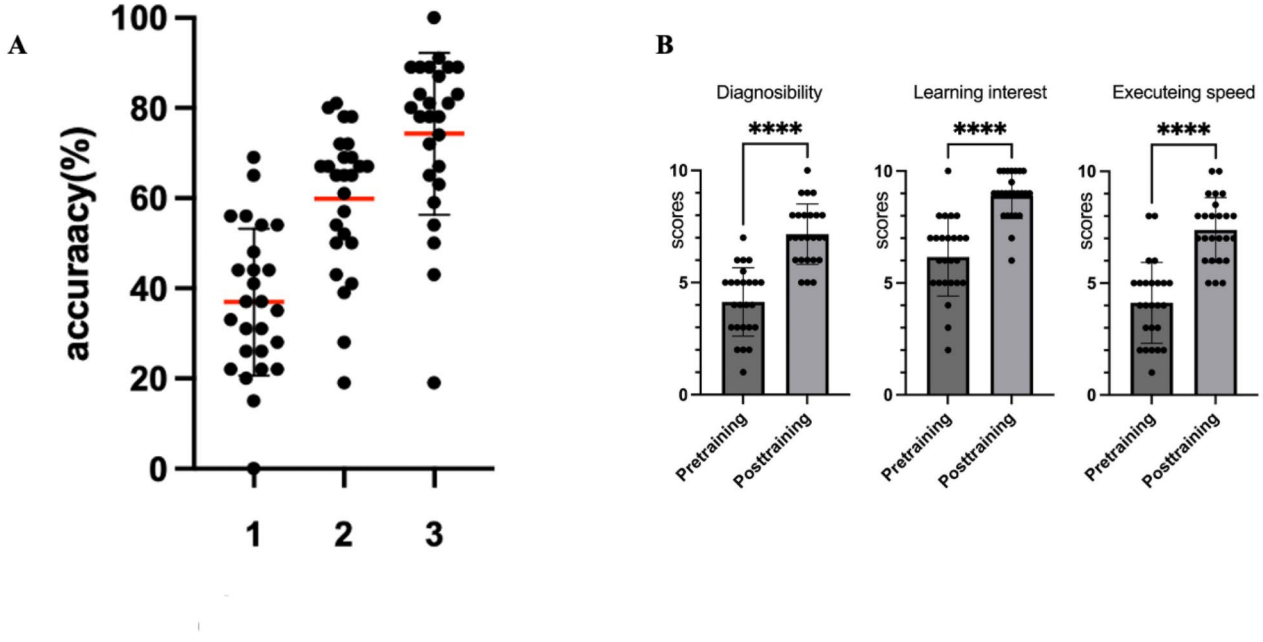

Fig. 6 **(A)** Comparison of the accuracy rate. **(B)** Comparison of self-efficacy (pre-training and post-training. The data is derived from questionaries completed by the participants, who self-evaluated their responses. Each questionnaire was structured on a scale of 10 marks. Participants assigned ratings to various aspects such as their perceived changes in diagnosability, level of interest in learning, and proficiency in executing PBS examinations

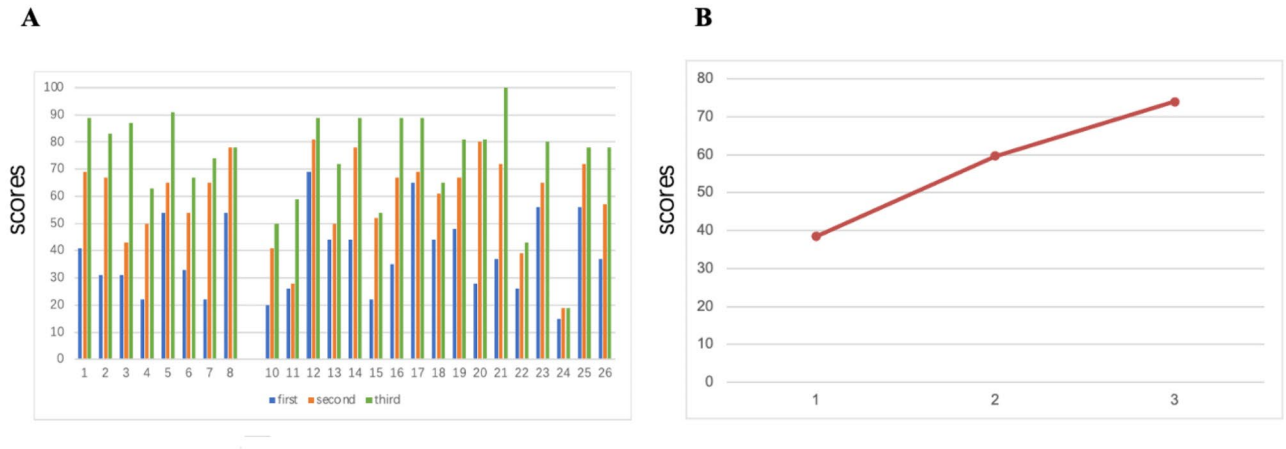

Fig. 7 (**A**) Change in the correct rate of each participant in the three exams. The data corresponding to the ninth group was deemed unusable owing to the lack of information. The X-axis delineates individual participants, while the Y-axis denotes the accuracy rate of the corresponding examinations. Distinct colors are assigned to represent the three different examinations. **(B)** Mean change in accuracy rate in the three exams. The X-axis demonstrates different examinations, while the Y-axis shows the mean change in accuracy rate(%). The average accuracy rate for the first examination was 38.4. The average accuracy rate of the second examination was 59.6. The average accuracy rate for the third examination was 73.9

of teaching software led to improvements in the grades of all participants. Notably, more than half of the participants demonstrated a increase of over 100% in their scores during the third attempt compared to their initial performance. The pass rates for the first, second, and third examinations were recorded at 8%, 62%, and 81% respectively ($n = 26$), with corresponding average scores of 38, 60, and 74.

While one respondent expressed skepticism regarding the software's capacity to guide practical clinical work, only three individuals (3/26, 12%) believed that the test outcomes using the software did not accurately reflect their actual clinical proficiency. However, a consensus emerged among almost all participants regarding the fidelity of the cell images provided by the software, which were deemed to effectively simulate the PBS inspection scenarios encountered in real clinical settings. Additionally, the user-friendly interface of the software was affirmed, with 100% ($n = 26$) of the participants expressing willingness to recommend the software as a valuable learning tool to their peers.

Discussion

The overall cohort of 26 participants dramatically improved their pass rates on the assessments from 8% (mean score = 38), on the first exam to 81%, (mean score = 74), on the final exam. nevertheless, the degree of enhancement varies across participants, potentially attributable to differences in their clinical experience. Individuals with greater clinical exposure are better equipped to identify and address knowledge gaps during the learning process, as they typically encounter a larger volume of blood cells. The software took one month to develop and helped participants achieve significant improvements in their performance. Because learning morphology requires a long period of accumulated experience, it is critical to enhance the ability of new recruits or interns in clinical laboratories to swiftly identify and diagnose hemocytes.

According to the findings of the questionnaire survey, a significant majority of respondents recognized the effectiveness of the teaching software in enhancing their clinical proficiency. They reported a notable boost in their diagnostic capability, learning interest, and execution speed and emphasized the pivotal role of the teaching software in aiding the diagnosis of PBS. Particularly noteworthy is the substantial improvement observed in the accurate identification of immature granulocytes, encompassing promyelocytes, myelocytes, and metamyelocytes, which hold significant clinical importance. Immature granulocytes denote prematurely released granulocytes from the bone marrow, typically occurring in response to infection and inflammation. Clinicians have placed significant emphasis on monitoring immature granulocytes in peripheral blood, as their presence signifies ongoing leukopoiesis, serving as an early indicator of potential infection, inflammation, or other stimuli affecting the bone marrow. This outcome underscores the crucial role of teaching software in enhancing the diagnostic proficiency of blood smears within a limited timeframe, enabling examiners to more precisely identify clinically relevant blood cells. The confirmed practicality of the software further underscores its utility in clinical practice.

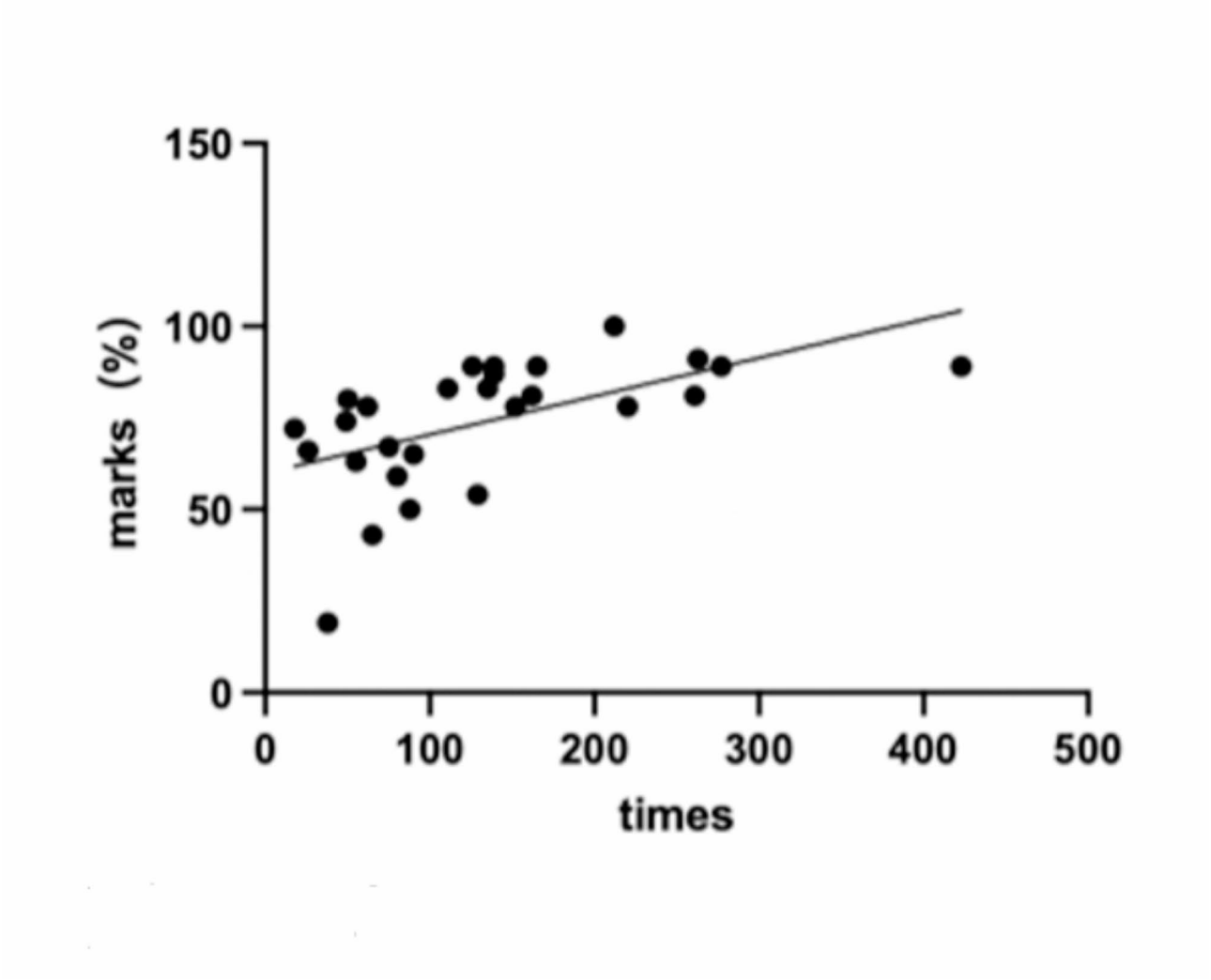

Fig. 8 Correlation between the frequency of attending lessons and the final marks obtained by participants (specifically, the results of the third test. The Spearman's correlation coefficient (Rs) is calculated to be 0.70, with a 95% confidence interval ranging from 0.42 to 0.85. The associated P value is less than 0.0001, indicating a highly significant correlation

Table 1 Feedback on the CELLink teaching software (10-point scale)

Items	Pretraining Mean	Posttraing Mean
1. What is your self-rating of your ability to diagnose blood cell morphology?	4.1	7.24
2. What is your self-rating of your interest in learning about blood cell morphology?	6.2	8.9
3. What is your self-rating of the speed of your PBS examination?	4.1	7.8

It is noteworthy that the score of one participant exhibited minimal improvement, remaining at 19 points in both the second and third exams, compared to the initial score of 15 points. This lack of significant improvement may be attributed to their relatively lower practice frequency, totalling 38 sessions. The absence of a maximum study time limit within the teaching software, which mandates a minimum of 2 weeks and 180 min, results in variations in the duration allocated to each study session. Consequently, some participants engaged in fewer study sessions compared to their peers. This observation underscores the importance of continuous practice and sustained long-term study efforts in influencing academic performance.

On the contrary, participants showed greater improvement between the first and second tests, than between the second and third tests. This phenomenon could be attributed to the software's provision of numerous cell images during the initial stages of use, which were readily assimilated by participants within a short timeframe. This underscores the software's significance in aiding inexperienced laboratory professionals to swiftly acquire

proficiency and commence their duties during the initial phase of use. Intriguingly, while some participants achieved progress exceeding 100%, others showed only a 30% improvement, potentially influenced by the duration of their tenure in the field. Experienced laboratory professionals typically possess a deeper understanding of PBS examination procedures and can effectively apply newly acquired knowledge, whereas those with limited experience may be constrained by their clinical exposure.

The findings of the questionnaire survey revealed a clear advantage in incorporating teaching software into the instruction of peripheral blood morphology. This advantage manifests primarily in the following aspects:

This teaching software transcends the inherent spatiotemporal constraints of traditional morphological laboratory instruction. Beyond the initial guided laboratory experience of reading PBS, students can utilize the online software to solidify their learning through independent practice. This flexibility allows for continued learning outside of the laboratory setting, at any time and location. Notably, for medical institutions in remote regions with limited teaching resources, such as microscopes, this software presents a compelling solution. By providing access to virtual microscopy through the software, it addresses the potential drawbacks of restricted study time and limited practical experience due to equipment constraints [12].

Building upon the aforementioned benefits, the software's functionalities hold the potential to cultivate advanced recognition and identification competencies among students in resource-scarce environments. These teaching strategies can help translate abstract concepts into concrete knowledge [13]. Furthermore, the software's design principles, rooted in HCI, contribute to increased student engagement and motivation [14]. The incorporation of engaging sound effects and a user-friendly interface fosters a more relaxed and stimulating learning atmosphere compared to traditional methods [15]. This is supported by the findings presented in Fig. 5, which demonstrate a significant improvement in student learning interest following the use of the software. Moreover, the software's examination mode leverages a leaderboard system to incentivize active learning and pursuit of academic excellence. This approach, as illustrated in Fig. 3, facilitates the monitoring of both individual and collective progress.

Simulate clinical work. In traditional morphological teaching, blood cells with characteristic features are typically chosen for instruction, facilitating easier memorization of cell recognition attributes by students [16]. However, in real-world clinical settings, variations arise due to individual patient differences, evolving treatment stages, alterations in blood smear staining, fluctuations in observation lighting, and other factors [17]. Consequently, the morphology of blood cells in PBS may deviate from typical norms or prove challenging to identify under microscope examination. Faced with complex and dynamic clinical scenarios, laboratory professionals must engage in prolonged analysis of smears, gradually accumulating experience over time.

Effectively improve the ability to accurately identify various blood cells by gaining a comprehensive understanding of cell morphology. The database of PBS morphology within this teaching software was constructed using authentic clinical blood cell images obtained from various patients under microscope examination. This comprehensive database allows inexperienced laboratory professionals to gain a thorough understanding of the morphological characteristics exhibited by blood cells, thereby enhancing their capacity to identify atypical cells encountered during clinical practice. Such utilization of authentic clinical data serves as one of the most effective methods for on-the-job training, facilitating practical skill development and proficiency enhancement.

Limitation

Nonetheless, the teaching software does possess certain limitations. Firstly, the sample size utilized in the study is relatively small, and the overwhelmingly positive evaluations of the software's quality by all participants may introduce potential biases, as randomness and contingency cannot be fully discounted. Secondly, the participants enrolled in the experiment span a wide range of ages, and the observed improvements in their grades may be correlated with variations in clinical experience. However, the study has not addressed these differences through subgroup analyses or group discussions.

Approximately half of the participants expressed the view that utilizing a mobile phone application would streamline and simplify the learning process. However, it is worth noting that the small screen size of mobile phones compromises image quality, leading to compressed visuals that hinder clear identification of cell particles. As of now, the software is exclusively available for use on computers. Efforts are underway among professionals to develop a mobile platform, aiming to enhance user convenience. In summary, the advantages offered by the teaching software hold the potential to facilitate more effective training of inspectors within hospitals while also yielding cost savings. Moreover, the applicability of the software extends beyond PBS morphology teaching, as it can also be utilized in morphological instruction across various laboratory fields, including urine and parasite detection.

Further development is warranted to incorporate additional functionalities into the teaching software. This includes features such as aiding in the differentiation of ambiguous cells, addressing contentious cell types, and

expanding the learning database. Moreover, personalized learning options tailored to individual users' needs are essential. To genuinely enhance proficiency, a dynamic approach is required. For instance, once a user consistently classifies a specific cell type correctly, the frequency of practice and examination for that cell should be reduced. Conversely, the frequency of practice for other cell types should be augmented, ensuring a comprehensive and adaptive learning experience.

Conclusion

To the best of our knowledge, this represents the inaugural self-developed teaching software tailored for PBS morphological detection. Based on the outcomes of the initial assessment reported in this paper, this multi-media learning system appears to have capacity to broaden learning opportunities, amplify learning efficiency, and reduce laboratory and educational expenditures. Additionally, we advocate for future advancements in teaching software, with a particular focus on enhancing personalization features. This emphasis on personalization is anticipated to yield a teaching effect characterized by reduced costs and enhanced outcomes.

Abbreviations

PBS	Peripheral blood smear
PUMCH	Peking Union Medical College Hospital
HCI	Human-computer interaction
Rs	Spearman's correlation coefficient

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12909-025-06953-x.

Supplementary Material 1: Appendix 1. The summary page within the teaching software

Acknowledgements

We would like to acknowledge the hard and dedicated work of all the staff that implemented the intervention and evaluation components of the study.

Author contributions

Conception and design of the research: Bin-Yao Zhang, Wei WuAcquisition of data: Geng Wang, Xin Wang, Bo-Shen Wu, Dan Liu, Qi-qi Zhang, Bai-Rui Li, Xin-Fei ZhangAnalysis and interpretation of the data: Geng Wang, Xin Wang, Bo-Shen Wu, Qi-qi Zhang, Lin Zheng, Bai-Rui Li, Xin-Fei ZhangStatistical analysis: Bin-Yao Zhang, Dan Liu, Obtaining financing: Wei WuWriting of the manuscript: Bin-Yao ZhangCritical revision of the manuscript for intellectual content: Bo-Shen Wu, Wei WuAll authors read and approved the final draft.

Funding

Administrative Commission of Zhongguancun Science Park (No. Z221100003522004.)

Data availability

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate

This study was conducted with approval from the Ethics Committee of Peking Union Medical College Hospital(Approval number: I-22PJ266). This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 23 July 2024 / Accepted: 5 March 2025
Published online: 18 March 2025

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