Commentary

Next-Generation Learning and Training: The Cy-TEST Experience

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INTRODUCTION

Historically, the founders of cytopathology transmitted their original observations and related their interpretations through detailed reports of the morphological details, which were occasionally supplemented by drawings in black and white that were only marginally supportive of the written descriptions.[1] However, at the basis of cytopathology education, there was—and still is today—daily practice at a microscope accompanied by an "expert"; this is a personalized, long, and expensive process of knowledge transfer inevitably biased by the subjective interpretation of the teacher. Moreover, the development of several schools of thought and local tendencies in past decades has caused severe drawbacks and strongly influenced the overall diagnostic reproducibility and perception of reliability of cytopathology among clinicians. The advent of color figures and photomicrographs in books and atlases, the availability of multihead microscopes, and the possibility of quickly sharing scientific evidence have strongly improved cytopathology learning and teaching worldwide. However, standardization and harmonization of cytopathology among different countries have not yet been reached despite the efforts of universities and scientific societies in collecting unique series of well-characterized cytological cases and in finding dozens of microscopes to organize courses and workshops for trainees. It is clear that such an approach is time-consuming, very expensive, and poorly performing.

Recently, scanners have become available to digitize histological and cytological slides and produce virtual slides that are navigable (just as at a microscope); this has improved case sharing and cut teaching costs drastically. Moreover, digital pathology has recently solved most technical problems with the quality of virtual slides, file storage, hardware requirements, and information technology architecture, and this has allowed research, teaching, and diagnostic applications.[2–6] Consequently, several educational sites and lesion encyclopedias have appeared on the Web. Nonetheless, teaching and learning cytopathology with virtual slides has received little attention. The reasons may be related to the difficulty of indicating the morphological details of single cells within the array of different cell types on display. This is particularly true for cervical cytology, in which significant, abnormal cells are often dispersed among a huge number of "normal" cells.

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THE ROADMAP TO A NOVEL TEACHING PLATFORM IN CYTOPATHOLOGY

To overcome these difficulties, we conceived an online, interactive application integrated within a learning management system that offers the functionalities of a microscope and allows the identification of cells of interest within uploaded virtual cytological slides. This program allows the demonstration of cytopathological patterns through a novel and effective approach. The prospects of this application, which is branded Cy-TEST and is freely available at https://cytest.crs4.it/moodle/ (see also the project Web site at http://www.cytest.eu/), are not limited to the teaching/learning process, and they are bound to expand to the assessment of diagnostic ability as well as the control of the reproducibility of diagnostic parameters.

The Cy-TEST project was planned during the late spring of 2014, was submitted to the European Union Erasmus + project for financial approval (2014-1-IT01-KA202-002607), and was started in September 2014 with the first meeting in Turin. The European Federation of Cytology Societies, Padua University and Turin University in Italy, Porto University in Portugal, and Imperial College in England are the active founding members, with the Consortium for Research and Continuing Education in Turin serving as an administration partner. The Data Intensive Computing group of the Center for Advanced Studies, Research, and Development in Sardinia (Pula, Italy) was selected to provide the technical support.

The Cy-TEST application is based on the following: 1) the Open Microscopy Environment OMERO server system, which is open-source software for the visualization, management, and analysis of biological microscopy images that enables the use of a wide range of bio-image formats and the management of image metadata (eg, arrows, circles, and squares of different sizes and colors) to demarcate and point to cells and/or areas of different sizes (ie, tags and regions of interest [ROIs]) within a virtual slide, and 2) Modular Object-Oriented Dynamic Learning Environment (MOODLE), which is an open-source learning management platform providing a set of tools for designing training environments that are robust, secure, modular, and highly customizable. In MOODLE, one can create a course on a specific organ or pathology, annotate images, define ROIs, and produce problems and questions.

Questions are presented in the form of multiple choices (Fig. 1) or are constructed in an interactive way that requires the student to focus on a single image or cells in the ROI, to recognize a specific type of cell alteration, and to drop 1 or more marks on the virtual slide as an answer (Fig. 2). Moreover, according to our experience with the Eurocytology project (http://www.eurocytology.eu/), it will be possible to activate the system in the many different languages of Europe.

In summary, the bonuses provided by Cy-TEST are as follows:

- Integration of virtual images with scientific information due to the link between the MOODLE and OMERO platforms.
- Interactive approach for teaching and quality assessment in pathology.
- Teaching and e-testing in different languages.
- Standardization and harmonization of cytological diagnoses at the international level.
- Quality assessment in cytopathology that is cheap, open, and easy to organize.
- Easily accessible and progressive self-assessment that is validated by a network of experts.
- Open-source system.
- Consensus on single cell features that can be practiced with no need for multihead microscopes.
- Bridging of the gap between cytopathology and histopathology.

Within the stream of a long, significant, but often conflicting history[7] at different levels of our young European Union (Parliament, the European Union of Medical Specialists, the European Society of Pathology, and the European Federation of Cytology Societies), we are trying to promote a shared platform at least in science and pathology practice. Unsurprisingly, we must overcome problems of language and tradition along with different national programs, but the goal is to reach a common European diploma that follows the mandate of the 1999 Bologna declaration (easily readable and comparable degrees; see http://ec.europa.eu).[8,9]

CY-TEST LIMITATIONS

One of the difficulties encountered in the Cy-TEST project was related to the collection of well-characterized and well-preserved cytological preparations covering all fields of cytopathology that were to be digitized with slide scanners. A multi-institutional collaboration was fundamental for addressing this point. Finding external experts to check and validate the exercises was another minor problem. Scanning
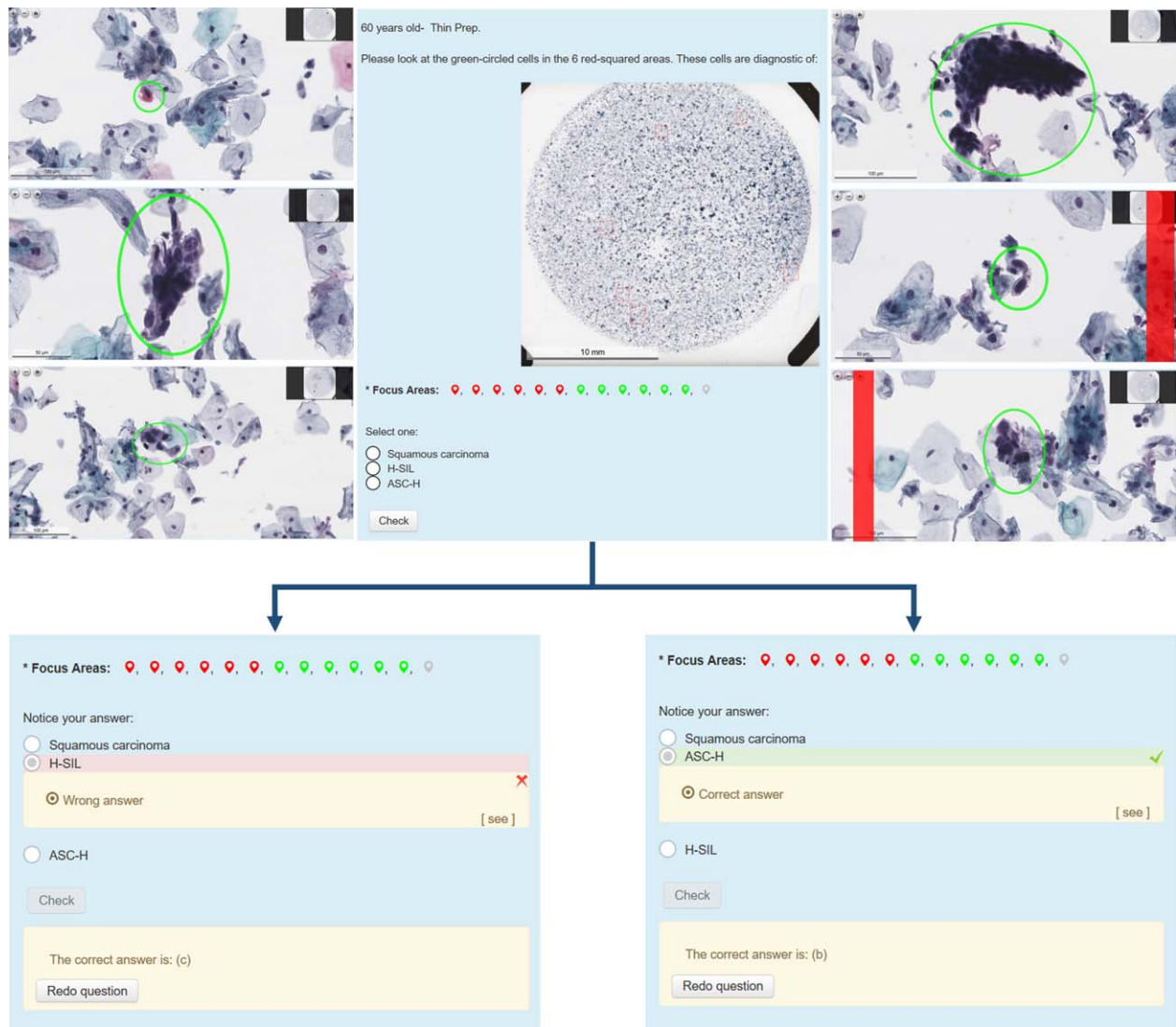
Figure 1. Classic multiple-choice exercise from Cy-TEST. The center of the top of the image presents a question related to a virtual slide of a Papanicolaou-stained, liquid-based preparation in which the cells of interest are marked with a green circle (with magnifications shown next to the exercise box). The user can move the slide and zoom in to see the cells better. In this case, there are 3 possible answers, and only 1 is correct. If the user chooses a wrong answer, the program announces that the result is wrong and what the right answer is (bottom left). If the user selects the correct answer, the program communicates the success (bottom right).

and presenting images at different foci is still a problem because although the recording of different levels of focus is technically feasible, the resulting images are often too heavy for practical use. This problem is being approached through the automatic selection of optimal focusing.

Like most Internet-based software, OMERO.insight, the Java client–based program used to upload virtual slides and apply tags and ROIs, needs to be updated (once a year), and sometimes this process produces some compatibility problems that need to be fixed. Some external users could not access the system because of firewall restrictions imposed by hospitals and institutions: this problem was easily solved with the requirement that institutional technicians open 2 specific gates. Moreover, the creation of the ROIs was quite intricate and needs to be improved. The full system (including 750 virtual slides and 1400 interactive exercises) needs only 2 TB; however, the server maintenance cost is approximately €10,000 per year, and that is without consideration of system administration. The open-source nature of both OMERO and MOODLE, on which Cy-TEST is based, should allow a quick system update and ensure the compatibility of the software with most of the digital pathology improvements for cytology that are expected to occur in the near future.
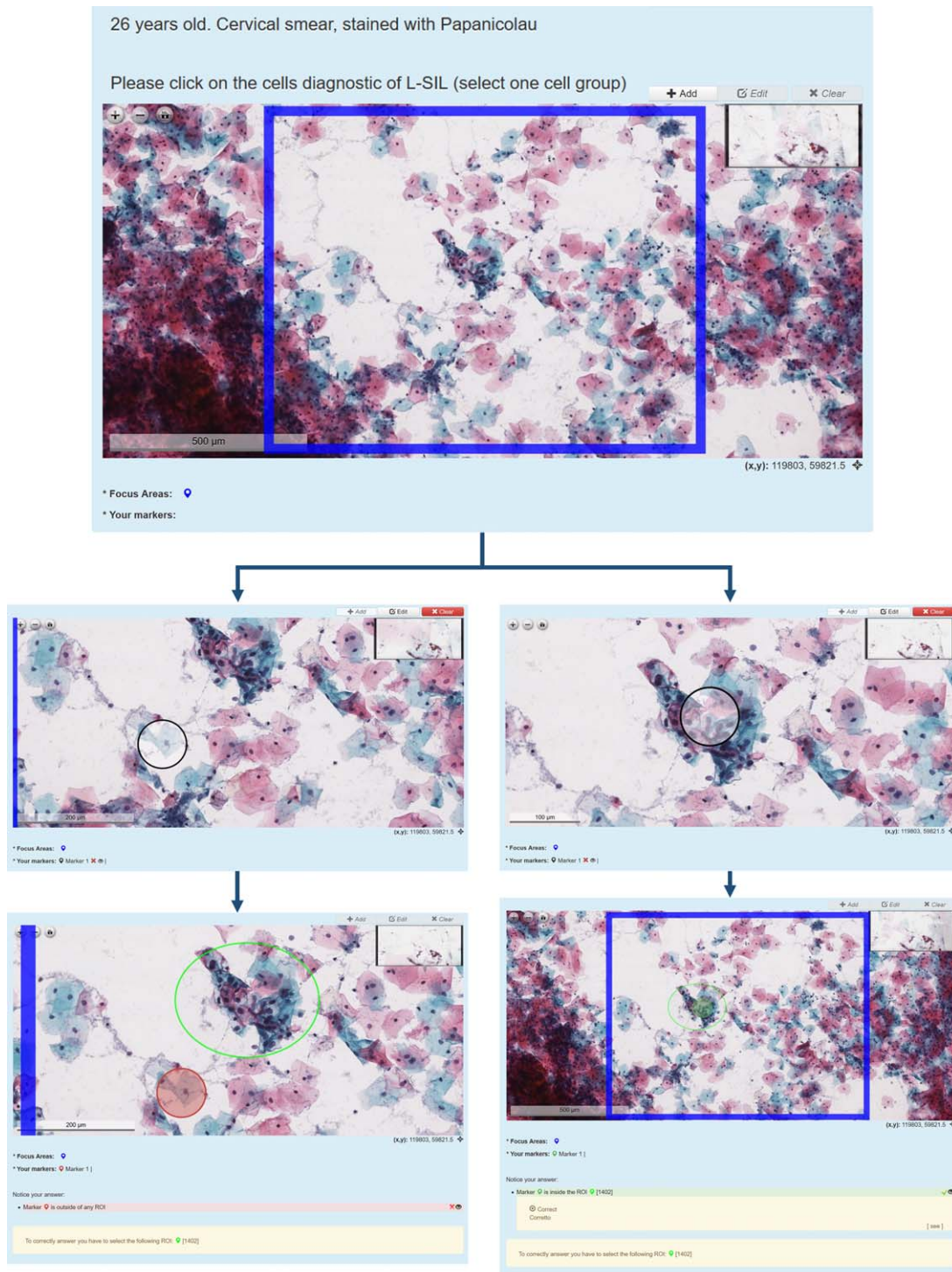
Figure 2. Cy-TEST interactive exercise. The top of the image shows a virtual slide of a Papanicolaou-stained cervical smear, in which a small region of interest is marked with a blue square. The user has to recognize and click on atypical cells inside the blue square. If the user clicks on the wrong cell (black circle on the middle left), the program displays a green circle around the correct cells and turns red the user's black circle around the wrong cells (lower left). On the contrary, if the user clicks on the correct cells, the black circle turns green, and the program communicates the good result.

PROSPECTS AND FUTURE DEVELOPMENTS

The Cy-TEST project, focused on teaching and assaying the cytopathology of lesions of different organs, is already approaching dissemination and will be completed in October 2017. Among its goals, the electronic version of the Quality Assurance, Training, and Examinations aptitude test (named E-QUATE) will soon be tested, and it hopefully will be adopted by the European Federation of Cytology Societies to assess the quality and level of diagnostic capacities in cytology according to European standards.

Exploiting the process of the demonstration of single cytological patterns via informatics and their interactive correlations with questions and comments, the original approach that has been realized with the Cy-TEST project offers opportunities for future developments and novel applications.

Here we can prospectively outline the following:

1. A strict correlation exists between cytological features and related histological patterns. This correlation, corresponding to the usual diagnostic process in which preoperative cytology paves the way to the ensuing histopathological examination of postsurgical specimens, is currently only seldom practiced in university courses, in which the 2 separate disciplines (cytology and histopathology) are sometimes taught in different contexts.
2. An added feature of the Cy-TEST software presents both histology and cytology slides of the same case and allows a description of the underlying correlating features. This novel application will thus permit us to teach and present diagnostic cytology cases as an integral part of pathological diagnoses and to link sequentially presurgical and postsurgical steps. In multiple-choice exercises, the definition of a given cytological feature is determined to be correct according to classical and well-accepted definitions. The validation of histopathological and cytopathological classification and diagnostic criteria and interobserver reproducibility tests were achieved through the discussion of cases with multihead microscopes, circulating slides and smears, or, more rarely, virtual images. So far, however, attention has been focused on cases rather than the features

of single cells because the available technology has been insufficient for such an approach. A specifically designed development of the Cy-TEST program (tentatively called a decoy quiz) allows us to present single cells (identified with color circles with the ROI device) and then ask for the related diagnosis (presented as an alternative). The system will then allow us to collect the different diagnoses offered by the experts participating to the trial and to automatically calculate the κ statistics and the reliability of the pathological definitions.

In conclusion, on the basis of Cy-TEST's pioneering achievements, we believe that a new era of learning, training, and testing in cytopathology and histopathology is coming.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

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