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Review Article

# Whole slide imaging for educational purposes

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## Abstract

Digitized slides produced by whole slide image scanners can be easily shared over a network or by transferring image files to optical or other data storage devices. Navigation of digitized slides is interactive and intended to simulate viewing glass slides with a microscope (virtual microscopy). Image viewing software permits users to edit, annotate, analyze, and easily share whole slide images (WSI). As a result, WSI have begun to replace the traditional light microscope, offering a myriad of opportunities for education. This article focuses on current applications of WSI in education and proficiency testing. WSI has been successfully explored for graduate education (medical, dental, and veterinary schools), training of pathology residents, as an educational tool in allied pathology schools (e.g., cytotechnology), for virtual tracking and tutoring, tele-education (tele-conferencing), e-learning, virtual workshops, at tumor boards, with interactive publications, and on examinations. WSI supports flexible and cost-effective distant learning and augments problem-oriented teaching, competency evaluation, and proficiency testing. WSI viewed on touchscreen displays and with tablet technology are especially beneficial for education. Further investigation is necessary to develop superior WSI applications that better support education and to design viewing stations with ergonomic tools that improve the WSI-human interface and navigation of virtual slides. Studies to determine the impact of training pathologists without exposure to actual glass slides are also needed.

**Key words:** Digital, education, proficiency testing, training, whole slide imaging

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## INTRODUCTION

Whole slide image (WSI) scanners are robotic microscopes capable of digitizing entire glass slides. These WSI devices automatically scan glass slides and employ software to combine individual scanned fields into a composite digital image. Today, there are several commercially available systems that can digitize glass slides containing tissue sections, cytology material, blood smears, and so on. The WSI produced is of excellent quality. However, WSI files are often much larger than other digital images typically used in healthcare. Also, unlike conventional digital image files, which typically contain a single view, WSI files are formatted as multi-resolution "pyramids" that allow for optimized real-time viewer performance of selected regions across all resolutions.[1] Images can be easily shared over the Internet or on optical discs (e.g., DVDs). The speed of loading digital images depends on the speed of the user's computer and network. When retrieved, the captured "virtual" image can be visualized on a computer monitor or handheld mobile device without the use of an actual microscope, (i.e., "virtual microscopy"). New human-computer interfaces (e.g., touchscreen displays and tablet technology) that enhance WSI viewing and navigation are especially beneficial for education. Moreover, image viewing software today permits users to edit, annotate, analyze, and easily share WSI (e.g., tele-conferencing). As a result, WSI has begun to replace the traditional light microscope, offering a myriad of opportunities for education, training, competency evaluation, and proficiency testing.[2-5] This review article focuses on applications of WSI in education and proficiency testing.

## GENERAL EDUCATIONAL USES

WSI have been used for a plethora of educational activities [Table 1]. Digital slides are more interactive than static images, easier to share with multiple users anywhere at any time when compared with glass slides, and they permit training materials to be standardized by offering the same digitized slide sets to all trainees. In addition to scanning slides, the creation of digital slide teaching sets ideally requires a mechanism to make the images available to users (e.g., hyperlinks to the files on a sever) as well as software to manage the files (e.g., search function) and link them to informative metadata (e.g., clinical content and educational text discussions). Disadvantages of using glass slides for teaching purposes include expense of microscopes (multiple or multi-headed for large groups), restricted access to trainees, loss of stain quality over time, and limitations of the type of glass slides that can be shared. Histology slides that are hard to prepare (e.g., calcified and decalcified sections of bone and teeth), one of a kind exotic cases, surgical pathology cases that do not lend themselves well to recuts (e.g., needle core or small skin biopsies), consult slides that must be returned, and specific cytology cases (e.g., irreplaceable Pap tests where only one glass slide exists) infrequently get incorporated into glass slide teaching sets. Now, with WSI, the most representative slides with the best quality material can reassuringly be included into teaching sets. Not only can such materials be easily added to WSI sets, but compared with glass slides these digital slides will not fade, break, or disappear. The portability (time and location), ease of maintenance, ability to annotate images (which can be selectively hidden from trainees), linking of educational content to the files, and utility of them to construct tests is a great boon for educational purposes. However, to ensure that not just computer savvy students excel, all will require adequate training to comfortably use virtual slide technology.

**Table 1: Educational uses of whole slide images**

| |
|---|
| Graduate education (medical, dental, veterinary school) |
| Pathology training (residency programs) |
| Allied pathology schools (cytotechnology) |
| Virtual tracking and tutoring |
| Tele-education (conferencing) |
| E-Learning |
| Virtual workshops |
| Tumor boards |
| Interactive publications |
| Examinations |

## GRADUATE EDUCATION

Several authors to date have documented the success of WSI in graduate education for medical,[6-12] dental,[13,14] and veterinary schools.[15-17] Scanned slides for dedicated teaching should be de-identified, prior to making the WSI available for general users. Overall feedback of students for these publications was highly positive. Both students and faculty indicated strong support for using WSI to teach histology, pathology, and cytology. Students complemented the quality of the images and ease of use of the software. Thumbnail images help students maintain their orientation regardless of location or magnification. WSI promoted more interactivity between students. Tutors seem to find it easier to explain issues and findings to students using computer displays. Also, students work faster with WSI, they were more likely to study slides in preparation for practical examinations when virtual slides were available, and the novelty factor of this new modality of teaching raised the students' interest. Therefore, it is not surprising to see in many schools light microscopes been totally abandoned for computers.

## PATHOLOGY TRAINING

For many of the aforementioned reasons, WSI has proved beneficial in training pathology residents.[18,19] Centralizing WSI resources (scanning and storage) and providing easy, secure web access to digitized slides makes it possible to standardize training (e.g., grading of tumors), offer self-paced virtual rotations, manage and archive conference materials (e.g., unknown cases), and assess competency.[20-22] Digital slide teaching sets have become popular at several institutions.[23,24] For example, at the University of Pittsburgh Medical Center over 4000 WSI have been created to date for pathology educational purposes, which encompasses most anatomical pathology subspecialties. At present, digital slide sets supplement traditional microscopy training. Perhaps in the future they may completely replace conventional microscopy. A scalable, web-based atlas-like tool (called PathRez) has been created to search this WSI database.[25] Tracking tools, incorporated into WSI, also have the ability to provide quantitative metrics to help evaluate resident competency at evaluating slides.[22] Exposing pathology trainees is important to avoid technophobia, as they are the future pathologists who are most likely to use WSI technology when they graduate. Also, it will provide them with the preparatory skills necessary to better navigate digital slides which are increasingly being used on formal tests (e.g., board examinations in the USA and Europe).[26] Residents and fellows are often recruited to help add useful but curated, peer reviewed and/or edited annotations and educational content to digital teaching sets. WSI have also been successfully employed to educate cytotechnology students.[27-29] Annotated digitized slides appear to be very useful for teaching cytotechnologists cytomorphology. However, there are differences between screening and interpretive functions when examining cytology slides which still need to be explored with WSI. For example, the implications of the relatively low resolution of some WSI systems at low (screening) magnification have not been adequately studied. Moreover, viewing through a conventional light microscope may provide a different perceived field width than what is seen on a monitor. It has also been shown that cytotechnologists may have trouble with place keeping when using WSI, and that greater exploration of WSI at low magnification significantly correlates with correct diagnoses for cytotechnologists.[30] Cytology WSI with annotation, such as those belonging to the International Academy of Cytology (IAC) online virtual slide library, perform better than those without annotation.[31] This may be because they require only interpretation skills from the participants, rather than both screening and interpretive skills for WSI without annotation.

## TRACKING AND TUTORING

With the advent of WSI, it is now possible to track and audit how someone views and navigates the slide to derive at their diagnostic interpretation.[32-34] This has allowed investigators to examine the process by which pathologists arrive at a given diagnosis using a combination of their slide exploration strategy (digitally recorded slide navigation with mapped search patterns), perceptual information gathering, and cognitive decision making.[35] Examining eye movements using eye-tracking cameras while viewing slides can provide further information about a pathologists' decision-making process. Feedback with such data provided to trainees can help improve their diagnostic skills. Software can track how one views a slide in four dimensions (*x* and *y* axes, time, and zoom), areas studied for given periods of time, and include the users' comments about the areas viewed. These systems have been used to compare trainees to expert pathologists. For example, we now know that while trained pathologists spend significantly less time than residents scanning virtual slides, they take more time than trainees to dwell on locations they subsequently chose for zooming. Also, unlike residents, pathologists frequently select areas for viewing at higher magnification outside of areas of foveal (central) vision.

Researchers have recognized that there are two types of slide exploration strategy: (1) a focused and efficient search, observed when the final diagnosis was correct; and (2) a more dispersed, time-consuming strategy, observed when the final diagnosis was incorrect.[35] This difference suggests that initial interpretation of a slide may bias further slide exploration. WSI tracking tools have also been particularly helpful with respect to tutoring and assessing trainees. For example, the educational system SlideTutor (http://www.slidetutor.upmc.edu/) provides a virtual apprenticeship designed to monitor the users work, intervenes with helpful advice when they make errors, and adapts its interaction to fit their specific educational needs. Studies have shown that using SlideTutor, students are able to improve their diagnostic and reporting performance by a factor of four after as little as 4 h of use of the system.[36]

## E-LEARNING AND VIRTUAL WORKSHOPS

The field of pathology in today's era of technological advances has increasingly made use of e-learning (i.e., electronically supported learning). Web 2.0 technologies have greatly improved out-of-classroom and in-classroom educational experiences. The virtual learning environment supports distance, flexible, and cost-effective learning. E-learning pathology applications today frequently include WSI media content. Virtual workshops are becoming a popular mechanism to provide continuing medical education, particularly since they offer participants a cheaper option than traveling to meetings and the fact that an interactive WSI augments problem-oriented teaching. Prior to attending a meeting, participants used to receive glass slides or kodachrome plastic projector slides beforehand about the cases to be shown. Today, posting digitized slides online has greatly lowered the cost for organizers and improved the quality of material being shared. There are several online educational slide sharing services (e.g., PathXchange) available, and public websites (e.g., vMic Pathorama, Slide2Go) that give users access to online virtual teaching sets.[37] Virtual atlases that promote web-based learning are also now offered by several societies including the Unites States and Canadian Academy of Pathology (USCAP), American Society of Cytopathology (ASC), and International Academy of Cytopathology (IAC).[38] The USCAP's online academy have a virtual slide box (WSI slide library of several hundred virtual slides categorized by organ system) and The Juan Rosai Collection of surgical pathology seminars (includes WSI of approximately 20,000 cases from 1945 onwards). The website for the Pathological Society of Great Britain and Ireland also contain virtual slides. There are also some journals, such as the International Journal of Surgical

Pathology[39] and Diagnostic Pathology, that have added access for readers to a WSI that accompanies an article (e.g., case reports). It is anticipated that in the near future textbooks too will begin to incorporate digitized slides for readers to access. Content creation and delivery are already available for mobile computers such as the iPad.[40]

## TUMOR BOARDS

Most hospitals routinely have tumor boards where clinicians meet for multi-disciplinary case presentations. Presenting the pathology findings in these cases is often a significant component of tumor board presentations. WSI has been successfully used for this purpose at several institutional tumor boards.[41,42] The entire histologic glass slide or all slides belonging to a case get digitized and presented in front of a live audience. The evidence to date has been positive, and apart from the novelty factor WSI presentations proved to be of a greater educational value for clinicians. For pathologists, the use of WSI at such board meetings involves less preparation time than photographing cases. In one report, pathologists saved an average of 1 h per week in preparing for these meetings, thus cutting their time by 50%.[43] Moreover, WSI permits real-time flexibility, making it easy to add on cases and show cases side-by-side. Also, because presenters have access to the entire slide, they are better equipped to address "on-the-spot" questions.

## PROFICIENCY TESTING

WSI are being used for performance improvement programs and have significant potential to be used in gynecologic proficiency testing. Using digital image technology (Digital Scope tool that uses the free Microsoft plug-in Silverlight) to simulate the use of a microscope in evaluating slides, the College of American Pathologists (CAP) now offer their Performance Improvement Program in Surgical Pathology (PIP) online. Web-based case review allows many users to simultaneously access digitized slides and promote timely evaluation. It is reassuring to see that pathologist's diagnostic scores do not appear to be compromised by converting to WSI.[44] As recertification in pathology becomes more important it is anticipated that WSI will be increasingly employed in some Maintenance of Certification programs. In cytopathology, the current gold standard for performing proficiency testing is manual screening or review of glass slides. Nevertheless, digital imaging is being recommended by several investigators.[45-48] As WSI would certainly be more cost effective and has improved standardization for proficiency testing, it has been shown that in order for such digital programs to work, prior training of participants on the technology is required. Complaints to date are related mainly to the lengthy time experienced by users to examine digital images. Some may also argue that WSI, by not reflecting real-world experience where cytologists screen and interpret material on glass slides, is not a true test of proficiency.

## MEDICAL EDUCATION AND EXAMINATIONS

In the context of standardized curricula and a growing number of medical students, new strategies have been employed to improve the student experience of learning pathology. As already alluded to before, the most significant technological innovation has been the introduction of WSI at medical universities around the world for web-based studies. At the Poznan University of Medical Sciences in Poland, investigators developed and evaluated a user-friendly online interactive teaching and examination platform called WebMicroscope to facilitate dental student access to pathology course material, including histological laboratory specimens. WebMicroscope using WSI as an Enhanced Compression Wavelet (ECW) file format, pioneered in aerial and satellite imagery, offers an alternative web-based method of teaching pathology.[49] The WebMicroscope server is used to host, manage, and deliver WSI-based digital slides to students during their laboratory practicals and examination. In this context, a dedicated web viewer interacts with an image server that serves out appropriate regions of the slide image. In this way, students can view digitized slides in real time without the need to download the entire image. The client module is based on a native, downloadable browser plug-in, or java script-based dynamic HTML. In the latter case, it does not require any specific downloads to the client workstation. Abandoning the use of conventional light microscopes and glass slides for training since 2005, educators at this university in Poland decided to rely on WebMicroscope to teach pathology to dental students. WSI can be visualized at any magnification and permits navigation in the *x-y* axis, which perfectly imitates using a traditional microscope and glass slide. The WebMicroscope allows students to independently explore the entire histological slide, as well as control the content and its rhythm of delivery. This interactive technology made microscopic laboratory studies in pathology more efficient and teaching resources more portable, independent of class schedules [Figure 1].[50] Although the initial equipment and software cost for creating virtual slides are high, this new technology has the potential to revolutionize the way individuals teach and learn from microscopic images. For teachers, using virtual microscopy allows one to derive more information about how students learn pathology, how instructive the laboratory practicals are, and which slides are of real didactic value for the students.

Examinations that apply WSI technology online require more sophisticated test management software. In the past, Poznan University faculty employed an examination

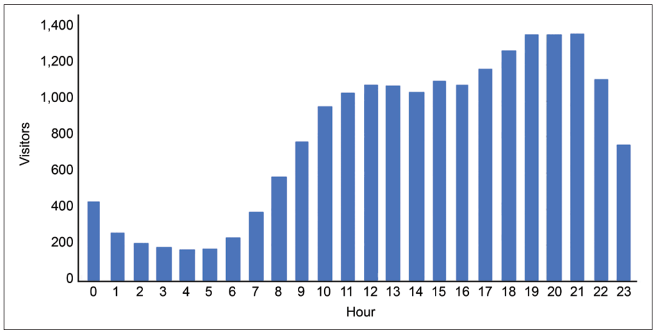


**Figure 1: Students slide views in a day are shown per hour. Self-study time is evident**

system that was restricted to the use of standard static images. This was technically less challenging and followed a routine that was similar to that of conventional paper-based examinations.[51,52] WSI is more demanding as it requires the use of innovative image serving and viewing software, and because of the enormous size of the images, a storage facility capable of storing hundreds of gigabytes. However, the effort is worthy because WSI reflects better current laboratory activities. Allowing many students to take their examinations using virtual slides poses a challenge, with many potential bottlenecks as network demand increases with multiple simultaneous users [Figure 2]. To overcome this WSI were stored on independent servers. Serving these slides as part of the practical examination was bandwidth and server intense, particularly if the image latency was to be kept to a minimum with many students accessing the images simultaneously. A successful examination system requires multiple image servers which are carefully load balanced. This implies that when one server gets busy due to user activity, another server takes over and provides the services that are being requested. For the practical pathology examination offered at Poznan University, multiple image servers were operated in tandem,[53] allowing the processing of multiple requests for images each second without students complaining of any delays during their exam. Using WSI allows students to still ask questions without specifically highlighting the key diagnostic features as it must be done in the field of view of a static image. Even if a question refers to a specific field of view, the student can zoom out and see that field in the overall context of the slide. This contextual information, readily available in WSI, is essential to teach students both how to find the key diagnostic fields within a whole slide and to perceive how a diagnostic field fits into the surrounding non-diagnostic slide context.

Each practical exam consisted of 50 multiple-choice questions per student. Every question was displayed together with the WSI and students had to provide an answer based on their interpretation of this slide. The scope of WSI offered was broad, designed to include all WSI used during the laboratory practicals. Questions and WSI were presented in a different order to every student.

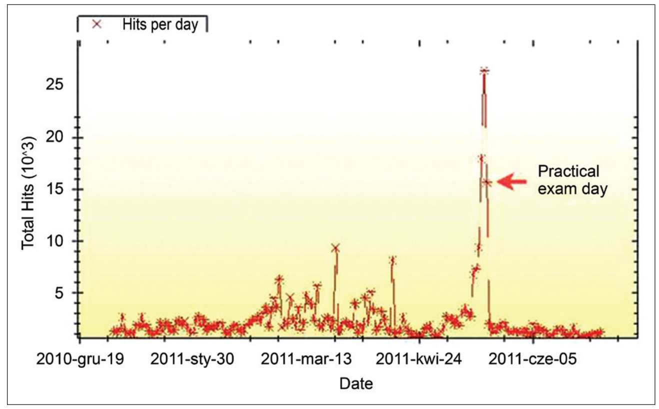


**Figure 2: Cumulative graph of total hits per day during the period of January-July 2011 (oral pathology course)**

**Table 2: Students' practical exam performance using whole slide images (WSI) from 2006 to 2012**

| Year | Number of students | Number of questions/ student | Number of WSI | Correct students' answers | | | |
|---|---|---|---|---|---|---|---|
| | | | | Avg % | SD % | Min % | Max % |
| 2006 | 8* | 50 | 50 | 98.0 | 2.7 | 88 | 100 |
| 2007 | 84 | 64 | 64 | 97.2 | 4.7 | 73 | 100 |
| 2008 | 92 | 50 | 81 | 92.1 | 4.4 | 76 | 100 |
| 2009 | 96 | 50 | 82 | 93.8 | 5.6 | 78 | 100 |
| 2010 | 101 | 50 | 103 | 93.4 | 8.0 | 44 | 100 |
| 2011 | 83 | 50 | 125 | 93.9 | 5.2 | 74 | 100 |
| 2012 | 85 | 50 | 125 | 91.3 | 7.4 | 62 | 100 |

*Only one group of students in academic year 2005-2006 participated in WSI based learning (Avg: Average, SD: Standard deviation, Min: Minimum, Max: Maximum)

For the examination in the academic years 2008-2012, 50% of randomly rotated WSI were used to prevent "fossilization" of the students. These rotations did not influence the performance of the students. Students were given unlimited time to complete the exam. There was no time limit per slide either. Students could also view slides or answer questions in any order. All sessions of the practical exam using WSI took place in a secure location and were continuously proctored by teaching assistants. All examinations were graded using the same scale. Participants were all dental students enrolled in the pathology course between 2005 and 2012. Students were also required to complete a short anonymous survey at the time of the exam. More than 90% of responders found the WSI-based laboratory practicals and the subsequent WSI practical exam to be useful and helpful in improving their understanding of pathology. For their practical examinations students got 94-98% of their questions correct [Table 2]. This provides clear evidence of the learning benefits derived from using WSI. This seven-year experience in developing and using an examination system that applies the WebMicroscope platform with WSI indicates that despite widely available self-study possibilities, good teachers still create substantial value and practical exam scores were helpful in identifying such teachers.[54] These findings signify that the WebMicroscope platform using WSI is a promising tool for teaching and creating examinations in pathology.

## CONCLUSION

It is obvious that in many countries, settings, and classrooms WSI has now replaced conventional microscopes. WSI is being successfully employed for undergraduate and graduate education, training of pathology residents, as an educational tool in allied pathology schools, for virtual tracking and tutoring, tele-conferencing, e-learning, virtual workshops, at tumor boards, with interactive publications, and on examinations. WSI supports flexible and cost-effective distant learning and augments problem-oriented teaching, competency evaluation, and proficiency testing. Newer human-computer interfaces such as touchscreen displays and tablet technology have proved to be especially beneficial for education using WSI. However, the current limitation with WSI is the length of time it takes to view slides. Not surprisingly, most users are not satisfied with the viewing speeds of available systems. This is partly related to the fact that large image files are difficult to manage. For example, the average size of a file for a WSI scanned at ×40 magnification (0.23 um/pixel) is 1-50 GB/image. The size would be even larger for a whole case that contains many slides. Poor PC performance, along with network limitations, can greatly hinder continuous viewing of a WSI. Table 3 lists some of the features a pathologist needs when viewing WSI for different activities, and potential solutions for a graphical user interface (GUI) to address them.[55]

Investigators at the Massachusetts General Hospital in Boston evaluated a novel WSI viewing station and tool that focused primarily on speed.[52] The prototype WSI viewer they developed was based on Sony's PlayStation®3 (PS3®) game console with wireless controllers. The central processing unit in the PS3®, called a Cell Broadband Engine™ (Cell BE), is capable of supporting a wide range of applications that require real-time processing. The Cell BE provides nearly full-speed memory access while simultaneously carrying out parallel computation. Moreover, the ergonomic buttons on these wireless controllers offer a unique solution for a WSI-human interface to navigate virtual slides. Using this PS3® viewer, these researchers showed that most operations were reflected on a display in about one-sixtieth of a second. Pathologists were able to comfortably operate this user-friendly WSI system after minimal (0-15 min) training. Interestingly, those participants who regularly played games at home required even less (0-3 min) training. In summary, most pathologists were satisfied with the functionality, usability, and speed of this WSI system. The most difficult situation encountered was simulating diagnostic sign-out. Nevertheless, the ultra-high speed achieved by adapting the Sony PlayStation®3 into a WSI viewing system is consistent with what would be needed to use WSI in daily practice.

Finally, as the authors are clearly the proponents of WSI for education and to some degree also for proficiency testing, in fairness this article addresses only a few of the barriers in utilizing WSI. Indeed, there are other sizeable barriers that still need to be overcome, such as the cost of WSI equipment which includes the scanner, software licenses, server hardware, storage, and information technology support on an ongoing basis. For many institutions, the expense of implementing all of the aforementioned components of a WSI system is presently far higher than the cost of a microscope, which may be negligible in many laboratories because they already have them. Also, Z-plane issues which are important

**Table 3: Requirements and solutions for whole slide images viewing systems (modified from reference[55])**

| WSI activity | Optimal features | GUI design |
|---|---|---|
| Signing out cases | View all slides | Move quickly between slides |
| | Navigate the entire slide | Easily navigate the entire image |
| | Change magnification frequently | Rapidly adjust magnification |
| | Integration with the laboratory information system (LIS) | Mark off reviewed slides |
| | Compare with stained slides | Simultaneously view multiple images |
| Consensus conference | View selected slides | Quickly select slides or thumbnails |
| | Use of pointers | Easy use of pointers |
| | Revisit areas of interest | Marking areas of interest to revisit |
| | Sharing quality images | Good image quality |
| | Different operators | Easily switch between operators |
| Slide seminar presentation | Intuitive controls | Simple to use |
| | Operation by every speaker | Available for all operators to use |
| | Ability to view slides in any chosen order | Quickly move between selected slides |

GUI: Graphical user interface

for depth of focus when evaluating cytology glass slides and blood smears need to be considered. This seems to be a stumbling block for many when they transit from glass to WSI.[56] If trainees are only exposed to WSI, is there any possibility that we could be doing our patients a disservice because these future graduates may not be familiar with the advantages of focus planes? Moreover, WSI is currently being used mainly in academic centers. Therefore, will such WSI-trained professionals be ill-equipped for community practice where glass slides are likely to be still used for some time. Clearly, studies to determine the impact of training pathologists and cytotechnologists without exposure to actual glass slides are needed. Further investigation is also necessary to develop superior WSI applications that better support education.

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