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Research Article

Web-based oil immersion whole slide imaging increases efficiency and clinical team satisfaction in hematopathology tumor board

Zhongchuan Will Chen, Jessica Kohan, Sherrie L. Perkins, Jerry W. Hussong, Mohamed E. Salama

Division of Hematopathology, Department of Pathology, ARUP Laboratories, University of Utah, Salt Lake City, Utah, US

E-mail: *Mohamed E. Salama - mohamed.salama@path.utah.edu
*Corresponding author

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Abstract

Background: Whole slide imaging (WSI) is widely used for education and research, but is increasingly being used to streamline clinical workflow. We present our experience with regard to satisfaction and time utilization using oil immersion WSI for presentation of blood/marrow aspirate smears, core biopsies, and tissue sections in hematology/oncology tumor board/treatment planning conferences (TPC). **Methods:** Lymph nodes and bone marrow core biopsies were scanned at ×20 magnification and blood/marrow smears at 83X under oil immersion and uploaded to an online library with areas of interest to be displayed annotated digitally via web browser. Pathologist time required to prepare slides for scanning was compared to that required to prepare for microscope projection (MP). Time required to present cases during TPC was also compared. A 10-point evaluation survey was used to assess clinician satisfaction with each presentation method. **Results:** There was no significant difference in hematopathologist preparation time between WSI and MP. However, presentation time was significantly less for WSI compared to MP as selection and annotation of slides was done prior to TPC with WSI, enabling more efficient use of TPC presentation time. Survey results showed a significant increase in satisfaction by clinical attendees with regard to image quality, efficiency of presentation of pertinent findings, aid in clinical decision-making, and overall satisfaction regarding pathology presentation. A majority of respondents also noted decreased motion sickness with WSI. **Conclusions:** Whole slide imaging, particularly with the ability to use oil scanning, provides higher quality images compared to MP and significantly increases clinician satisfaction. WSI streamlines preparation for TPC by permitting prior slide selection, resulting in greater efficiency during TPC presentation.

Key words: Hematopathology, microscope projection, oil immersion, tumor board, whole slide imaging

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INTRODUCTION

Whole slide imaging (WSI) is a technology that is increasingly used in pathology for education and clinical applications such as telepathology, tumor board/treatment planning conference (TPC) presentation, and may even have utility in establishing primary diagnoses.[1] While there are anecdotal reports[2-4] of increased satisfaction associated with using WSI to present cases at TPC, objective

peer-reviewed studies measuring the perceived increased satisfaction or to define preparation time required to scan slides and annotate fields of interest for presentation at TPC are lacking. In addition, there have been no published data on experience in using WSI technology in hematology/oncology TPC in which detailed cytologic features of peripheral blood smears and bone marrow aspirates are often essential diagnostic features that need to be presented to the clinical audience. As such, peripheral blood and bone marrow aspirate smears are often displayed at high magnification under oil immersion, which adds a level of complexity and increased resources when translated to performing oil immersion-based WSI. In contrast, surgical pathology cases presented using WSI usually only requires ×20 and ×40 magnification scanning to be sufficient for most diagnostic and presentation purposes. Although there are several devices that use WSI technology in hematopathology, for instance CellaVision DM96 (CellaVision, Durham, NC, USA) and the Bloodhound Integrated Hematology System (Constitution Medical, Westborough, MA, USA), that combine automated smear preparation, cell counting and cell sorting, these instruments are used primarily as ancillary tools for rapid visualization and verification of blood differential counts rather than for acquisition of high quality WSI digital images for diagnostic use or presentation in TPC.

We recently developed a workflow that employs WSI in our weekly hematology/oncology TPC using oil immersion scanning for peripheral blood and bone marrow aspirate smears. Prior to implementing WSI, we used exclusively a microscope projection (MP) system for presenting cases at TPC. In this report, we share our experience with WSI in TPC presentation and attempt to objectively determine whether the use of WSI increases clinical team satisfaction and assess relevant time metrics of various components of WSI compared to a traditional presentation process.

METHODS

Cases were presented at TPC using two different methods: Traditional MP and WSI [Figure 1]. A 24 h cutoff prior to TPC presentation was requested for cases to be presented by WSI. Any case requested following this cutoff were presented using MP. As such, most TPC sessions contained presentations by both modalities. We also compared WSI to MP by surveying the clinical team regarding satisfaction with WSI compared to MP. In addition, the efficiency of both methods in terms of the time required of pathologists for preparation and presentation was compared. Two pathologists were involved in the preparation and presentation of cases included in this study.

Traditional Microscope Projection Method for Pathology Slide Presentation in Treatment Planning Conferences

The traditional MP method for showing cases at TPC involved a setup that included a 2 megapixel DP21 microscope camera (Olympus America, Center Valley, PA, USA) mounted on a BX41 microscope (Olympus America, Center Valley, PA, USA) with 2X, 4X, 10X, 20X, 40X, and 60X hi-dry objectives permanently located in the conference room. The camera was connected to a computer running Windows 7 with Olympus CellSens software (Olympus America, Center Valley, PA, USA) installed, allowing for display of the real-time image feed from the camera. The computer video output was in turn attached to a standard overhead VGA projector (Sony Corporation, New York, NY, USA). In this method, the pathologist was responsible for selecting the appropriate slides to show at TPC and physically carrying the slides to the TPC room to be presented [Figure 1].

Whole Slide Imaging Method for Pathology Slide Presentation in Treatment Planning Conferences

The WSI method involved the pathologist selecting slides for scanning and dotting the scanning areas before TPC. The slides were then picked up by WSI technicians dedicated to scanning slides for the department, although not exclusively for TPC. The technicians and scanners were located in the same building as the pathologist, and TPC cases received priority for scanning over other educational or research cases. Using the pinning tool in Aperio eSlide Manager (Leica Biosystems, Buffalo Grove, IL, USA), a US Health Insurance Portability and Accountability Act-compliant web-based server/viewer of scanned slides, the pathologist then annotated the appropriate fields in each case to be shown at TPC. Once in the TPC room, the pathologist logged into the eSlide Manager interface via a standard web browser (Internet Explorer, Google Chrome or Mozilla Firefox) and loaded the case to be presented. The previously annotated fields were then simply retrieved by moving through the pins and the selected fields were presented in the exact order and magnification originally intended [Figure 2].

Whole Slide Imaging Scanning Methodology and Timing

An Aperio XT slide scanner (Leica Biosystems, Buffalo Grove, IL, USA) was used to scan all tissue sections (everything apart from bone marrow aspirate smears and peripheral blood smears) at ×20 magnification without oil immersion, following manufacturer instructions. For 83X oil immersion scanning of bone marrow aspirates and peripheral blood smears, an Aperio CS-O scanner (Leica Biosystems, Buffalo Grove, IL, USA) was used. The scanning area for smears was usually 9 mm^2, but also ranged from 4 mm^2 to 81 mm^2. Most

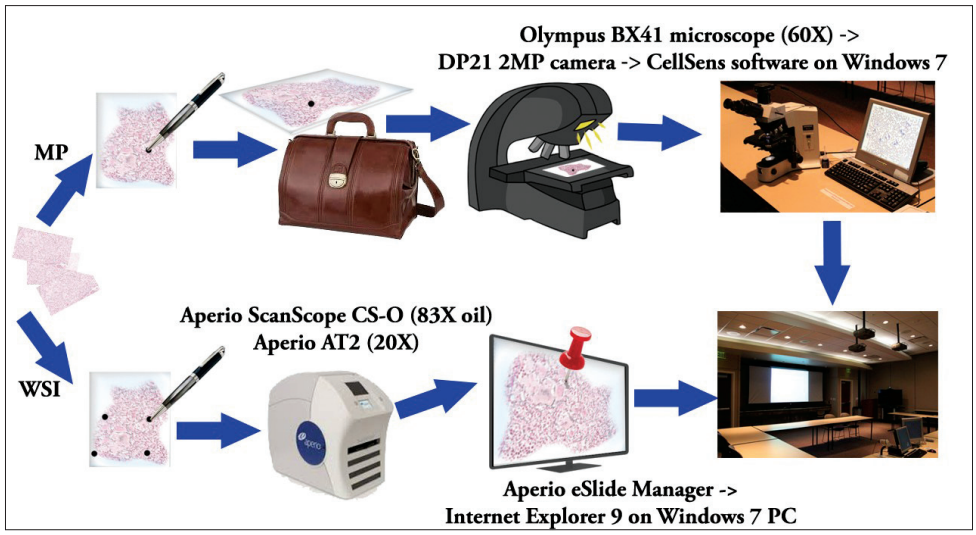

Figure 1: Schematic diagram illustrating workflow process for microscope projection (MP) and whole slide imaging (WSI) tumor board presentation methods. In MP, the slide is dotted to indicate fields of interest; it is then placed on a separate slide tray and physically transported to the conference room. The projection system consists of an Olympus BX41 microscope with a DP21 2 megapixel camera which is connected to a computer running CellSens software that captures the live video feed from the camera. With WSI, the fields of interest to be scanned are delineated using 4 dots. The slides are then scanned using an Aperio ScanScope CS-O scanner to scan at ×83 magnification under oil immersion, or using the AT2 scanner at ×20 magnification. The scanned slides are uploaded onto eSlide Manager and the fields to be displayed at treatment planning conferences are preannotated using the pinning function. At TB, eSlide Manager is opened via Internet Explorer. In both the MP and WSI methods, the computer screen is projected for viewing by attendees using a standard overhead VGA video projector

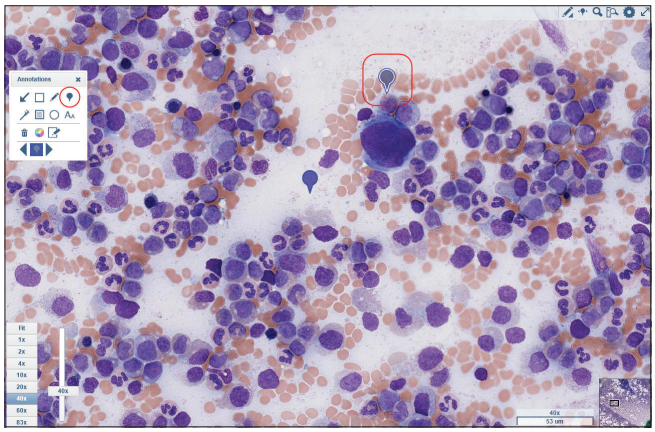

Figure 2: Screenshot of pinning tool in eSlide Manager (with pinning tool and placed pin circled in red). An animated screen capture video sequence illustrating the pinning process may be viewed at http://youtu.be/N988KAmCWgs. An animation illustrating the process for retrieval and display of previously pinned slides may be viewed at http://youtu.be/yy7zTHSv50k

slides were adequately represented with a single selected area, but occasionally several areas on the same slide were selected for scanning to show salient features that could not be captured in one small field. The scanning process generally followed manufacturer instructions, apart from added steps to enhance image quality and focus. These steps comprised manually adding focus points, starting at a focus offset of −0.2 on a 4 mm^2 area. The scanned image was reviewed by the technician for proper focus, and the focus offset was increased in increments of 0.2 until the image with the most optimal focus was captured. The entire selected area was then scanned using the optimal focus offset. The offset varied between slides due to differing thickness of mounting media and coverslips. The final scanned images from both scanners were then uploaded to Aperio eSlide Manager, grouped according to case accession number. Average timings for scanning were obtained on a tray of 20 slides for the 20X scanner and separate timings for scanning of different slide areas was obtained for the oil immersion scans based on 20 slides.

Clinical Team Satisfaction Evaluation

To assess clinical team satisfaction, a survey [Figure 3] was sent to clinical attendees at TPC, which included attending oncologists, fellows, residents, and oncology nurses/physician assistants.

Pathologist Time Requirement / Process Efficiency

To objectively determine the time resources needed for each method, all cases presented since the introduction of WSI were timed using a stopwatch for both preparation time and presentation time. Preparation time was defined for MP as from the instant the pathologist picked up the first slide for preview prior to TPC to the placement of all selected slides on a separate slide tray to be presented at TPC. For the WSI method, preparation time consisted of two separate times: time from picking up the first slide to placing all appropriately dotted slides in the tray for scanning, then the instant eSlide Manager was loaded to the moment all appropriate annotations with the pin tool

was completed. Time required for scanning was recorded separately as noted above.

Preparation times were compared between methods based on different denominators including slides selected, total number of slides in cases to be presented and total number of cases.

Presentation time was defined for both methods as the time required for the pathologist to present the pathologic findings. This did not include the time required to answer questions from the clinical team following presentation of findings. The denominator was the number of slides presented.

Percentage of Slides Presented Using Whole Slide Imaging

The numbers of cases presented by WSI and MP were noted over the course of 13 TPC sessions, along with reasons and the number of occurrences in which cases were presented using MP instead of WSI. Furthermore, technical difficulties with both MP and WSI methods were noted descriptively when they occurred.

Statistical Analysis

Statistical analysis was performed using the Student's *t*-test with SAS version 9.3 software (SAS Institute, Cary, NC, USA).

RESULTS

Over the course of 13 TPC sessions, 59 cases were requested. Of these, 48 cases (81%) were successfully scanned and presented using WSI. Nine cases (15%) were unable to be presented using WSI as they were late additions past the cutoff time. Two cases (3%) were unable to be presented due to scanner malfunction that required vendor servicing.

Satisfaction Survey

A total of 12 responses were received from 16 surveyed clinical attendees (75% response rate), who all reported significantly increased satisfaction with WSI in all categories evaluated on the survey ($P < 0.01$ in all categories) [Figure 4]. Furthermore, free-text feedback, received from attending hematologists, described overwhelmingly positive comments regarding WSI ("new system") compared to MP ("old method"), including "the new system is superb: High resolution, focus on important areas of the slides, much faster and much more efficient than the old method. It will allow teleconferencing with outside doctors and as such promote outreach," "The new system is awesome (the pathologist) was able to focus more on describing the slide, diagnostic work up (immunohistochemistry, etc.) rather than trying to find the area of interest in the slide looking into the microscope. I am very impressed with the new system." Examples of screenshots comparing the image quality of WSI and MP for various slide types and tissues are shown in Figures 5-7. Selected photographs of the actual projected images on the overhead projector are shown in Figures 8-10. Seven respondents (58%) noted decreased motion sickness with WSI compared to MP, while five respondents (42%) reported not experiencing motion sickness with either modality.

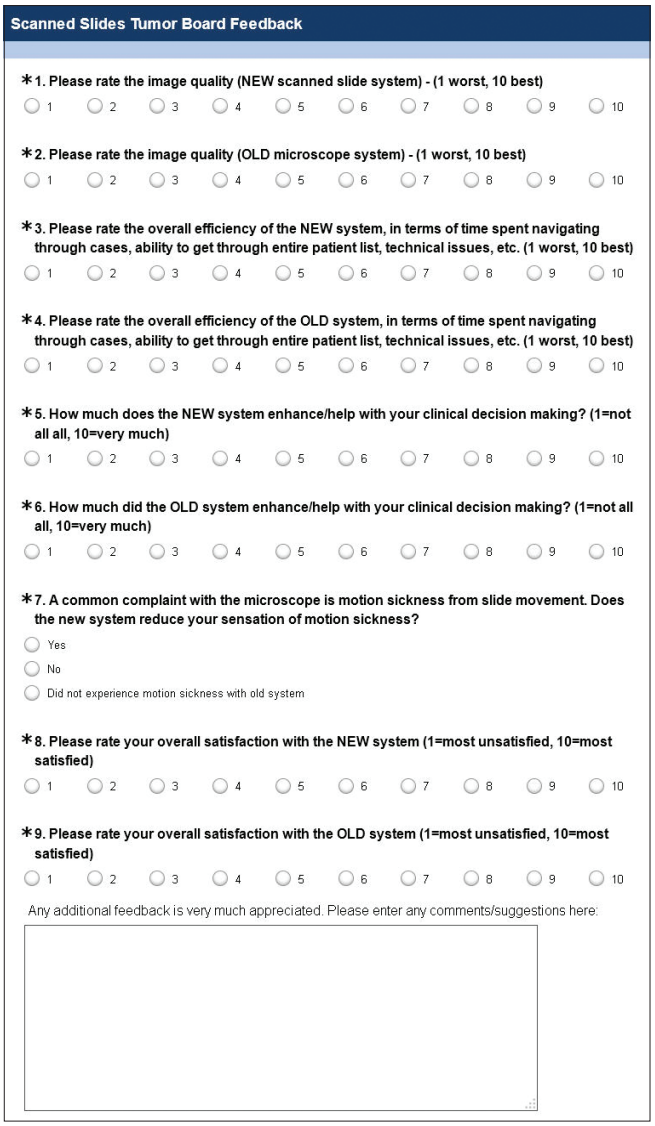

Figure 3: Survey form used to assess clinical team satisfaction

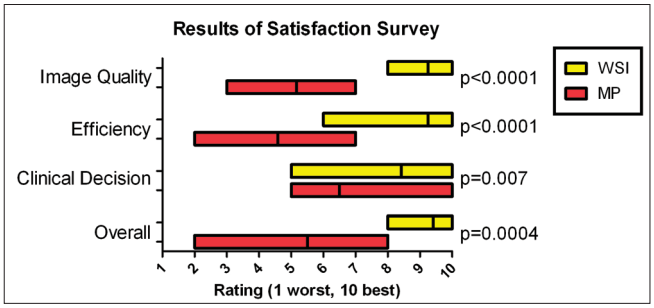

Figure 4: Results of satisfaction survey (bars represent minimum, mean, and maximum)

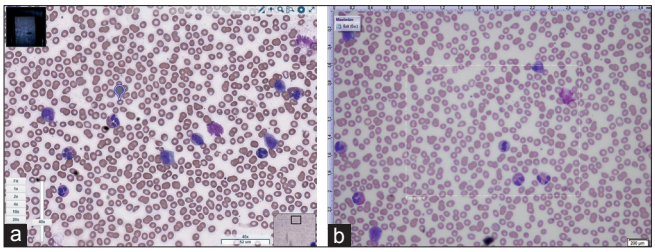

Figure 5: Screenshots of peripheral blood smear as displayed on computer monitor at ×40 magnification. (a) Whole slide imaging, (b) microscope projection

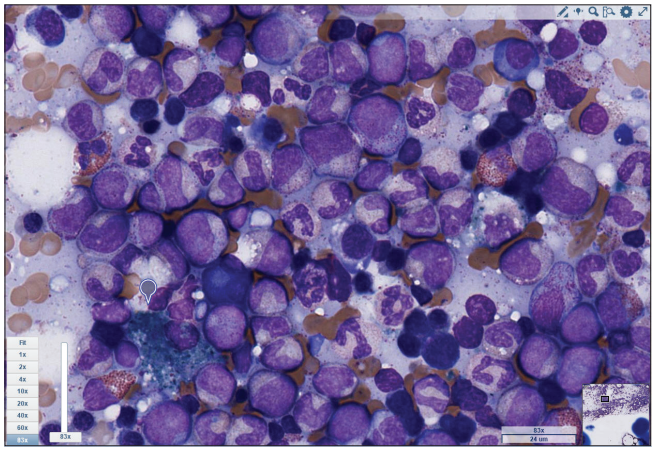

Figure 7: Screenshot of bone marrow aspirate smear scanned at ×83 magnification using oil immersion whole slide imaging as displayed on computer monitor

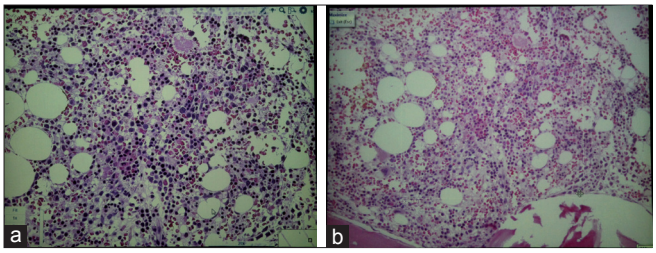

Figure 9: Photographs of projection screen showing projected image of H&E bone marrow core biopsy section at ×20 magnification using (a) whole slide imaging, and (b) microscope projection. Both photographs were taken under identical lighting conditions and with identical camera settings

Preparation and Presentation Times

Preparation and presentation times were available for a subset of the cases (41 of 59; 69%) presented using WSI. There was no significant difference in preparation time for both modalities across all denominators [Table 1]. However, the presentation time required for WSI (mean: 0.45 min/slide) was significantly less ($P = 0.03$) than that for MP (mean: 0.77 min/slide) [Table 2]. In our experience, prior to implementing WSI, many cases were unable to be partially or fully presented using MP due to lack of time. In fact, at the first TPC session in which the WSI system was implemented, one clinician remarked that "this is the first time we were able to go through all cases and finish on time!"

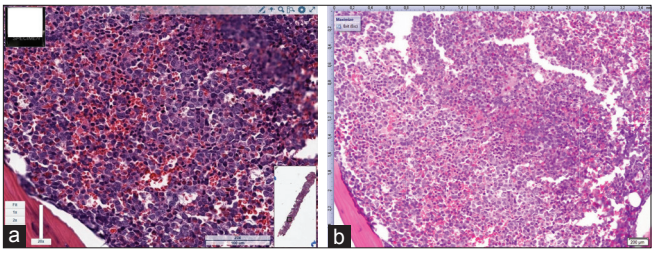

Figure 6: Screenshots of H&E bone marrow core biopsy section as displayed on computer monitor at ×20 magnification. (a) Whole slide imaging, (b) microscope projection

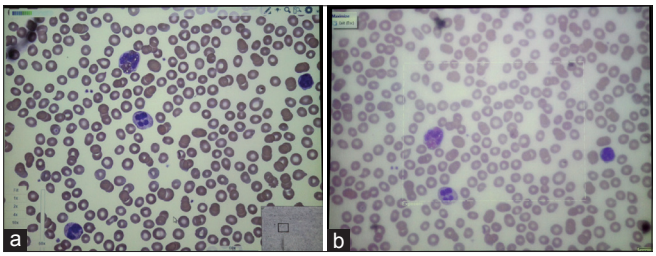

Figure 8: Photographs of projection screen showing projected image of peripheral blood smear at ×60 magnification using (a) whole slide imaging, and (b) microscope projection. Both photographs were taken under identical lighting conditions and with identical camera settings

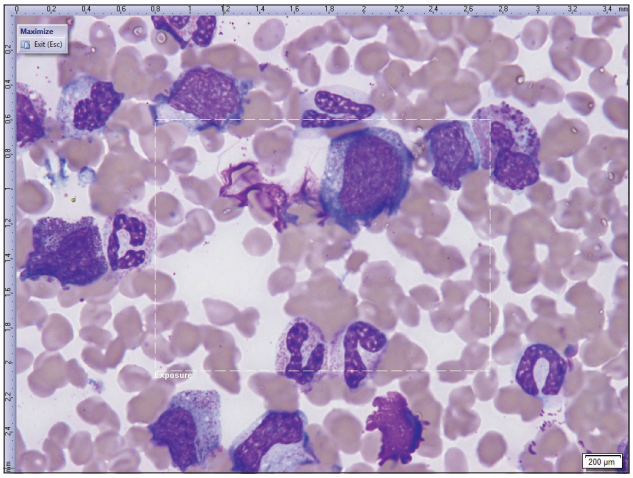

Figure 10: Screenshot of bone marrow aspirate under 100X oil immersion microscope projection as displayed on computer monitor

Scanning time

Scanning time on the automated Aperio AT2 scanner (Leica Biosystems, Buffalo Grove, IL, USA) for 20X slides required 45 min for a tray of 20 slides, or an average of 2.25 min/slide. Scanning time for 83X oil immersion was considerably longer due to the need for greater manual intervention, and was based on the area scanned [Table 3], with larger areas requiring more time. Of note, the 2 mm × 2 mm scanning time included the calibration time required for offset focusing of the slide, and this time was an integral component of the times for all larger scanned areas. The average "hands-on" time required of a technician for 20X automated scanning was

Table 1: Preparation time comparison between modalities according to various denominators

Parameter	MP	WSI (total time)	WSI (pre-scan slide selection/ dotting time)	WSI (post-scan eSlide manager annotation time)
Cases presented	19	22		
Slides (selected/total)	71/188	84/196		
Preparation time/presented slides in minutes: Mean (range)	1.39 (0.26-5.0)	1.14 (0.80-1.97)	0.49 (0.45-0.58)	0.65 (0.36-1.47)
Preparation time/total number of slides in minutes: Mean (range)	0.32 (0.13-0.83)	0.51 (0.39-0.72)	0.23 (0.17-0.30)	0.28 (0.19-0.53)
Prep time/number of cases in minutes: Mean (range)	2.64 (1.03-6.67)	3.85 (2.32-4.85)	1.77 (1.0-2.48)	2.08 (1.0-2.94)

WSI: Whole slide imaging, MP: Microscope projection

Table 2: Presentation time comparison between modalities

Parameter	MP	WSI
Total slides presented	110	135
Slides presented per TPC: Mean (range)	12.2 (4-42)	13.5 (4-25)
Total pathology presentation time per TPC session in minutes: Mean (range)	7.74 (1.85-20.67)	5.97 (1.17-12.07)
Presentation time/presented slides in minutes: Mean (range) (P=0.03; Student's t-test)	0.77 (0.37-1.31)	0.45 (0.29-0.53)

WSI: Whole slide imaging, MP: Microscope projection, TPC: Treatment planning conferences

Table 3: 83X oil immersion scanning times in minutes

Area	Preparation/ offset time	Scan time	Total time
2 mm×2 mm	3.9	4.5	8.4
5 mm×5 mm	3.9	7.1	11
7 mm×7 mm	3.9	9.6	13.5
9 mm×9 mm	3.9	12.7	16.6

0.54 min/slide, which included wiping, loading, taking snapshots, and naming/assigning slides. The technician "hands-on" time to scan a slide under 83X oil immersion ranged from 8.4 to 16.6 min, depending on the scanning area which ranged from 4 mm^2 to 81 mm^2 [Table 3]. The technician could not leave the oil immersion scanner unattended during the entire scanning process which included wiping, loading, depth of field adjustment, taking snapshots, and naming/assigning slides. As a typical bone marrow case generally consisted of one peripheral blood smear and one bone marrow aspirate smear to be scanned at 83X with a 4 mm^2 scanning area, and one core biopsy slide to be scanned at 20X, the overall scanning time for an average bone marrow case was approximately 20 min, with the technician "hands-on" time representing approximately 17 min. A typical tissue or lymph node case consisted of at least 4 slides to be scanned at 20X, but often had greater numbers of slides due to immunohistochemistry slides. The overall scanning time for an average case to be scanned entirely at 20X varied with the number of slides, but the "hands-on" time required of the technician for a tray of 20 slides usually did not exceed 10.8 min (20 slides × 0.54 min) as the technician could leave the AT2 scanner unattended once the automated scanning routine was initiated.

Technical Difficulties with Microscope Projection and Whole Slide Imaging During Treatment Planning Conferences

The problems with the MP system included loss of connection between camera and the computer software, the computer image capture software not being able to load, or the high-powered oil immersion objectives not being able to project properly through the camera. In each of these cases, the impact was major with cases not being able to be presented. If technical support was able to repair these issues during the TPC, it would result in a delay that prevented pathology findings from being presented.

The main problems with the WSI system included not being able to load the internet browser due to malware on a computer in the conference room, or a slow wired internet connection. However, the impact was usually none or at most moderate, since we could switch to any other computer in the room that could load the internet browser. A laptop computer connected to wireless internet was brought to TPC to be connected to the projector as a backup in the event all computers in the conference room failed. Occasionally, the eSlide Manager Server connection was slow, which mostly delayed the viewing of each slide by a few seconds, but was resolved by remotely rebooting the eSlide Manager server. The difficulties encountered with WSI only slightly delayed, but never completely prevented presentation of pathology findings, whereas defective software connection between the microscope camera and computer occasionally completely prevented presentation using MP.

DISCUSSION

Our study is the first to objectively compare WSI to a traditional method of TPC presentation. It is also unique

for using oil immersion scanning to scan blood/marrow smears at high power.

In our study, WSI generally performed well in every aspect. Although WSI required slightly more time from pathologists to dot each slide for scanning and then annotate fields in eSlide Manager with the pin tool, there was no statistically significant difference in the total time spent by the pathologist preparing for TPC. More importantly, WSI allowed for more efficient use of presentation time during the TPC itself, allowing for more cases to be accommodated and completely presented. In particular, the pinning tool function in eSlide Manager allowed for rapid transition between fields of interest in the virtual slides (screen capture videos demonstrating pinning function available at http://tinyurl.com/WSIpinning), eliminating considerable time wasted switching slides (particularly when multiple special stains or immunoperoxidase staining slides were presented) and searching for the field of interest in the MP system, which also contributed to reduction of motion sickness. In addition, many tabs in the web browser can be preloaded with all the cases to be presented in the TPC session, eliminating the need to waste time to switch back to the master case accession list to search for the next case to be presented.

Both pathologists involved in preparation and presentation of cases in this study are recent graduates who are very computer-literate but whose exposure to WSI was limited to end use of scanned virtual slides in examinations or on educational websites. Neither had used WSI for TPC presentation nor had any experience with eSlide Manager prior to this study. The training time for demonstrating the entire process to the pathologists was approximately 30 min. Thereafter, no further training was required apart from minimal explanations for minor updates to the eSlide Manager interface.

Despite the added cost and additional scanning time required for WSI, we feel the advantages of WSI significantly outweigh the greater resources needed. Certainly, it would be cost-prohibitive for a pathology department to deploy WSI solely for TPC presentation, but TPC presentation is a significant incremental benefit once added to a preexisting WSI system. First, clinical team satisfaction, in particular with regard to image quality, was much higher. This is not only due to the much higher resolution of the scanned slides compared to MP [Figures 5 and 6], but also due to the ability to scan slides under oil immersion at 83X [Figure 7], allowing for clear images of bone marrow aspirate slides. As the microscope in the conference room only had a 60X hi-dry objective, high definition or clear high power views of bone marrow aspirates were not possible with MP without the inconvenience of bringing a 100X oil immersion objective and switching it with another objective on the microscope prior to TPC. Unless a particular finding absolutely necessitated projection using the 100X oil objective, changing objectives was avoided due to the trouble and risk of damage or oil contamination of other objectives from excessive manipulation. In general, in our experience, 100X oil immersion generated the best image quality out of all the lenses on the MP system [Figure 10], almost matching the quality of 83X WSI images, but the inconvenience of using 100X MP in our setting precluded its routine use. As such, its lack of routine use is a limitation of our study, as satisfaction survey results did not take into account comparison of 100X oil immersion MP to 83X oil immersion WSI. Nevertheless, throughout several TPC sessions, we were able to demonstrate findings in many cases using WSI with oil immersion scanning that could not be shown using MP due to not anticipating the need to bring the oil immersion objective or the actual immersion oil. More importantly, during our study period, there were no cases that required demonstration with MP due to an inability to show all findings by WSI.

Second, the higher efficiency of WSI and the pinning feature allowed for rapid movement between images and cases resulted in reduced presentation time in TPC session, which indirectly results in savings to the healthcare system primarily as healthcare providers including pathologists, clinicians, and nurses are potentially able to attend to other duties should TPC finish earlier due to the shorter presentation time. As an example, taking into account that 13.5 slides on average were presented in each TPC, and that WSI resulted in an average presentation time savings of 0.32 min/slide compared to MP [Table 2], the overall time saved per TPC session using WSI is estimated to be 4.3 min. In our experience, 12 clinicians and 5 pathologists on average attend each TPC session, which translates into 73 physician-minutes saved per TPC by using WSI instead of MP. If we estimate that 7.5 of 13.5 slides are scanned at 20X and the remaining 6 slides at 83X with a 4 mm^2 scanning area, the total technician "hands-on" time per TPC would amount to approximately 54 min. Thus, the amount of technician-minutes spent per TPC session translates into a greater amount of physician-minutes saved, which achieves significant costs savings due to higher remuneration for physicians compared to technicians.

Third, the ability to provide redundancy with access of eSlide Manager from any computer with an internet connection and web browser allowed for virtually guaranteed capability to show TPC cases, even when one computer had technical difficulties, unlike with MP systems that cannot be easily relocated to another computer in the event of failure due to complex hardware connections, driver and software installation requirements that cannot be performed quickly during TPC. For further redundancy in the WSI system, a laptop containing the scanned slides copied to the local hard drive eliminated any issues with inability to access eSlide Manager due to internet connectivity problems.

CONCLUSIONS

Whole slide imaging brings about significant potential and future developments[1,5,6] not feasible with MP, including the possibility of joining TPC by remotely located clinicians in the community to maintain follow-up and continuity of care for patients that they may have referred to a tertiary cancer center or to claim continuing medical education credits, or expert consultation on scanned slides by remotely located pathologists.[7,8] WSI also allows for long-term archival of TPC cases slides for education[9-16] and research, and potential cost savings in the future due to decreasing digital storage costs compared to increasing real estate costs needed for physical facilities to store glass slides.

In summary, using WSI for TPC presentation is a value-added benefit to a preexisting WSI system that results in increased clinical team satisfaction and more efficient use of TPC time.

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