ORIGINAL ARTICLE

Feasibility of using the Omnyx digital pathology system for cytology practice

Matthew G. Hanna, MD[a], Liron Pantanowitz, MD[b],*

[a] Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, New York
[b] Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania

Introduction Whole slide imaging systems have focused mostly on surgical pathologic evaluation. However, for pathology laboratories to become fully digital, cytology slides will also need to be digitized, managed, viewed, and analyzed. Our aim was to determine the feasibility of using the Omnyx whole slide imaging system for various purposes in cytology.

Materials and methods Our institution implemented the Omnyx digital pathology system, which was tested for feasibility and not implemented for clinical use in cytology. Glass slides (n = 18), scanned using various whole slide scanners, were uploaded into the Omnyx system. The system was evaluated for its feasibility with cytology case management, digital slide navigation and annotation, telecytology, and cytologic−histologic correlation.

Results The Omnyx software was able to manage cases similar to a laboratory information system. Users were able to electronically distribute, search, and sort the clinical cases. A graphic dashboard approach and virtual slide tray is available for end users to evaluate cases. The ability to create custom folders and drag-and-drop images into these folders fulfilled clinical, quality assurance, education, and research needs. Innovative tools for digital slide navigation and annotation (eg, auto-pan, adding text to annotation, hiding annotations, image coregistration) offered innovative methods to work with slides. Omnyx also provided a mechanism for sharing images with others to perform teleconsultation.

Conclusions We have demonstrated the feasibility of using the Omnyx whole slide imaging system for various purposes in cytology practice. The application supported, not only case management, but also the ability to perform cytologic−histologic correlation and telecytology. The viewer offered many features that improved digital slide navigation and annotation.

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*Corresponding author: Liron Pantanowitz, MD, Department of Pathology, UPMC Cancer Center Pavilion, Suite 201, 5150 Centre Avenue, Pittsburgh, PA 15232; Tel.: (412) 623-3746; Fax: (412) 623-4779.
E-mail address: pantanowitzl@upmc.edu (L. Pantanowitz).

Introduction

A digital pathology system is composed of 2 key integrated components: a whole slide scanner used to digitize glass slides and a workstation at which whole slide images can be

viewed on a monitor.[1,2] To be effectively used in a pathology laboratory, additional components will often be required, including a server to store digital files and software to assist with image management. For routine clinical practice, a digital pathology system will also need to be interfaced with the laboratory information system. Whole slide imaging (WSI) can be used for multiple clinical applications, such as primary diagnosis, slide archiving, telepathology, and image analysis. If well implemented, a fully integrated digital pathology system could enhance workflow in the laboratory and improve efficiency, workload balancing, and sharing of cases.[3,4]

Most pathology laboratories around the world that have deployed whole slide imaging systems for "fully digital" clinical work have primarily targeted surgical pathologic evaluation.[5-7] More recently, some laboratories have also started validating WSI for routine cytology practice.[8] Although high-level similarities exist between surgical pathology and cytology services, their samples, slides, and workflow differ significantly. Unique factors that should be addressed when using WSI in cytopathology include image acquisition challenges (eg, focus, resolution) and complex cytology workflow (eg, multiple slide preparations, screening)[9-11] (Table 1). Moreover, a cytology laboratory must comply with several regulations such as prospective repeat screening of negative Papanicolaou (Pap) test case results, 5-year retrospective reviews of all Pap test slides for newly diagnosed high-grade squamous intraepithelial lesion or cancer cases, and cytologic−histologic correlations.[12]

To the best of our knowledge, no studies have specifically addressed the usage of digital pathology systems to support cytology clinical workflow and quality assurance

Table 1 Digital cytology workflow needs.

Cytology requirement	Omnyx system functionality
Case assembly (multiple slide types)	Histologic workstation with case management suite
Cytotechnologist screening	Digital slide navigation and annotation
Slide focusing	Ability to import z-stacked whole slide images from other vendors
Case sign out	Pathologist workstation with case management, flexible worklists, and laboratory information system interface
Quality assurance (eg, 5-year review)	Patient timeline and access to digital archive
Cytologic−histologic correlation	Multiviewer (side by side) and image coregistration
Telecytology	Image collaboration such as live screen share and conferencing

(QA) needs. Therefore, the aim of the present study was to demonstrate the feasibility of using a whole slide imaging system for various purposes in cytology.

Materials and methods

Our institution implemented the Omnyx digital pathology system (Omnyx Inc, subsequently purchased by Inspirata, Tampa FL) for clinical use. Glass slides were scanned using various scanners (eg, Omnyx VL120, Aperio ScanScope XT, Hamamatsu Nanozoomer 2.0 HT) and uploaded into the Omnyx system (Dynamyx). We evaluated 10 cytology cases in the Omnyx system, including 1 that incorporated a corresponding surgical pathology case. The number of slides ranged from 1 to 4 slides per case (total 18 slides evaluated). Most cases included only 1 liquid-based Pap test slide. However, nongynecologic cases were also assessed. The types of cytology slides evaluated included ThinPrep (Papanicolaou stain), cytospin (Diff-Quik stain), direct smear (Diff-Quik stain), cell blocks (hematoxylin and eosin stain), and immunohistochemistry-stained slides. The Omnyx digital pathology system was integrated with the anatomic pathology laboratory information system (CoPathPlus, Cerner Corp). Details of this integration have been previously reported.[13] The Omnyx system was implemented and validated for primary diagnostic use in surgical pathology. However, the system was tested for both surgical pathology and cytology workflow. Although the Omnyx system was tested for cytology workflow feasibility, it was not validated for digital cytology primary diagnosis. The reported experience in the present study was accordingly based on feasibility testing alone. Omnyx was deployed and validated in clinical production to manage WSI digitization, digital case workflow, and image viewing.[14] Digital workflow includes 3 general users: an administrator (eg, information technology analyst), histology end user (eg, histotechnologist or scan technologist), and pathologist workstation (eg, pathology resident, cytotechnologist, sign-out pathologist). The administrator has full access to all modules and permissions in the system. The histologic end-user privileges include glass slide scanning, case assembly, and QA (eg, checking the scanned image quality). The pathologist workstation permits the end user to view cases (eg, worklists, digital slides, and interfaced patient data) and manipulate images (eg, add annotations) and includes some reporting functionality (eg, incorporate snapshots and text boxes). A dedicated histology workstation was used for image quality review and digital case assembly. The Omnyx pathologist workstations included 2 side-by-side monitors (HP Z24s generic PnP [plug and play] monitors with 3840 × 2160 resolution). The left display allows end users to view text-based, case-level information, and the right screen is dedicated mostly to displaying whole slide images.

The pathologist workstation was assessed using end-user testing performed by both a pathology trainee (M.H.) and a

cytopathologist (L.P.). In particular, the WSI system was evaluated for its feasibility with case management (for clinical, QA, and educational uses), digital slide navigation and annotation, telecytology, and cytologic−histologic correlation.

Results

Case management

The case management system included 3 components: histology workstation (eg, to scan slides, assemble cases), pathologist workstation (eg, WSI review), and a module for system administrator use (eg, to create workgroups, reset passwords). The application managed the following key digital workflow components (Fig. 1): case creation and assignment, user worklists, case lists (arranged by case, specialty, or priority, including urgent, rush, or routine), case status (eg, active or signed out), case review, and documentation (eg, saved annotations, snapshots, comments). The case worklist was color coded and customizable (eg, sorted, filtered) by the end user. Users were given access to relevant patient metadata such as clinical details (eg, clinical history, gross description), gross photographs (Fig. 2), old cases (with and without digital slides), and, if available, attachments (eg, scanned documents). The end user was permitted to create subfolders (eg, QA folder, teaching folder) into which they could manually drag-and-drop whole slide images for later review. If a previous case was available, the digital pathology system allowed this archived case to be promptly retrieved. All the information for the entire previous case was readily accessible in the digital pathology system, including the previous diagnosis and any previously scanned slides. This permitted real-time cytologic−histologic correlation to be performed at the time of sign-out (Fig. 3). From a QA perspective, this is equivalent to setting cases aside for later review (ie, for cytologic−histologic correlation) or to provide feedback to trainees or cytotechnologists. The functionality allowing flagging or segregating cases into folders offers flexibility for workflow related to QA; however, it is unlikely to entirely replace laboratory information system-driven QA needs (eg, for tracking workload limits, percentage of cases screened). The case management system offers an "evidence tray," in which snapshots and annotations of a whole slide image can be stored (Fig. 4). This evidence tray can be used as a gallery to store many representative static images (eg, those saved by a cytotechnologist screening a case).

Digital slide navigation

When the Omnyx viewer is launched, the application fills the entire screen. This facilitates viewing of a case, including having all the digital slides that belong to a case presented to the user in a virtual slide tray that mimics a real slide tray. This also mimics the manual workflow with a microscope. When screening a cytology slide, users can use the keyboard (auto-pan), a mouse (click and drag), or programmed trackball input device to navigate. The user is able

Figure 1   Case management suite. Cases are sortable and searchable in various lists. These cases can be arranged by priority (red, urgent; yellow, rush; blue, routine).
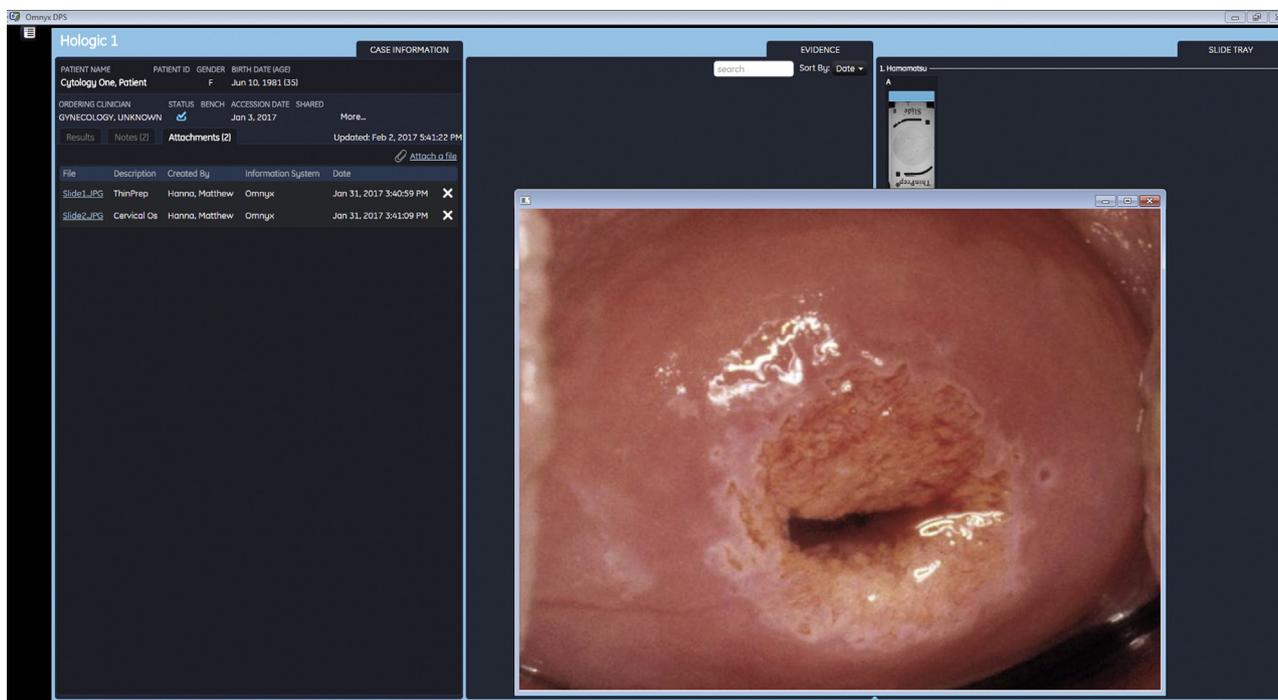
Figure 2 The case management system has multimedia capability, including the incorporation of gross images (uterine cervix case shown).

to pan and digitally zoom. Users can rely on a visible thumbnail overview for quick navigation to specific regions of interest or use the Omnyx tissue jumper tool to automatically move to new groups of cells or tissue pieces (Fig. 5). In cases with multiple, dispersed tissue fragments, the tissue jumper tool can be used to "jump" from 1 piece of tissue directly to another. This feature allows for easier navigation of multiple small pieces of tissue on a slide, eliminating the need to pan over dead space (white slide background). Software to track screening patterns is also
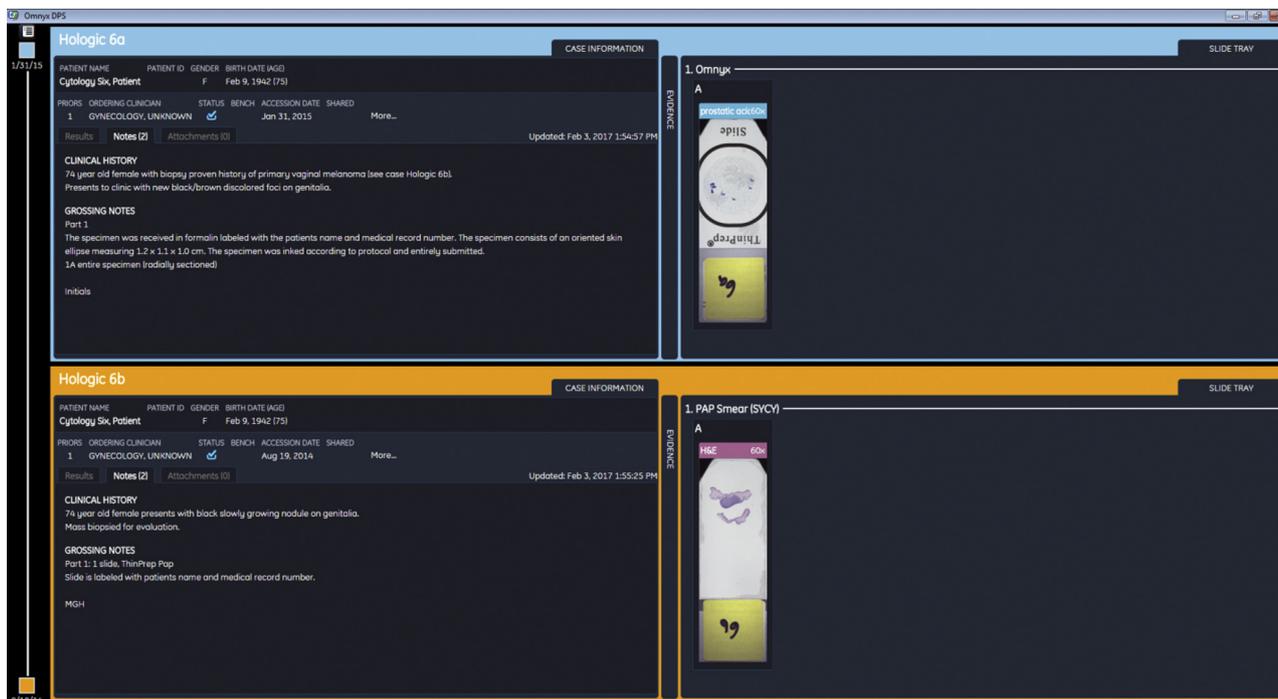

Figure 3 Ready access to archived files for case comparison. A current (case 6a; blue) can be compared with an archived case (case 6b; yellow). Both cases can be displayed for review and evaluation.
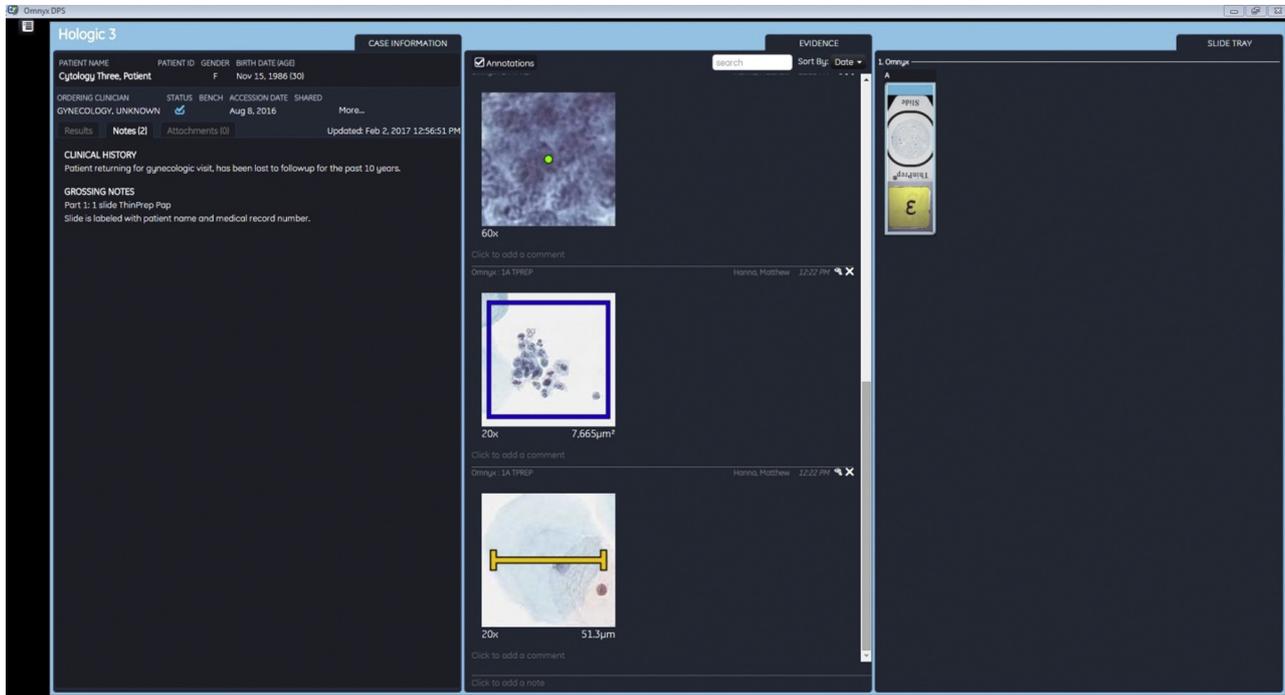
Figure 4   Annotations and snapshots for each case can be saved within an evidence tray (middle column of this screenshot).

available. Coregistration of multiple digital slides is possible, in which colocalized areas can be synchronized between slides (Fig. 6). For example, this can be used for more efficient and accurate comparison of regions of interest in cell blocks with many immunohistochemical stains. The tool must be selected by the reviewer to activate the coregistration functionality. The tool denotes the position, magnification, and rotation settings for the current slide and uses the coordinates when navigating across all coregistered WSIs of the same tissue block. It also provides scrolling

buttons the reviewer can use to move between different WSIs for facile comparison of multiple WSI files.

Slide annotation

The Omnyx digital pathology system was able to replicate dotting of digital slides for screening using virtual annotations. Such annotation tools include various shapes (eg, rectangle, ellipse, arrow, dot) or a freehand drawing tool for
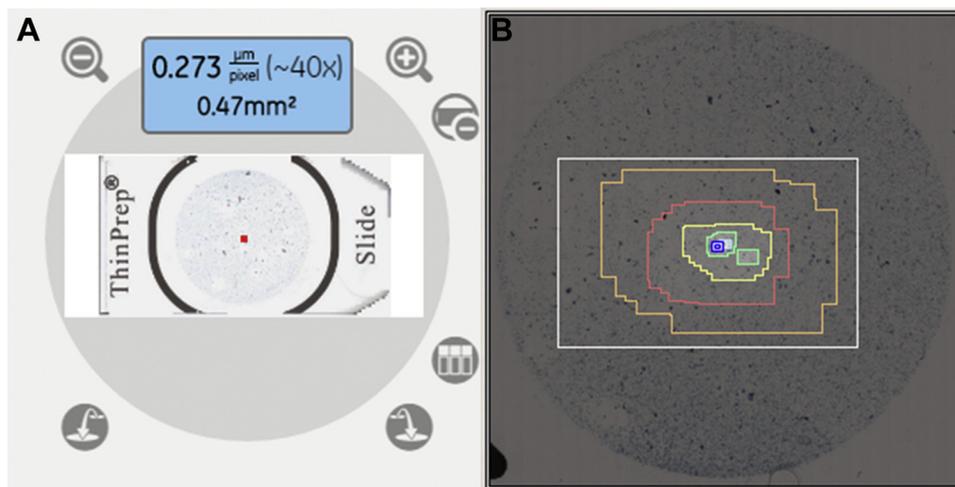
Figure 5   Whole slide image navigation tools. A, Thumbnail representation of an entire digital slide. The red dot indicates the current field of view. The end user can use this thumbnail for navigation or use the tissue jumper buttons on the bottom left and right to automatically navigate to new cellular areas. B, NDPviewer software (Hamamatsu) shown tracking panning and zooming activity; each color represents a different magnification.
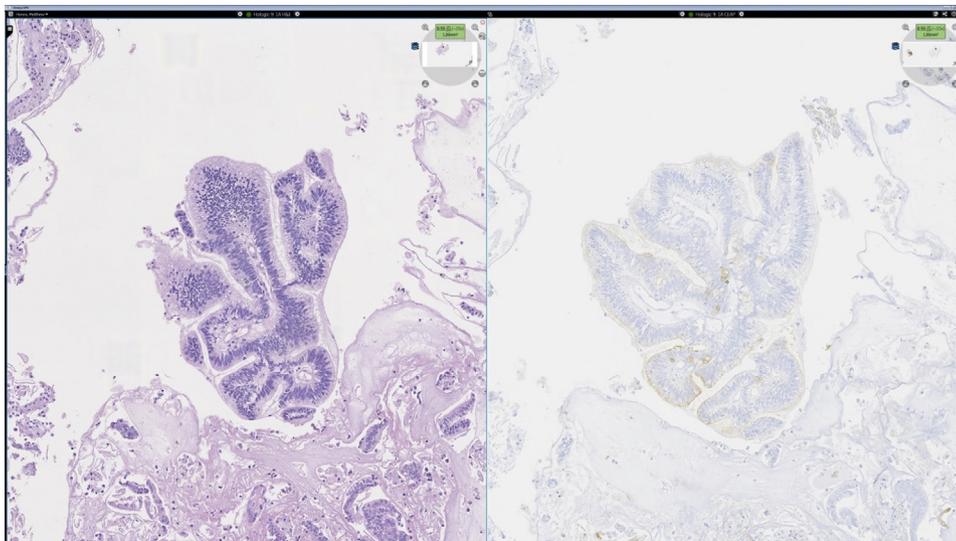
Figure 6 Image coregistration is shown of Left, hematoxylin and eosin stained cell block and Right, immunohistochemistry stained sections. Pan and zoom functions move both slides simultaneously, allowing for useful comparison of the same regions with different stains.

the user to mark cells of interest. Each annotation is saved as a "layer" that is not directly embedded into the WSI file itself. This allows for multiple users to add their individual annotation layers while preserving the original image file. The annotations are indexed and act as hyperlinks to the specified location. Each annotation can be displayed in different colors and can include the addition of text, allowing a cytotechnologist to communicate valuable findings. Virtual annotations can be turned on or off to show or hide the annotation layer. They can also be designated as private or public to be viewed by many users. Annotations can accordingly be used to fulfill education needs.

Telecytology

Within the Omnyx system, it is possible to share digital slides with other internal users or individuals outside one's institution. For teleconsultation, a link is generated that can be shared via electronic mail with another user to allow them to access a specific digital file or case hosted on a server. For internal consultations, active online Omnyx users can be searched to identify whether another user is potentially available for review (Fig. 7). Digital slides can also be shared with multiple users for real-time collaboration. Just as with viewing a slide at a conventional multi-headed microscope, users can discuss a shared case while viewing the digital slide, simultaneously navigate the slide, add virtual annotations for all to see, and anonymously poll attendees (eg, ask them to grade a neoplasm).

Cytologic—histologic correlation

The Omnyx digital pathology system offers tools that permit real-time (prospective) cytologic—histologic correlation to

be performed during sign-out and retrospectively as part of a QA program. In addition, current cases can be viewed live and side-by-side with previous cases for comparison purposes. Cases can also be saved to customized QA folders for later cytologic—histologic correlation. This can be performed with digitized cytology and/or surgical pathology slides.

Discussion

Whole slide imaging hardware and software tools to date have been largely geared toward surgical pathology. However, cytology specimens are an important component of anatomic pathology practice. Hence, for pathology laboratories to truly become fully digital, cytology slides will also
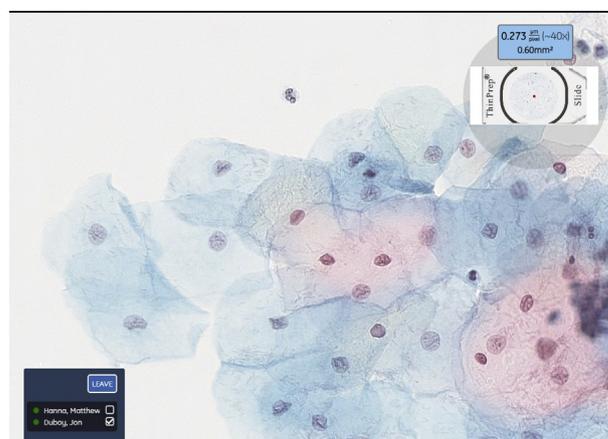

Figure 7 Real-time case collaboration. The Omnyx 2.0 system has a case-sharing module such that other online users can be invited to review a case. Remote user system control selection is shown at the bottom left of the screen.

need to be digitized, and the digital pathology systems used to manage and view these digital slides will need to support the unique workflow of cytopathology. The Omnyx system was implemented and validated at our institution for primary diagnostic use in certain subspecialties of surgical pathology (eg, gastrointestinal pathology, pediatric pathology). However, our department did not have the opportunity to become fully digital before the company dissolved.

The challenges experienced with implementation were mostly technical, including establishing an interface between the laboratory information system and the Omnyx system. Operational difficulties were also identified that related to initially implementing a hybrid glass and digital workflow versus a fully digital workflow.[15] The present review of the Omnyx software application has demonstrated that this digital pathology system can accommodate many needs for cytology practice. The sooner pathology departments embark on scanning their glass slides and move toward digital workflow, the greater will be their archived image database. This, in turn, will promote more seamless QA in cytology such as the ability to undertake cytologic–histologic correlation with older cases and the performance of 5-year reviews. No digital pathology platform, including the Omnyx software, has an integrated QA module yet that specifically supports cytology regulations (ie, 5-year review, 10% rescreening of negative gynecologic results, tracking of workload requirements). However, if leveraged effectively, digital pathology systems such as Omnyx could enable more efficient workflow by flagging certain cases and adding digital annotations that can be made available (or hidden) for subsequent QA review.

The Omnyx software's capability to manage cases provides many of the functions expected of a laboratory information system. The ability to electronically manage, distribute, search, and sort clinical cases is more efficient and allows the laboratory to eliminate the use of paper. The combined graphic dashboard and virtual slide tray approach for sign-out activity are familiar for end users, because it represents the actual slide tray workflow they are accustomed to using with glass slides at their microscope. The ability to integrate the Omnyx system with our laboratory information system and also plug-in algorithms (eg, Visiopharm) for image analysis provided an end-to-end solution that supports complete digital workflow. To extend our digital ecosystem, we installed a single sign-on solution (Caradigm) on several clinical workstations that shares patient context across various systems, including Omnyx, the anatomic pathology laboratory information system, and the electronic medical records.

The ability to create custom folders and drag-and-drop images from any case into these folders fulfills many clinical, QA, education, and research needs. Folders and subfolders can act as repositories for single digital slides or complete cases. Compared with the manual workflow, which is dependent on glass slides, digital workflow is more efficient and reliable.[16] For example, quick access to archival cases

will help decrease the turnaround time, especially when searching for misplaced slides. For slide navigation and annotation, digital tools (eg, auto-pan, adding text to annotations, hiding annotations, image coregistration) offer innovative methods for working with slides that were previously not possible using a conventional light microscope. The Omnyx system also offers multiple mechanisms for sharing images with others ranging from the creation of secure hyperlinks to a tool that permits many users to simultaneously view the same digital slide. The Omnyx system further supports cytology workflow by allowing slides from different vendors to be imported that have been scanned on multiple tissue planes (ie, z-stacking). Also, the viewer permits the viewing of z-stack images scanned from other vendors. The Omnyx system also has a user interface for patient specimens with timeline views that allows for quick access to a previous patient cytology specimen (ie, this can be used to promptly access archival images to perform a 5-year review). The system offers the ability for multiple digital slides to be viewed side-by-side, which can be used to perform cytologic–histologic correlations or to compare cell block cytomorphology with matching immunohistochemistry stains of cellular material on 1 monitor.

The present report was limited to describing the digital cytology workflow experience for only the Omnyx system. However, other vendors offer digital pathology platforms with similar accompanying software. Some of these vendors offer both hardware (WSI scanners) and software, and others provide only software systems. Platforms that offer case management software with equivalent functionality to that described in the present review include the Philips IntelliSite Pathology Solution, which is sold with the Ultra Fast Scanner and display (available at: https://www.usa.philips.com/healthcare/solutions/pathology), and the 3DHISTECH Track and Sign system, which supports a comprehensive digital workflow (available at: https://www.3dhistech.com/track-and-sign). Stand-alone commercial case management software includes Insipirata's PathologyNEXT Digital Pathology Cockpit (available at: https://www.inspirata.com/transforming-digital-pathology/) and Sectra's enterprise picture archiving and communication system (available at: https://sectra.com/medical/solutionarea/digital-pathology/). Additionally, certain vendors offer basic image management software but not true case management software. This functionality is limited to database tracking management of images and associated metadata, such as the Leica eSlide Manager (available at: https://www.leicabiosystems.com/digital-pathology/gestione/aperio-eslide-manager/) and the Hamamatsu NDPserve (available at: https://www.hamamatsu.com/eu/en/product/type/U13173-03/index.html).

Conclusions

We have demonstrated the feasibility of using the Omnyx whole slide imaging system for various purposes in

cytology. The application effectively supports, not only case management, but also the ability to perform cytologic—histologic correlation and telecytology. The viewer offers many features that enable digital slide navigation and annotation.

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Conflict of interest disclosures

M.G.H. made no disclosures. L.P. serves on the medical advisory board for Leica and Ibex and as a consultant for Hamamatsu.

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