Technical and Informatics Considerations in Implementing a Digital Pathology System: Recommendations for UC Davis Medical Center.

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Abstract

Background

Although digital pathology (DP) technology has existed for over 20 years, recent advances now allow DP systems to be used for primary diagnosis and as automated image analysis tools, where they play valuable roles. Adoption has been slow, however, with pathology laboratories slowly transitioning to DP systems. Due to the advantages its use brings, it is important that UC Davis Health (UCDH) strengthen its current DP implementation.

Objectives

The purpose of the thesis to identify and discuss informatics issues presented within other organizations DP systems. Furthermore, discuss with how those identified informatics barriers were addressed with UCDH's DP system implementation. Concluding with identifying future enhancements to strengthen UCDH's DP system.

Methods

Mixed methods were used to accomplish the objectives, beginning with an article search to identify and discuss informatics issues presented within other organization's WSI validation studies. Inclusion criteria was designed to identify studies conducted within contexts similar to that of UCDH. Studies were selected with cases involving either histopathology or surgical pathology, and digital images were acquired and viewed on a DP system of the Leica BioSystems Aperio brand. We applied the knowledge learned from the literature by conducting informal interviews and first-person observations to discuss UCDH's implementation of its digital pathology system, and discuss how informatics issues identified in literature were mitigated.

Results

The literature review identified six informatics and technical issues with other organization's DP systems. UCDH focused on four of six key components mitigate barriers to its DP implementation. (1) Reducing image quality issues due to technology by procuring advanced computer hardware and displays (2) Reducing image quality issues due to slide preparation by developing histology lab quality assurance protocols, (3) reducing dissatisfaction with WSI viewer by updating the software, and (4) offering user training sessions prior to DP implementation, so users can gain prior DP experience.

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Table of Contents

List of Figures

List of Tables

List of Acronyms and Abbreviations

AI	-	Artificial intelligence
CAP	-	College of American Pathologists
CLIA	-	Clinical Laboratory Improvement Amendments
CMS	-	Centers for Medicare and Medicaid Services
COTS		Consumer off-the-shelf
CPU	-	Computer processing unit
DP	-	Digital pathology
EAU	-	Emergency Use Authorization
Aperio eSM	-	Aperio eSlide Manager
EMR	-	Electronic medical record
FDA	-	Food and Drug Administration (U.S.)
GPU	-	Graphics processing unit
H&E	-	Hematoxylin and Eosin
IMS	-	Image management system
IT	-	Information technology
LDT	-	Laboratory-developed testing
LIS	-	Laboratory Information System
ML	-	Machine learning
POUQA	-	Point-of-use quality assurance
RAM	-	Random access memory
TAT	-	Turnaround time
UCDH	-	University of California, Davis Health
WSI	-	Whole slide imaging

Chapter 1

Introduction

Although digital pathology (DP) technology has existed for over 20 years, recent advances now allow DP systems to be used for primary diagnosis and as automated image analysis tools, where they play valuable roles. Adoption has been slow, however, with pathology laboratories slowly transitioning to DP systems. Due to the advantages its use brings, it is important that UC Davis Health (UCDH) strengthen its current DP implementation, which is still underway.

UCDH's Department of Pathology and Laboratory Medicine began building a DP system for its surgical pathology laboratory with the ultimate objective of adding a whole glass imaging (WSI) library so that clinicians could view slides digitally at cancer tumor boards and collaborate during diagnostic sign-outs. The first milestone toward this objective was procurement of a high-capacity glass slide scanner to use for digitizing surgical pathology cases. However, when the COVID-19 pandemic hit and federal and state agencies issued emergency shutdown orders, UCDH had to quickly adapt to allow administrative staff to complete their job duties remotely. UCDH's Pathology Department was ordered to minimize its on-premises staff, and so only pathologists on clinical service were allowed to be onsite in order to sign out cases. However, in April 2020, the U.S. Food and Drug Administration (FDA) granted CLIA-licensed pathology labs a temporary waiver to allow sign-outs remotely on non-FDA validation DP systems. As a consequence, UCDH's objective pivoted to implementing a digital pathology system for remote diagnosis.

Unfortunately, two circumstances outside of UCDH's control occurred, acting as barriers to its DP implementation. The first consisted of pandemic-related supply chain constraints,

which delayed UCDH's obtaining the computer hardware needed for its implementation. Secondly, due to departures and retirements, UCDH's Pathology Department experienced a shortage in surgical pathologists. With the easing of these constraints in the first half of 2023, however, UCDH is ready to finalize its DP system implementation and begin its full utilization. The objective of this paper is thus to identify and analyze technical and informatics barriers associated with implementing a DP system so as to pinpoint potential issues UC Davis Health may encounter as it continues to strengthen its digital pathology program.

Histopathology Workflow

Histopathology is the examination of tissues or organs removed from a patient during surgery to aid in diagnosing any diseases the patient could have, and an understanding of the basic histopathological workflow and the tools used during it, particularly for surgical pathology cases, is necessary to understand the critical role a DP system plays. The specimen is accessioned by the pathology lab, where it is examined by a pathology assistant or pathologist. This process consists of the following procedures.

Gross examination begins with the tissue's being viewed under the naked eye, at which time any abnormalities or variations in color or texture are recorded. It then undergoes a process known as *fixation*, during which it is treated with preservatives to prevent degradation before the examination is completed. Tissue processing then proceeds, with the tissue's being embedded using paraffin wax in cassette blocks, which are sliced into thin sections in a procedure known as *microtomy*. These sections are mounted on glass slides and stained with liquid dyes reactive to certain proteins so as to aid definition of cellular structures. Once the slides have dried, laboratory staff assemble them into a slide book that is then delivered to the pathologist, who reviews each slide using conventional microscopy (microscope) under different magnifications.

The aim, again, is to identify any abnormalities in the cells or tissue that are determinates of disease. The pathologist renders a final diagnosis based on the microscopy examination and other health-related information concerning the patient.

What is Digital Pathology?

Digital Pathology has had several interchangeable names over its 20-year history: whole slide imaging (WSI), virtual microscope, computational pathology, and telepathology. Definitions aside, DP's primary objective is to capture a high-resolution digital replica of a glass slide containing patient tissue such as that discussed in the previous section. Moreover, DP systems were designed to mimic microscopes, producing digital replicas of such quality that a pathologist need no longer view the actual physical glass slide to conduct his examination. Subsequent sections will discuss the importance of this characteristic, along with other benefits of DP and its potential future.

Components of a DP System

A DP system has three components, image acquisition, software, and image viewer, and these are discussed, end to end, below.

Image Acquisition

As indicated previously, the primary purpose of DP systems is to capture high-resolution, color images of conventional glass slides. These digital slide replicas, which are called whole-slide images (WSIs) (Lujan et al., 2021), are acquired by means of a whole-slide scanner.

When DP technology was developed over 20 years ago, whole-slide scanners were retrofitted microscopes with video cameras mounted on them (Çatalyürek et al., 2003). These microscopes were fully motorized to capture image stripes of a glass slide at a series of different

magnifications. The system's custom-developed software would then stitch together these image stripes to emulate the image of the glass slide (Cucoranu et al., 2014).

Today's WSI scanners employ a similar technology. Where an *objective* is the lens or system of lenses in a microscope closest to the object being viewed and a *high-power field* (HPF) is the field of view under the maximum magnification power of the objective, today's scanners consist of a high-power field objective and cameras. Moreover, over the years, advances in automation have the WSI scanners' image quality, decreased their slide-scanning time, and increased their slide capacity.

For instance, the UCD Department of Pathology recently purchased two Aperio GT450s (Leica Biosystems, Vista, CA); one GT450 can hold 450 glass slides and, provided the area of the tissue on the glass slide being scanned is 15mm-19mm, has a scanning speed of 32-60 seconds at 40 magnification. Thus, each GT450 can scan 40-81 glass slides within one hour's time.

Software

The second component of a DP system is its software, which is known as its image management system (IMS). The IMS serves as the system's image repository, storing the images the WSI acquires and so allowing clinicians to access and manage them. Each IMS incorporates a database that can contain image data, patient metadata, and image file storage locations. Included are such slide attributes as acquisition date, case number, and slide ID as shown on the slide label. Patient metadata can include patient demographics and medical data relevant to that patient's surgical pathology case, e.g., anatomical site from which the tissue was collected and the slide-staining protocols employed.

The IMS can also include image analysis tools such as vendor proprietary algorithms capable of detecting certain characteristics of tissues. For example, an algorithm can perform histology pattern recognition, differentiating tissue subtypes within a WSI and automatically highlighting the different tissue subtypes. Such algorithms can greatly assist a pathologist's review.

The IMS in UCDH's DP system is the Aperio eSlide Manager (Leica Biosystems Vista, CA), which will be discussed in greater detail in upcoming sections.

Image Viewer

Because a pathologist will spend the majority of their time using it to interact with digital slide images, the final and arguably most important component of a DP system is its image viewer. This is considered to be software and is usually a module within the IMS. As the image viewer's primary objective is to mimic what the pathologist does with a conventional microscope, it displays the digital slide image as if it were being viewed under a microscope.

Image viewers have a number of helpful tools and features that can assist a pathologist in thoroughly examining a tissue sample and so making a diagnosis. The viewers' panning, zooming and rotating capabilities allow the thorough examination of the sample from any viewpoint. They also provide the pathologist with the means to measure, annotate, calibrate the color of, and take static image snapshots of the sample or any portion of it.

UCDH has two image viewers, both manufactured by Leica Biosystems (Vista, CA)—the Aperio WebViewer and the Aperio ImageScope. The former is the primary web viewer and is embedded in the IMS (eSlide Manager), whereas the latter is Leica's client-installed image viewer. In the past, the features of the WebViewer were inferior to those of the ImageScope.

Today, however, the ImageScope's only advantages over the WebViewer are its capability for additional gamma color configuration and additional WSI file format support.

Benefits of Digital Pathology

Use of DP confers significant benefits to the practice of pathology to the ultimate benefit of the patient. These are discussed below.

Decreases Time to Develop a Diagnosis

As previously mentioned, digital pathology entails production of a digital replica of a glass slide, which, in the conventional microscopy workflow, a pathologist views to produce a diagnosis. Production of a physical slide can take a significant amount of time that replacing it with a WSI eliminates.

Although in some contexts physical slides can be produced on-site, they must still be assembled into books, also called 'slide trays' or 'slide jacks,' and producing digital replicas eliminates this necessity. In other locations, physical slides are created off-site and must be couriered back to their original location, creating further delay. In addition, glass slides may sometimes be broken or lost in transit, postponing the pathologist's examination and final diagnosis until they can be recreated.

A further decrease in time needed for a pathologist to make a diagnosis results from the ease with which the pathologist can view WSIs relative to physical slides. With DP, the pathologist can effortlessly toggle back and forth between slide images, whereas, with physical slides, he or she would have to laboriously mount each slide on the microscope stage to be viewed one at a time as in traditional microscopy. As has been documented (Williams et al., 2018), this ability to view slides side by side also increases pathologist efficiency.

Enables Telepathology

A far-reaching consequence of DP is that it enables telepathology, the practice of pathology at a distance. When first coined in 1986, the term *telepathology* meant practicing pathology indirectly, i.e., via an image on a television screen rather than directly through a microscope ("Teaching by Television," 1951). Today, with advances in telecommunications, a computer monitor and WSI viewer have replaced the television in telepathology, whose meaning as now shifted to the practice of pathology at a distance. Because it resulted in reduced staffing in health facilities in order to maintain social distancing, the COVID-19 pandemic provided a forced telepathology opportunity, compelling pathology labs to implement remote diagnoses. A softening of regulatory mandates to allow pathologists to sign-out cases remotely further encouraged use of telepathology.

Telepathology facilitates sharing of expertise, both in diagnostics and in pathologist education, ultimately benefiting patients.

Diagnostics

A primary consequence of telepathology is that it allows more than one pathologist to view a patient's slides simultaneously, a need that occurs in surgical pathology when a second opinion or consultation is required, either due to regulatory protocol or a request submitted to the attending pathologist. In a conventional microscopy workflow incorporating physical slides, the consulting pathologist would have to wait until the attending pathologist finished viewing a patient's slides before having access to them. If the consulting pathologist were not in the same geographic location as the attending pathologist, the slides would have to be commercially shipped, again risking breakage or loss and adding time to a final diagnosis and thus further delaying initiation of the patient's treatment plan.

With its potential to revolutionize the way consultations and second opinions are carried out, telepathology has the potential to decentralize pathology expertise, enabling experts to share their expertise with other health centers in a matter a minutes and thus providing patients accurate and timely diagnoses regardless of geographic location or distance.

The ability to practice pathology at a distance that DP allows may serve to ease pathologists' caseloads, which have increased significantly in recent years due to increases in the need for cancer diagnoses and the shortage of pathologists in the United States (Metter et al., 2019). Whereas the workloads of specialist physicians are limited by the number of patients who can be seen within a workday, those of pathologists, which consist of managing all clinical specimens within their specialty within a specified timeframe, lack this practical constraint, meaning that they can continue to grow, virtually without limit. Thus, the ability to share expertise regardless of distance that telepathology allows will assume increasing importance.

Medical Education

Along with its growing role in diagnostics, telepathology has revolutionized pathology education and training, replacing traditional classrooms with virtual microscopes. Pathology students can access WSI virtual teaching sets from their computers, allowing them to learn and practice at their own pace. WSIs can also be shared by multiple students in live sessions, allowing remote mentoring and supervision. This format proved invaluable during the COVID-19 pandemic, when pathology residents were forced to remain at home to satisfy social distancing mandates (Hassell et al., 2021).

Within the pathology community, telepathology also promotes continuous professional development and collaboration among practicing pathologists, allowing them to share their experiences with complex cases so that other pathologists can learn and expand their expertise.

Allows Automation of Image Analysis

Driven by scientific and technical expertise in machine learning (ML) and artificial intelligence (AI), digital pathology has also led to the emergence of a novel, automated image-analysis methodology. Currently, sophisticated deep learning methods are being developed and implemented to automate routine analysis of digital images, thereby freeing pathologist resources to read more complex cases that cannot be diagnosed by machine (Khalid et al., 2021).

AI image analysis tools also collect the quantitative data needed for the development of advanced precision medical applications that will enable full automation of diagnostics for use for high-volume, routine surgical pathology cases. Today, AI image-analysis technologies are available to assist pathologists in rendering a diagnosis.

For example, software development company Paige AI (Paige AI, Inc. New York NY) developed Paige Prostate, the first FDA-validated AI image-analysis tool designed to identify an area of interest, i.e., cancer, on prostate biopsy WSIs. The Paige Prostate AI algorithm was trained to identify and mark areas of suspected cancer for review by a pathologist (FDA, 2021).

WSI Regulation and Facility Accreditation

DP-related federal regulation falls under the aegis of two regulatory bodies—the Centers for Medicare and Medicaid Services (CMS) and the Food and Drug Administration (FDA), and the College of American Pathologists (CAP), the professional organization representing pathologists and laboratory professional, gives accreditations to pathology laboratories. Since these shape the landscape in which UCDH will develop its DP system, the current and expected future statuses of DP-related regulations and the CAP accreditation are pertinent to this study.

In general, the CMS oversees both surgical pathology labs that participate in Medicare and Medicaid programs and all clinical laboratories through the Clinical Laboratory

Improvement Amendments (CLIA) program. CLIA guidelines related to use of WSIs are limited, but, prior to the COVID-19 pandemic, CLIA mandated that all diagnostic reporting be completed within a CLIA-licensed facility (CLIA, 2020). Pathologists were therefore required to not only perform pathology sign-outs within their laboratory facility but also read slides, physical or digital, on-site.

The FDA regulates certain tests performed in surgical pathology labs. In April 2016, the FDA released guidance related to assessing technical performance of WSI-related devices so as to allow evaluation of use in a clinical setting for primary diagnosis. In April 2017, the FDA approved the first DP system to be marketed for primary review and interpretation of digital slides—Philips IntelliSite Pathology Solution (Philips Medical Systems Nederland B.V.). In May 2019, Leica Biosystems followed, receiving FDA approval for its Aperio AT2 DX WSI system.

However, at the beginning of the COVID-19 pandemic (April 2020), the FDA granted Emergency Use Authorization (EUA) for CLIA-licensed labs, including UCDH's surgical pathology laboratory, to use non-FDA-approved DP systems for remote reviewing and reporting. The order was intended to prevent disruptions to pathology sign-outs during the pandemic while also reducing pathologists' exposure to the COVID-19 virus by increasing the availability of WSI-related devices. Unless final guidance is revised prior to that date, EUA will remain in effect only until November 7, 2023, (FDA, 2020). Currently, UCDH does not possess an FDA-approved DP system but has been using its non-FDA-validated DP system for remote sign-outs under the temporary waiver issued in 2020 under the FDA's EUA.

Using its own laboratory-developed testing (LDT), UCDH now performs it own internal validation of its WSI scanner and other DP-related equipment. This study's aim was therefore to conduct and so assess the validity of UCDH's DP system .

Accreditation by CAP also directly affects UCDMD's development and installation of DP systems. CAP's core functions are ensuring the quality of pathology services provided patients, promoting patient safety, encouraging professional development, and providing advocacy within the field of pathology and laboratory medicine. Through the CAP Laboratory Accreditation Program, CAP offers accreditation to laboratories that comply with its standards and inspects accredited laboratories annually to ensure compliance (CAP, 2022). All the laboratories within UCDH, including the surgical pathology lab, maintain CAP accreditation.

Purpose of Validation

According to guidelines established by the College of American Pathologists (CAP) in 2013, every pathology laboratory planning to use DP for clinical diagnostics, whether in-house or externally, is required to perform an internal validation whose goal is to emulate real-world testing of the entire DP system. Moreover, the test must assess intra/interobserver variability by establishing *diagnostic concordance* between digital and glass slides, meaning that a pathologist reaches the same diagnosis by reading a case's digitized slides as by reading the corresponding physical slides. In April 2021, CAP updated these guidelines to include nine good practice statements and the following three recommendations for the DP validation process:

(1) It must include a set of 60 or more cases per application or use case so as to establish trust in WSI use, identify and mitigate any risk associated with NP technology, and balance the time and resources required for the lab to perform the validation.

(2) A diagnostic concordance of at least 95% should be achieved for each observer.

(3) A washout period of two or more weeks should be observed between a pathologist's viewing of the digital and the physical slides so as to reduce potential recall bias (CAP, 2022).

In furtherance of this validation process, the purpose of the thesis is to discuss the validation methodologies used to evaluate diagnostic concordance between physical and digitized slides in the surgical pathology laboratory at UCDH. Moreover, identify and discuss informatics issues presented within other organization's WSI validation studies. Concluding with how the identified informatics barriers were mitigated with UCDH's digital pathology system implementation. To achieve its purpose, this study included a review of the relevant literature, which is presented in Chapter 2. Then, Chapter 3 discusses the background and current state of UCDH's surgical pathology sign-out workflow. Then, Chapter 4 discusses implementation and recommendations to improve their digital pathology system, and Chapter 5 provides an outlook of future implementations and suggested enhancements to improve UCDH's digital pathology program.

Chapter 2

Literature Review

A literature review was conducted by searching the electronic databases PubMed and SCOPUS on February 15th, 2023, using the following key words and terms, Whole Slide Imaging, Digital Pathology, and Digital Microscope. Below, the acceptance criteria and a description of the papers thus found are discussed.

Inclusion Criteria

The aim of the literature search was to identify studies conducted within contexts similar to that of UCDH. Consequently, abstracts of papers retrieved were screened for the following inclusion criteria:

(1) Paper topic was a validation study evaluating diagnostic concordance between digital slides and physical slides viewed with a BLM microscope.

(2) The cases for which degree of concordance between physical and digital slides was determined involved either histopathology or surgical pathology.

(3) Digital images discussed were acquired and viewed on a system of the Leica BioSystems Aperio brand.

Table 1 below lists the papers that met the criteria above. These were further reviewed for reports of such informatics-related issues as image quality, image acquisition (scan) failures, delays in scanning or case turnaround time (TAT), and negative user experiences in viewing and navigating slide images in the IMS.

Results

Of the 442 records the initial search yielded, 17 articles matched the criteria for inclusion. The publication dates of the 17 ranged between 2008 and 2023, and all were published in

English, with 11 from North America, five from European countries, and one from western Asia. 41% (*n*=7) of the studies included a mix of surgical pathology cases, with the remaining ten focusing on a subspeciality (see Table 1). The washout time between readings taken via a BLM and a WSI ranged from one week to one year, with 35% (*n*=6) not specifying the washout period. Each of the studies employed one or more Lecia BioSystems WSI scanners for image acquisition, and all but one used Aperio ImageScopes for digital-image viewing. All studies reported one or more informatics-related issues related to use of the DP system, and these are discussed in the next section.

Discussion of Findings

For clarity, we categorized informatics and technical issues identified into the following six components (see table 1 for which component was mentioned in each study). 53% (*n*=9) mentioned turnaround time (TAT), i.e., the time taken for a pathologist to complete a surgical pathology diagnosis report measured from when the specimen is biopsied from the patient to when the pathologist signs-out the final diagnosis, was slower or perceived slower reading WSI, 41% (*n*=7) mentioned image quality issues due to technology, 35% (*n*=6) reported slides required higher magnification, 29% (*n*=5) mentioned user dissatisfaction with the DP system and/or WSI viewer, 29% (*n*=5) mentioned image quality issues due to slide preparation, and 17% (*n*=3) mentioned impacts from prior user DP experience or training.

Image Quality

Although not found to be a major source of diagnostic discordance between physical and digital slides, image quality was nonetheless a common theme in a majority of the studies selected. Specific issues related to image quality were technology, magnification, and preparation of the physical slides. These are discussed in detail below.

Table 1

17 Papers Meeting the Literature Review Criteria

Author(s)	Specialty	Informatics Issues Addressed
Alassiri et al. (2020)	Neurology	Efficiency
Al-Janabi et al. (2013)	Pediatric	Image Quality – Technology Magnification User Satisfaction Efficiency
Al-Janabi, Huisman, Vink, et al. (2012)	Dermatology	Image Quality – Technology Magnification User Satisfaction Prior User Experience
Bauer et al. (2013)	Mixed	Magnification
Bauer et al. (2015)	Frozen Section	User Satisfaction Efficiency
Brunelli et al. (2014)	Mixed	Image Quality - Tech
Ferreira et al. (2023)	Mixed	Slide Preparation Prior User Experience Efficiency
Fine et al. (2008)	Mixed IHC	Magnification Efficiency
Gage et al. (2013)	Gynecologic (GYN)	Image Quality - Tech Slide Preparation Efficiency
Gui et al. (2012)	Gastrointestinal (GI)	Image Quality - Tech Magnification Efficiency
Hanna et al. (2020)	Mixed	User Satisfaction
Hanna et al. (2019)	Mixed	Slide Preparation User Satisfaction Efficiency
Kim et al. (2020)	Mixed	Image Quality - Tech
Mutter et al. (2022)	Gynecologic (GYN)	Slide Preparation
Krishnamurthy et al. (2013)	Mixed	User Satisfaction
Velez et al. (2008)	Dermatology	Image Quality - Tech Magnification Slide Preparation Efficiency Prior User Experience
Williams et al. (2018)	Brest	User Satisfaction Prior User Experience

Technology

Seven (*n*=7) validation studies reported diagnostic discordance due to the displays they used to view WSIs. An extremely important component of a digital pathology system, these displays form the visual gateway to diagnostic analysis using WSIs. Specifically, participants reported difficulty identifying certain cell structures and differentiating tissue type, e.g., identifying eosinophils (disease-fighting white blood cells) and their size and shape (Velez et al., 2008). This difficulty was attributed to differences in the physical and digital slides' color balances, and the cause was found to be the displays used to view the digital slides and their lack of the refractile qualities needed to fully emulate the colors of the physical slides' contents.

Type of monitor and monitor features were found to affect the degree of diagnostic discordance experienced; in particular, high-resolution, wide-panel monitors enhanced diagnostic analyses using WSIs (Al-Janabi, Huisman, Nap, et al., 2012; Gui et al., 2012). Unfortunately, research is lacking regarding which display types work best in digital pathology (Abel et al., 2020). Moreover, whereas early DP systems used high-end consumer grade monitors, systems currently being validated by the FDA for primary diagnosis utilize medical-grade, self-calibrating monitors (FDA, 2020), and hence may lack the ability of high-end monitors to accurately reproduce color.

Magnification

Six (*n*=6) validation studies reported minor degrees of diagnostic discordance due to the inability to view digital slides at sufficiently high degrees of magnification. Digital slides scanned at 20x magnification were either prone to focus imperfections or failed to enable identification of certain structures. For example, in one study, nucleated red blood cells (NRBS) within placenta tissue were not detected when the slide was scanned at 20x (Al-Janabi et al.,

2013). However, rescanning physical slides at 40x to obtain digital slides greatly mitigated magnification discordance.

The number of slides requiring higher magnification levels was extremely low. For example, the pathologist in one study requested that slides for only 10 of 168 cases be rescanned at a higher magnification (Gui et al., 2012), suggesting that, in the majority of cases, 20x magnification is adequate for an accurate diagnosis. Moreover, all the studies reporting magnification issues were published between 2008 and 2014 and so used early WSI scanner technology.

The default magnification of these early scanners was set at 20x (Zarella et al., 2019) for several reasons. Scanning at a higher magnification produces large-sized image files and requires longer scan-per-slide times to enable capture of additional image layers (Ghaznavi et al., 2013), thus increasing the network storage required to store and the time needed to produce digital slides, respectively. However, today's WSI scanners are equipped with advanced image-rendering technology and tissue finder algorithms that greatly improve image quality while also increasing scanning speed. Moreover, improvements in network infrastructure technology and reduced storge costs have eliminated the relatively high storage costs of high-magnification digital slides when WSIs first became commercially available. Thus, whereas early scanners were assumed to need to be capable of producing digital slides only as good as the physical counterparts from which they were made, today's WSIs can actually improve upon their physical originals.

Slide Preparation

Five (*n*=5) validation studies reported diagnostic discordance due to issues related to preparation of the glass slides. As discussed earlier, in slide preparation, specimen tissue is

embedded in paraffin wax cut from cassette blocks that is then sliced into very thin slices and mounted onto glass slides. If the tissue is too thick, too much glue/mounting media was used, or air bubbles were caught between the glass slide and coverslip during preparation, the digital slide may be out of focus (Ferreira et al., 2023). For instance, one study found that tissue folds, small air bubbles, dust particles, and other imperfections negatively affected scanner algorithm performance (Velez et al., 2008). In particular, such slide imperfections were found to impact image quality for cases that required viewing to be at medium or high magnifications.

In two other studies, the tissue's being mounted on an extreme edge of its glass slide negatively impacted the WSI scanner's tissue identifier algorithm (Gage et al., 2013; Mutter et al., 2022). Positioning the slide label so that it overlapped the slide's coverslip was also found to affect the digital slide's image quality because it created a gap between the glass slide and the coverslip that prevented a proper seal from forming and so led to infiltration by air bubbles and foreign artifacts.

Efficiency

Although the majority of studies did not include formal measurement of the time expended in reading both the digital and physical slides, in nine (n=9) validation studies, study participants perceived reading a digital slide as taking a greater amount of time than did reading a physical slide. Moreover, of the three (n=3) studies that did include time tracking, reading digital slides was found to take longer than reading their glass counterparts. In one of the larger, mixed specialty validation studies, each pathologist was found to need one hour and six minutes longer on average to read digital slides than to read the corresponding physical ones (Hanna et al., 2019). In a medium-sized, fixed-specialty study (i.e., gastrointestinal), reading digital slides took 50% to 400% longer than reading the physical slides (Gui et al., 2012). In a smaller, fixed-

specialty (i.e., prostate) study, reading the digital slides for complex cases took longer than reading the corresponding physical slides, with the maximum difference in times in excess of 15 minutes (Fine et al., 2008). Amongst all the studies, the relative slowness experienced in reading digital slides was due either to image quality (poor resolution, inadequate magnification) or to user difficulty with the image viewer, which is discussed in the next section. Whether the relatively greater amount of time required to read digital slides versus physical ones is perceived or actual, minimizing TAT in surgical pathology cases is essential.

User Satisfaction with Image Viewer

Although five (*n*=5) validation studies mentioned unsatisfactory user experiences during use of the image-viewing software, none attributed diagnostic discordance to these experiences. Four mentioned user discomfort with using a mouse to navigate an image within the WSI viewer software, and one study participant noted that the Aperio ImageScope (Leica Biosystems, Vista CA) controls do not mimic a traditional microscope's knobs (Krishnamurthy et al., 2013). Therefore, for instance, within a WSI viewer, focus is adjusted with a series of mouse clicks and drags rather than with the knobs of a traditional microscope. In addition, whereas a microscope's user selects the object to be magnified with its nosepiece, the WSI viewer's mouse scroll wheel is used for this purpose in viewing WSIs, and participants in three studies suggested that the mouse was not an appropriate tool for navigating digital slides (Al-Janabi, Huisman, Nap, et al., 2012; Bauer et al., 2015; Krishnamurthy et al., 2013). However, the mouse peripheral is an integral component of modern-day computers, and little has been proposed to replace it in WSI navigation.

Moreover, makers of DP systems have introduced improvements with regard to using on-screen controls and keyboard shortcuts. With the introduction of touchscreens and mobile

devices, use of touch controls to navigate slide images is a possibility, but the relatively small screen size of these devices make reading WSIs for diagnostic purposes infeasible (Brunelli et al., 2014). Furthermore, with any transition to a novel technology to accomplish a task, users become increasingly accustomed to the tool as they use it. As reading slides digitally becomes more prevalent, pathologist will gain the muscle memory needed to use the WSI viewer's navigation tools just as they once did when first learning to read physical slides with a traditional microscope. Based on the feedback of study participants reported in the studies shown above, DP vendors should solicit user feedback on their WSI viewers to add to and improve their slide image-navigation features.

Impacts from Prior User Experience

Some of the reviewed studies report participants' prior experiences reading digital slides in assessing their current comfort levels with using digital rather than physical slides. The primary difference cited by these participants, who at that time had had little or no experience in reading WSIs, was increased pathologist TAT.

Two (*n*=2) studies included design frameworks intended to measure the impact a user's prior experience with reading WSIs had on their current comfort with doing so. Unsurprisingly, the authors of one study that measured TAT differences during their previous and current experiences with digital slides concluded that less WSI experience led to longer TATs (Velez et al., 2008). The other study observed the impact of conducting a pre-validation WSI training session consisting of two phases, the first including a one-hour, individual training session to familiarize the participant with the digital viewer and the other consisting of an observed practicum session with the trainer. The participant provided feedback during this second phase, which also included a mock validation study requiring the participant to view and diagnosis 20

complex cases on physical and digital slides. Following completion by all study participants, a group discussion was held to discuss findings, including ways to identify and mitigate potential pitfalls of WSI use. The study concluded that this individual training and validation methodology allowed participants to develop competency and confidence reading digital slides, which were measured by evaluating the overall diagnostic discordance between the training cases and the validation study. The study also found that TAT did not increase with reading slides digitally, suggesting that their efficiency increased as they gained experience with navigating WSI software (Williams et al., 2018). However, as all study participants completed both phases of the training, the validation study lacked a control. Including a participant who did not complete the training phases could have provided additional evidence that the training increased diagnostic concordance, decreased TAT, and increased user experience level.

Validation Methods

Validation methodologies to compare outcomes from reading between physical and digital slides varied widely across the studies. Six (n=6) were conducted outside the United States, and so the methodologies employed were under the guidance of different government and regulatory agencies. However, the studies conducted within the United States (n=11) cited the 2013 published CAP guidelines, and the majority of these studies used a case selection methodology modeled on the lab's workflow and caseload, thus following CAP's recommendation to perform real-world testing. However, some studies used statistical methods selected by the researchers to determine the number of cases required to adequately measure degree of diagnostic discordance (Bauer et al., 2013). As the validation studies reviewed varied from small subspeciality labs to large medical centers having multiple labs, variations in case volume and number of slides read was anticipated. Moreover, since certain specialties typical

require more slides per case for a pathologist to render a diagnosis, case slide volume tends to vary greatly amongst surgical pathology subspecialities.

However, the variation in methodology used to evaluate diagnostic concordance among the studies was surprising. The majority employed either a cross-sectional evaluation design, in which all participants were given digital and physical slides for the same cases and evaluated these independently to arrive at two distinct diagnoses, or a retrospective design using cases for which the participant had previously rendered a diagnosis based on viewing physical slides and so needed only issue one based on viewing WSIs for that case. In both cases, the sets of diagnoses were compared to discern level of diagnostic concordance.

Still another source of variation amongst the studies was the size of the wash-out period, which ranged from one week to one year, with six studies not reporting washout period length. As mentioned previously, the purpose of a washout period is to reduce observer recall bias. One study added additional bias controls by using a randomized design methodology, in which slides were read more than three times and were mixed with altered identifiers so that a participant was unable to determine which slides were repeated (Gage et al., 2013).

Post-Validation Survey

Three (*n*=3) of the studies reviewed conducted surveys following study completion using structured questionnaires to assess informatics related to digital slide use. The studies asked specific questions designed to measure participants' satisfaction with the WSI software and viewer and comfort level with issuing a diagnosis for pathology cases based on digital slides (Hanna et al., 2019, 2020; Velez et al., 2008) (see the example in Appendix A). These questionnaires were a valuable tool for the reviewers to gather perspective on several elements of their Digital Pathology system implementations.

1. Feedback Collection: The surveys allow stakeholders to provide their feedback on the digital pathology system. This insight helps identify what's working well and what areas need improvement.

2. Performance Evaluation: The surveys help assess the system's performance, including its efficiency, accuracy, and ease of use. This data can be used to gauge whether the system is meeting its intended goals and if any adjustments are needed.

3. User Experience: The surveys help capture user opinions about the system's interface, navigation, and overall usability, which can drive interface refinements or additional training.

4. Problem Identification: The surveys enable users to report any issues, glitches, or unexpected challenges they've encountered while using the system. This aids in troubleshooting and addressing technical problems promptly.

5. Adjustments and Optimization: Feedback from surveys can guide refinements and optimization efforts to enhance the system's functionality, performance, and user satisfaction over time.

6. User Adoption and Training: Surveys help assess how well users have adapted to the new system and identify areas where additional training or support might be required.

7. Continuous Improvement: Implementing a digital pathology system is not a one-time event. Surveys enable a continuous improvement cycle, helping organizations iteratively enhance the system and adapt to evolving needs. These questionnaires were apparently a valuable tool for the reviewers.

In furtherance of these findings identified and discussed from the reviewed WSI validation studies, we now need to discuss how UCDH mitigated these informatics issues with

its Digital Pathology implementation. To achieve this, we'll begin discussing the current state of UCDH's surgical pathology sign-out program in the next chapter.

Chapter 3

Current Status of DP Implementation at UCDH

Methodology Utilized

The aim of the remaindering chapters is to discuss UCDH's implementation of its digital pathology system. Moreover, applying mitigation strategies to the informatics barriers identified and discussed in the literature review. Concluding with providing additional recommendations and enhancement to bolster UCDH's digital pathology system. In furtherance, this was accomplished by the following data collection methods.

(1) First person informal interviews with UCDH surgical pathology subject matter experts.

(2) Firsthand knowledge from the author of this paper, whom the lead information technology analyst for UCDH's digital pathology implementation and clinical application portfolio.

(3) Additional support from the reviewed literature.

Background

UCDH's Department of Pathology and Laboratory Medicine's surgical pathology laboratory is located at UCDH's Medical Center in Sacramento California. Fifteen attending pathologists and approximately 40 staff members support the surgical pathology lab, and this team processes approximately 30,000 cases annually, with biopsies comprising half the cases and resections the other half. The differences between biopsy and resection are explained in the next

section. The attending pathologists share both general service rotations and specialty rotations amongst three teams:

- Team A: Gastrointestinal and Liver,
- Team B: Gynecologic and Endocrine,
- Team C: Breast, Head and Neck, Gentio-Urinary, Lung, Soft-Tissue Bone.

Two attending pathologists manage Renal and Neuropathology subspecialty cases in conjunction with their general service rotations. UCDH Dermatopathology, however, falls under a different clinical service line's reporting structure. The dermatopathology lab recently added DP capability with the recent acquisition of a Leica Aperio GT450 WSI scanner. However, for clarity, implementation of and recommendations for the surgical pathology lab only are addressed in this dissertation.

Biopsy vs. Resection

Biopsy and resection describe different types of tissue specimens obtained from patients for pathological examination. A biopsy refers to the removal of a small piece of tissue or cells from a particular area of the body for microscopic examination and is usually performed to diagnose or determine the nature of a disease or condition. On the other hand, resection, also known as surgical resection, refers to the removal of a larger portion or an entire organ or tissue mass during surgery. Moreover, a resection is often performed to remove tumors, suspicious lesions, or diseased tissues. Resections are more extensive than biopsies, as the goal of resections is to eliminate the entire affected area. Explaining the differences between biopsies and resections is necessary so as to properly understand the surgical pathology diagnostic workflow at UCDH.

For surgical pathology cases that involve resection, a biopsy is performed on the suspected tissue, so the Pathologist can identify the specific type of cancer they are dealing with. The diagnostic order in which the biopsy is reviewed first is important for several reasons, the most important being the preliminary diagnosis. In this case, since a pathologist reviews the biopsy first to verify the presence of cancer and identify its type, he or she compiles a preliminary diagnostic report to share with the patient's care team. This report is important, as it allows the patient's care team to begin making decisions on the appropriate treatment plan and therapies. Moreover, having a preliminary diagnosis allows the pathologist to perform informed diagnostic analysis on the resected tissue to determine if all the cancerous tissue has been removed.

Virtual Tumor Board

A virtual tumor board is a multidisciplinary team meeting of healthcare professionals, including oncologists, radiologists, and pathologists to discuss and collaborate on the diagnosis, treatment, and management of cancer patients. Unlike traditional in-person tumor board meetings, virtual tumor boards take place online using video conferencing. Before the advent of WSI, clinicians physically attending a tumor board meeting would either look through a multi-head microscope to view the contents of the physical slides or use a microscopy video camera to project the image of these contents on a screen. Today, clinicians review WSIs and other relevant medical data over web-conferencing screen sharing, allowing experts from different locations to come together and share their insights, review patient cases, and collectively determine the most suitable treatment options for individual cancer patients. As clinicians can quickly retrieve images from the IMS, use of WSIs allows tumor boards to be more efficient. Something we'll discuss even further with UCDH Pathology's WSI workflow.

Workflows

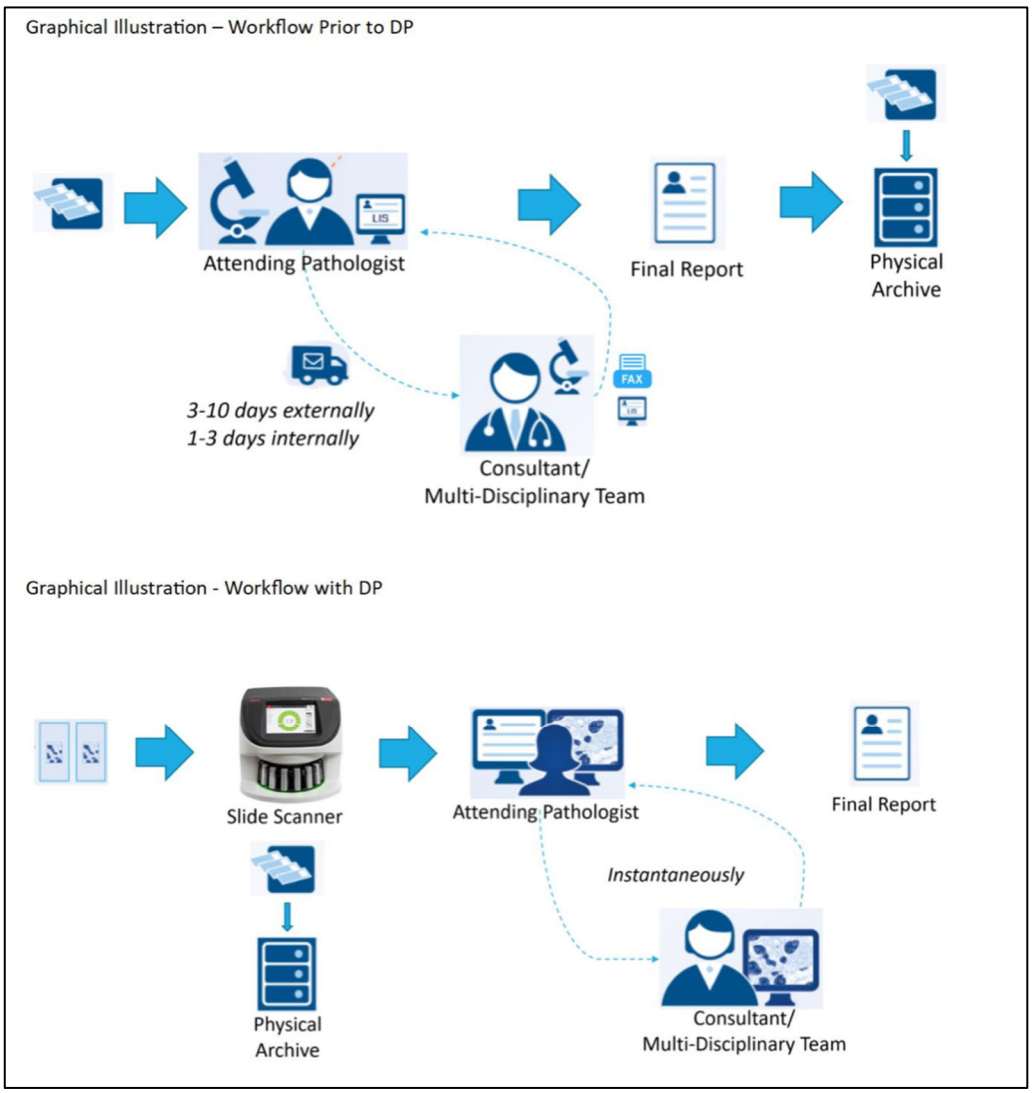
The workflows prior to DP system implementation and following it are presented below. See Figure 1 for a graphical representations of both workflows.

Prior to WSI Implementation

Prior to UCDH's implementation of its clinical DP system, the workflow was typical of any other surgical pathology department reading physical slides (see Figure 1). Once histology technicians finish preparing these, they assembled the slides for each case in slide books. Then, using the physician-scheduling system to determine the attending pathologist on duty that given week, they assigned the case to the appropriate pathologist within the Laboratory Information System (LIS) Division section and delivered the slide books to that pathologist's office or mailbox. The pathologist then prioritized his or her caseload via the LIS outstanding list to determine which case required a diagnostic analysis. The pathologist then reviewed the patients' demographics, medical data relevant to the surgical case, and any historical surgical cases that could be helpful to understanding the progression of the relevant disease. The pathologist loaded each glass slide on their microscope to perform their visual analysis. Combining their visual findings with the patient's histological media information, the pathologist then rendered a diagnosis. Once the case was complete or was determined to require an interobserver to view it, the pathologist returned the slides to the slide room staff, who checked in each individual slide using the LIS, and either assigned and delivered the slides to the consulting pathologist or filed the physical slides. (See Appendix B for swim lane workflow)

Figure 1

Pre- and Post-DP System Workflows (high-level)



Workflow After WSI Implementation

Prior to the implementation of UCDH's clinical DP system, meetings were held separately with two distinct stakeholder groups to discuss and plan the workflow changes that it would entail. The first stakeholder group manned the histology lab, and the second consisted of surgical pathologists. The workflow of the histology lab group was more greatly impacted by the DP implementation because the histology lab drives the pathologist caseload. The AP director

and histology lab leadership met to thoroughly discuss the workflow changes to slide preparation and management that would be necessary. The biggest concern was the impact the changeover would have on slide delivery throughput to the pathologist.

Since UCDH's possessed only one GT450 scanner, two challenges emerged, the first being scanning lead-time. The GT450 could take up 12 hours to scan 450 H&E slides, depending on the amount of tissue on each slide. The second issue was scanner capacity; it was apparent that insufficient time and capacity were available to scan complete resection cases in order to meet preliminary diagnosis throughput deadlines. To resolve this issue, the histology lab adjusted histology technician schedules to begin tissue processing earlier. In this way, slides could be loaded into the GT450 by afternoon so that it could scan the physical slides overnight so that the digital slides were available to pathology the next day. Moreover, since there was insufficient capacity for the GT450 to scan entire resection cases, the biopsies were loaded first, so the pathologist could begin diagnostic analysis and render a preliminary diagnosis. Therefore, the previous day's resection slides were loaded into the GT450 after the biopsy slides were unloaded. (See Appendix C for swim lane workflow)

Virtual Tumor Board Workflow

UCDH was already using WSIs prior to implementation of the clinical DP system. However, the manual workflow involved was inefficient and difficult for an attending pathologist to manage. Cases that were identified to be presented to a tumor board needed to be manually scanned by either slide room staff or the presenting pathologist. The case slides were scanned by the department's existing Aperio AT2 scanner and assigned to a shared datagroup with the Aperio IMS. The WSI scanner and IMS were not configured to read the slide barcode label, digital images were assigned to a folder in the IMS that corresponded with the tumor

board's date. When the tumor board convened, the presenting pathologist could log in to the legacy IMS to retrieve the digital images for their case. However, implementation of the clinical DP system eliminated this cumbersome workflow, because all surgical pathology slides are now scanned directly into the digital library, making the digital slides readily available to the attending pathologist, who can use tumor board assignment workflow within the IMS to flag individual case slides to their respective tumor board. Moreover, this allows the presenting pathologist to easily retrieve the digital slides for each case in order to present it to the board. Furthermore, if a case is not flagged appropriately or a last-minute case is added, the presenting pathologist can retrieve the digital slides by searching the IMS using the surgical pathology case number. This workflow improvement not only eliminated slide handling and inefficiency but also increased pathologist satisfaction with and buy-in for the clinical DP system.

Chapter 4

Implementation and Recommendations

A number of suggestions and recommendations will ensure the continued success of UCDH's DP system, and these are covered below.

Validation Methodology

The literature review found variation in validation methods but concluded most followed the CAP constructs delineated in its original published guidelines for validating DP systems for diagnostic purposes. UCDH pathology handled the validation of its DP system for diagnostic purposes by using a Laboratory Developed Test (LDT) to validate the diagnostic concordance of signing out pathology cases remotely. As previously mentioned, UCMDC Pathology did not purchase an FDA validated IVR digital pathology system. Therefore, UCDH Pathology structured its LDT using the 2021 CAP guidelines for validating WSI systems for diagnostic purposes. The Anatomic Pathology Chair was responsible for case selection and overall oversight of the DP system validation. Ninety-nine surgical pathology cases were selected at random from the LIS database across all specialties so as to emulate the lab's typical weekly case mix, thereby more than satisfying the CAP's recommended 60 cases for validating DP systems. The 99 cases selected included 294 specimen parts consisting of 1430 slides stained with either hematoxylin and eosin (H&E) and immunohistochemistry (IHC). Three attending pathologist participated in the validation by reading the same 99 cases digitally. These 99 cases had also been diagnosed previously using physical slides more than 12 months prior to the start of the validation, thereby more than satisfying CAP guideline's third recommendation, which suggested a two-week washout period. To further reduce potential participant recall bias, participants received anonymized spreadsheets that contained only the index case number,

minimal clinical information, and basic patient demographics (i.e., gender, age, race.). The participants read each case digitally using the Aperio WebViewer software and recorded their diagnoses on a spreadsheet along with three other metrics; quality of the tissue, quality of the WSI, and viewing speed. Although all three metrics were scored on a 5 point Likert scale, a formal TAT study was not performed. At the conclusion of the validation, the AP chair collected the spreadsheets from all participants and used Kappa statistics to calculated diagnostic concordance between the diagnosis read on physical and digital slides.

Kappa statistics, also known as Cohen's kappa coefficient, is a statistical measure used to assess the agreement between two raters, known as inter-rater reliability studies in medicine (McHugh, 2012). Moreover, satisfying CAP's second validation recommendation of interobserver variability. UCDH surgical pathology laboratory achieved a 98.97% diagnostic concordance between physical and digital slides, with no major discrepancies identified, thereby satisfying CAP's DP system validation recommendation of 95% or greater diagnostic concordance.

Digital Pathology Workstation

As identified in the literature review, displays are the visual gateway to performing diagnostic analysis using WSIs. As of the writing of this paper, there has been a lack of literature assessing what display characteristics are optimal for WSI use in diagnostics (Abel et al., 2020), particularly in light of the constant improvements in monitors available on the market since the introduction of DP system. When first commercially available, these systems included high-resolution medical grade monitors.

Display resolution, which determines the fineness of detail visible to a viewer, is measured in the number of pixels that can be displayed on a screen, which is expressed as the

number of pixels in the horizontal by vertical dimensions. Thus, for instance, 1920x1080 (Full HD or FHD) resolution, has 1920 rows of pixels across the screen and 1080 columns of pixels down the screen, whereas 3840x2160 resolution (4K Ultra HD) has 3840 rows and 2160 columns (Abel et al., 2020). However, the resolutions of today's consumer off-the-shelf (COTS) monitors are equal to or exceed those of medical grade displays, and a higher display resolution permits finer detail to be shown and so enhances a viewer's ability to distinguish small structures within tissue samples.

Moreover, the FDA regulates the types of displays in FDA-cleared WSI scanners. UCDH pathology currently does not possess an FDA-cleared whole-slide imaging scanner for primary diagnosis. Therefore, UCDH's Information Technology and Pathology Departments were tasked with procuring an adequate COTS display that would allow a pathologist to identify color and tissue-architecture variations in order to maximize the diagnostic concordance between physical and digital slides. However, the monitor is only one component that determines the quality of a WSI reader. Additional sources of image degradation affecting what a pathologist sees are the workstation, the graphics card, and network performance.

Assessing the current computer equipment used by 15 surgical pathologists, UCDH's IT Department found that the majority of their standard displays were over 10 years old and thus exhibited degradations in image color and brightness, with some experiencing image distortion due to the presence of dead pixels. Moreover, the workstation computers themselves were only adequate for performing the clinical administrative tasks needed to access electronic medical records (EMR), utilize the components of the Microsoft Office suite (e.g., email), and use basic web conferencing tools such as Microsoft Teams and Zoom. Furthermore, UCDH's IT Department had received pathologist complaints regarding workstation performance while

screensharing static images over Zoom. Therefore, UCDH's IT and Pathology Departments sought to build a standardized DP workstation for use by the latter's pathologists by defining the following COTS components.

Diagnostic Display

According to prior studies, a higher resolution display decreased pathologist diagnosis time (Abel et al., 2020), as these provide a larger field of view, allowing a pathologist to view an entire WSI at the same time and so more easily distinguish color and architectural variation in the tissue. As the medical displays used in prior studies were manufactured prior to 2015, today's COTS displays matched or, in most cases, exceeded the resolutions of these earlier medical displays. Therefore, the Samsung Ultra High Definition 4K monitor (3840x2160) was selected as the primary diagnostic display to include in the standardized DP workstation.

Administrative Display

UCDH's Pathology Department requested that each digital pathology workstation be equipped with three displays, with the primary display being utilized for diagnostic purposes. Prior studies have noted that pathologists prefer this number (Randell et al., 2015). The two additional displays improve pathologist diagnostic efficiency, as they enable pathologists to simultaneously view the reference data used to assist with surgical pathology case sign-out. Typically, such administrative displays are used for the Laboratory Information System and secondary reference materials.

However, procurement of three (3) 4k monitors was considered cost prohibitive, increasing a workstation's cost by more than 75% compared to a workstation having one high-definition display. Therefore, including two 32" Samsung HD monitors (1920x1080) was

recommended. However, supplier incentives and other considerations were made to procure two (2) Samsung 4K monitors per workstation, as will be discussed below.

Figure 2

Comparing Monitor Specifications

Monitor Specifications Comparison			
Component	Leica Minimum	Standard UCDH Display	UHD/4K Display
Size (viewable diagonal)	>=24 inch	23.5 inch	32 inch
Resolution	Min 1920 x 1200 Max: 3840 x 2160	Max: 1920 X 1200	Max: 3840 x 2160
Display Technology	IPS	IPS	VA
Connectivity	HDMI/DisplayPort/USB-C	HDMI/DisplayPort/VGA	HDMI/DisplayPort
Max Luminance	>=170 cd/m2	250 cd/m2	270cd/m2
Color Space (mode)	sRGB	72% NTSC (sRGB equivalent)	sRGB

Computer

As previously discussed, WSIs are large high-resolution images files, requiring significant computing power for the pathologist to view and navigate efficiently. The computer must have enough processing power for these image files to load quickly and be free from image rendering latency. When a pathologist views an image in a WSI viewer, image navigation should be smooth when panning and zooming, and the image should render without delay or pixelation. Three major components of the computer influence rending performance: the central processing unit (CPU), available random-access memory (RAM), and the graphics processing unit (GPU), and these are discussed below.

- CPU - A powerful processor is essential to efficiently process and allow manipulation of digital slides. Therefore, a multicore processor would be suitable for handling WSI computational demands.

- RAM - WSI software requires a significant amount of memory to load and manipulate the high-resolution digital slides. Additional RAM is therefore preferable as it allows smooth performance, especially when multiple slides are being viewed simultaneously at high magnifications.
- GPU - A dedicated graphics card can significantly enhance the visualization and manipulation of digital slides. GPUs accelerate image rendering and provide smoother navigation, zooming, and panning within the WSI viewer software.

After reviewing the required minimum specifications of the Aperio eSM and Aperio WebViewer application and comparing the latest specifications to the standard workstations used throughout the health system (see figure 3), UCDH's IT Department determined that the standard computer specifications satisfied the Aperio's minimum requirements but lacked the recommended GPU equivalency. Therefore, with considering optimal Aperio WebViewer performance and future growth of UCDH's digital pathology technology portfolio, UCDH's IT Department recommended procuring customized workstations with specifications in (figure 3).

These advanced components were selected to ensure optimal performance throughout the workstation's expected useful life of five years. Moreover, UCDH IT determined that all the workstation monitors should be the same size so as to reduce eyestrain and support user ergonomics. Furthermore, with vendor financial incentives and to minimize support-related issues due to mismatched display resolutions, UCDH IT was able to procure two diagnostic displays per workstation, thereby providing pathologists with an acceptable visual experience when viewing digital slides. Moreover, workstations utilizing multiple displays with varying dimensions and resolution specifications are known cause flickering and scaling issues. To address the differences in resolutions, the computer operating systems often apply scaling, which

can sometimes result in blurry or pixelated visuals with some application menus and dialogue boxes. Scaling can also affect the way applications and fonts appear, potentially causing readability problems.

Attending Pathologist were provided an opportunity to test a demonstration digital pathology workstation, so they could decide on opting for two or three display configuration for their office.

Figure 3

Comparing Workstation Specifications

Workstation Specifications Comparison			
Component	Leica Minimum	Standard UCDH PC	Digital Pathology PC
CPU Processor	Intel i7	Intel i5	Intel i9
Hard Disk Space	10GB Free	250GB Total	500GB Total
Memory (RAM)	16GB	8GB	32GB
Network Card	1GB	1GB	1GB Dual
Video Card (GPU)	NVIDIA Quadro T2000 equivlient (4GB dedicated)	Intel Integrated Graphics	NVIDIA RTX A2000 (6GB dedicated)
Support Number of Displays	N/A	2 Display Port, 1 VGA	4 Mini Display Port

Figure 4

Demonstration Digital Pathology Workstation

Figure 5

Digital Pathology Workstation Deployed in Pathologist Office

Slide Processing Impact to Image Quality

Some validation studies discussed in the literature review reported diagnostic discordance due to image quality issues related to glass slides preparation. Even though the validation performed by UCDH's Pathology Department did not find any major issues with image quality related to slide processing, the pathology lab is not immune to slide-processing defects. Discussed below are issues leading to poor image quality, and recommendations are made to minimize their effect or eliminate them altogether.

Events

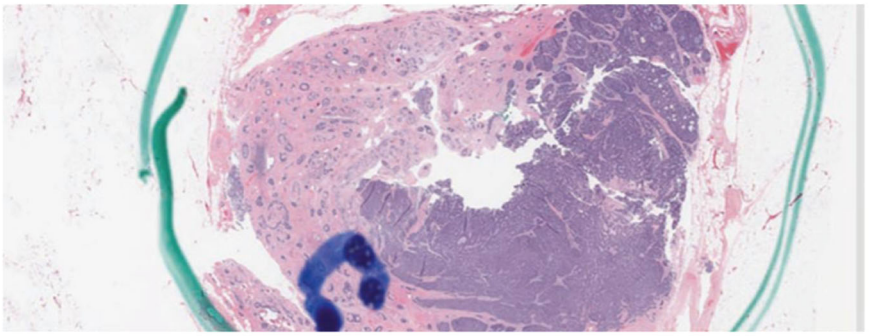
Cleaning Slides

Occasionally an attending pathologist annotates a glass slide's coverslip to highlight an area of interest of the tissue, and such markings interfere with the Aperio GT450 scanner's tissue finder and image-processing algorithms, impacting image quality by either causing portions of the slide to be ignored or degrading image quality at certain magnification levels. MoreoverTo

combat this, it is recommended that histology laboratory technicians clean every slide before they are loaded into the Aperio GT450. Techs should clean slide by using large a large cellulose soft tissues sheet with one drop of isopropyl alcohol. This cleaning process will also ensure that tissue-mounting media and stain residue are removed from the slide. Mounting media can also build up on the automated handling components of the GT450, and so cleaning this off of slides increases the time interval between maintenance and minimizes service repairs, decreasing scanner downtime.

Figure 6

Slide Annotated with a Sharpie and Excess Mounting Material

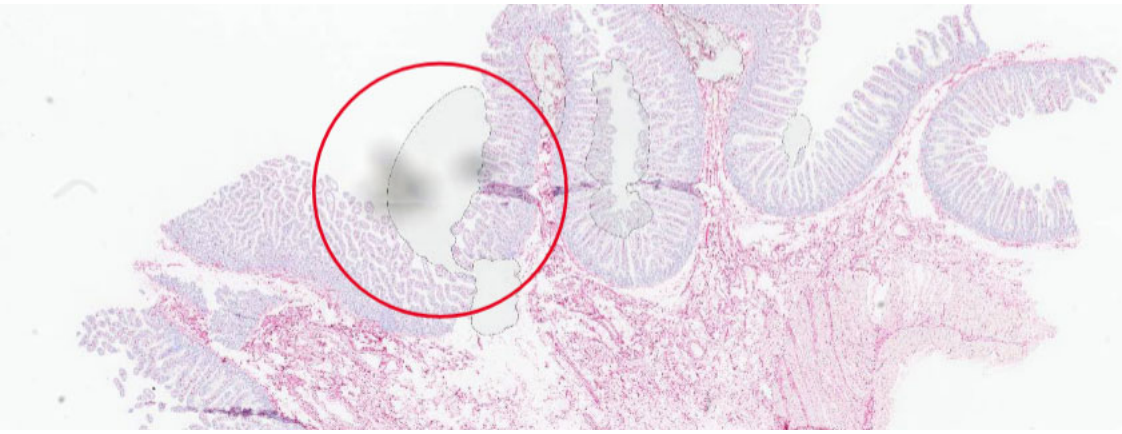


Tissue Mounting on Physical Slides

Tissue that is placed on the extreme edges of a glass slide can affect the digital slide's image quality. Moreover, when the tissue reaches the edges of the slide, the Aperio GT450 image processor may omit a portion of the tissue when rendering the digital image. Tissue placed on the edges of the slide may interfere with the slide coverslip and prevent full formation of a seal, allowing introduction of foreign artifacts between the tissue and coverslip and thereby degrading image quality. To prevent this situation, it is recommended that tissue-mounting standards based on proper specimen tissue mounting techniques be formulated and lab technicians trained in these.

Figure 7

Example of Foreign Artifact



Use of Incorrectly Sized Slide Labels

As with tissue placement, the slide label can also interfere with formation of an optimal coverslip seal on the tissue. The surgical pathology lab prefers large slide labels, since these have more surface area on which patient demographics and stain protocols can be printed. Unfortunately, all but one set of staining instruments are validated to process slides having a large-size label. Due to the instrument's automation and slide-handling clips, slides with large

labels will not achieve an optimal coverslip seal, possibly leading to not only the potential to introduce foreign artifacts but also impacting the quality of the tissue staining, thereby potentially degrading the quality of the digital slide and causing improper staining of the tissue. Therefore, it is recommended that slide labeling standards be formulated and the staff educated in proper label size usage and that advisories be posted on the label printer specifying what size of label should be used.

Slide processing quality does not end with the slide's being scanned by the Aperio GT450. Histology technicians should log in to the IMS and visually view each slide image to confirm the image's quality is optimal. As previously discussed, TAT is an extremely important consideration in any surgical pathology laboratory. The pathologist assigned to a case may not review the digital slides for hours or days, and, therefore, if digital image quality issues prevent the pathologist from rendering a diagnosis, TAT will be significantly impacted due to the wait for the glass slides to be delivered to the pathologist or reprocessed and/or rescanned. Any impact on TAT will delay critical results to the patient's care team, potentially adding delays with starting necessary treatment.

Image Viewer Experience

As discussed in the literature review, the image viewer is one of the most important components of a DP system. As in the case for UCDH's Pathology Department, the Aperio WebViewer becomes the pathologist's microscope and so must provide a seamless transition from reading a slide under traditional microscopy. Moreover, every aspect of the DP system between the IMS (Aperio eSlide Manager) and the image viewer (Aperio Viewer) needs to considered, as these can significantly affect the rapidity and ability of the pathologist to sign-out a case. For instance, at UCDH's initial implementation of its Aperio eSlide Manager and

WebViewer, user experience was unsatisfactory with respect to the WebViewer's display of slide order.

In a traditional microscopy workflow, a case's physical slides are assembled into a slide tray and placed in order of block and then slide ID (see figure #8). Surgical pathology cases can contain multiple specimen parts, which are placed on cassettes (tissue blocks) and assigned an alphabetical value. As these blocks are sliced to create slides, each tissue slice mounted on a slide is assigned a sequential numeric slide ID. A pathologist reads cases in block and then slide order to track and understand what slides are being read. When a pathologist opens a surgical case in Aperio eslide Manager, Aperio WebViewer mimics the slide book. Unfortunately, the eSM software version lacks the capability to sort slide order of block and slide ID, slides were displayed in order of acquisition by the GT450.

It was initially suggested to scan slides in order of block and slide ID, but that was quickly determined to be impractical due to the histology lab's processing workflow. Furthermore, if a slide was ordered to be rescanned due to reprocessing or scan quality, the rescanned slide would break the desired sorted view within the WebViewer. Following negotiations with the vendor, UCDH was placed on the Aperio eSM version 12.5 early adopter list, and this version upgrade included functionality to sort slides within the Aperio WebViewer. Approximately after a year after the initial implementation, UCDH implemented Aperio eSM 12.5 version and configuring the Aperio WebViewer sorting defaults to display slides in ascending order by case number, then block ID, and then slide ID. Pathologist satisfaction with Aperio WebViewer increased immediately after the Aperio eSM upgrade.

Figure 8

Example of Slide Tray

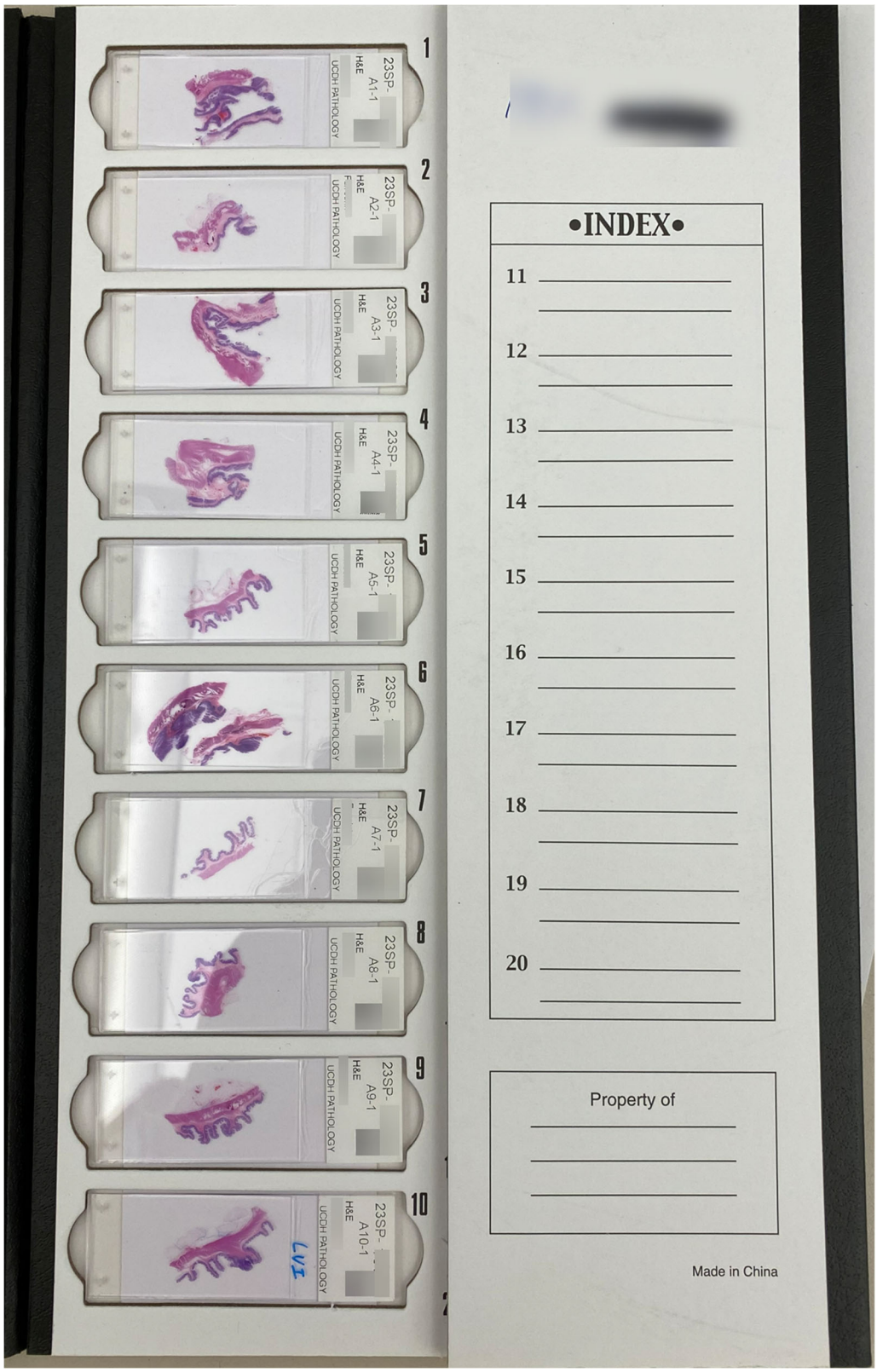


Figure 9

Aperio WebViewer Without Slide Sorting Feature

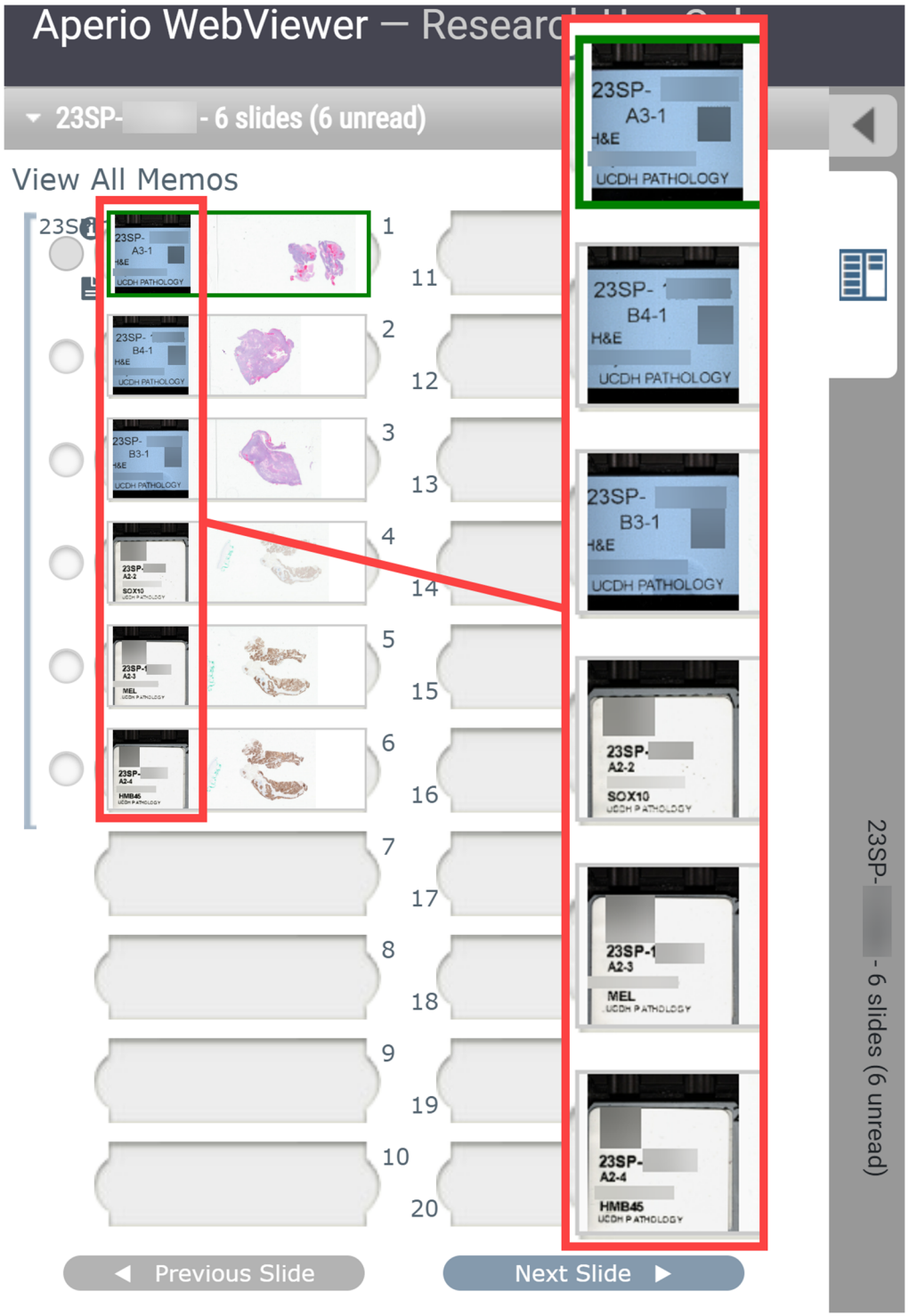
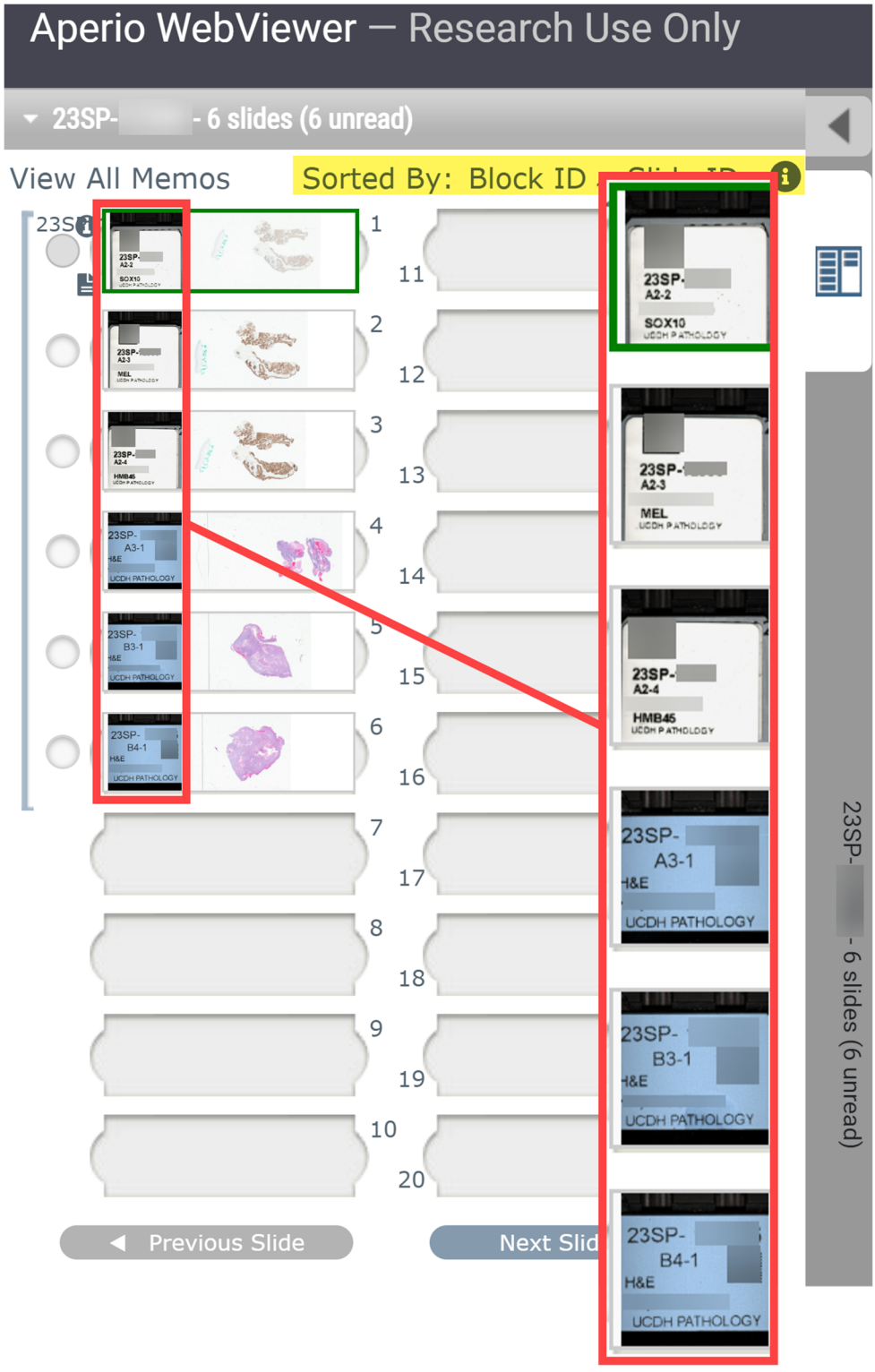


Figure 10

Aperio WebViewer with Slide Sorting Feature Enabled



Training Sessions (Pre-Validation and Continued Education)

Among the validation studies discussed in Chapter 2, only a few discussed requiring participants to attend training prior to reading digital slides. In any laboratory-instrument or clinical-application implementation, user training is an integral part of the project's success and user acceptance. UCDH's Pathology Department selected a mix of training types and formats, including vendor lead training and organizational lead follow-up training, in order to solidify the nuances of UCDH Pathology's laboratory workflow.

UCDH Pathology selected two distinct stakeholder groups to receive training, of both operators and pathologists, with training material and format designed specifically for each of the two groups. The operator groups consisted of histology technicians and pathology assistants who are primarily responsible for loading glass slides into the GT450. The pathologist group consisted of surgical pathology attendings and AP faculty on clinical service who could potentially sign-out cases digitally. Prior to the delivery of the Aperio GT450, both groups received Leica-created training materials to familiarize themselves with the basic components of the Aperio GT450, eSlide Manager, and WebViewer.

The operator group training was conducted once the GT450 system was operational, and the pathologist group training was scheduled for six weeks later. This scheduling gap allowed histology to scan live case slides to build the digital library, so that participants of the pathologist training group could be trained in real-world examples. Moreover, this lead time allowed histology to become more familiar with the GT450 and provided UCDH's IT Department to create workflows and training documentation. Detailed information regarding each group's training is discussed next.

Operator Group

Vendor-led operator training was conducted onsite shortly after delivery and successful configuration of the GT450 within the UCDH's IT environment. Leica representatives began each training session with a PowerPoint presentation providing an overview of the Aperio GT450 system. The presentation included slide preparation pitfalls that can lead to poor image quality and scanner errors. Leica representatives continued training with a live demonstration of the physical operation of the GT450. The demonstration included identifying all physical components of the GT450 and loading glass slides into the GT450. Further demonstrations covered preventative maintenance topics and simulated scenarios triggering scanner errors and providing troubleshooting steps needed to resolve these issues.

Leica concluded each training session by having each participant open and close the GT450 service cover, so that each participant would know how to resolve a scanner error. Shortly following the vendor-led training sessions, UCDH's Pathology Department held internal follow-up training sessions designed to cover the standard operating procedures (SOP) related to daily GT450 maintenance, case slide scanning methodology, eSM workflows, and slide preparation quality assurance.

Pathologist Group

Vendor-led pathologist training was conducted onsite and virtually, two 90-minute sessions were offered for scheduling convenience. The training sessions covered basic eSM navigation and focused heavily on the features and functions of the Aperio WebViewer. As with operator training, Leica representatives began each session with a PowerPoint presentation providing an overview of the Aperio GT450 system. Live demonstrations were then covered,

including basic navigation within the Aperio eSM application, case search, flagging of individual slides for virtual tumor boards, and advanced searching workflow to retrieve flagged slides.

The remaining hour of training focused the feature and components of the Aperio WebViewer. The main objective of the training was to demonstrate how the WebViewer's navigation controls are analogous to the controls of a conventional microscope. Pathologists were shown the general layout and toolbars of the Aperio WebViewer, and demonstrations of the Webviewer's tools (listed below) using live patient slides. Vendor-led training concluded with a question and answer session, in which each participant demonstrated that he or she was able to log into the Aperio eSM environment and open a case with the WebViewer.

The following controls were covered:

- Zoom: Allows adjustment of the magnification level to view different parts of a virtual slide in great detail.
- Pan: Enables movement to the viewable area of the slide, allowing navigation around the entire scanned tissue.
- Focus: Adjusts the focus on the virtual slide to bring specific areas into sharp focus.
- Annotations: Allows for adding, editing, or removing annotations on the digital slide to mark important features or make notes.
- Measurement: Enables measuring distances, areas, or angles on the slide for quantitative analysis. Measurements can be left as annotations, allowing other pathologist to view should interobserver/collaboration be needed.
- Slide Navigation: Provides options to quickly jump to specific areas or slides within a multi-slide scan.

- Thumbnail/Overview: Offers a thumbnail (macro image) of the entire slide, allowing quick navigation to specific regions of the digital slide.
- Magnifier: A small, movable magnifier window that shows a zoomed-in view of the area around the cursor, a useful tool for detailed inspection.
- Image Adjustments: Controls for adjusting brightness, contrast, and color balance to optimize the visualization of the slide.
- Image Capture: Allows user to take a static high-resolution snapshot of the digital slide, to include in sign-out reports or presentations for various purposes.
- Conferencing: Allows sharing the digital slide with colleagues in real-time, each participant can take navigation control and make annotations; this is useful should interobserver/collaborations needs
- Multiple Slide View: Allows for multiple slide images to be displayed simultaneously, enabling comparison and increased efficiency.

Post-Implementation Surveys

In the literature review, some of the validation studies indicated that complex cases read digitally require peer review and collaboration for rendering a diagnosis (Gage et al., 2013). Another validation study utilized focus groups to review and discuss complex cases after the validation study (Fine et al., 2008). Moreover, the focus group discussed factors that interfered with participant's diagnostic analysis, related primarily to degraded digital image quality related to glass slide preparation defects. The feedback thus obtained was taken back to the lab to develop process improvements to mitigate slide preparation quality issues. One validation study recommended ongoing continued education to review diagnostic concordance between physical

and digital images, in an effort to increase efficiency and pathologist buy-in to digital sign-out of cases (Gui et al., 2012).

Therefore, under the recommendation and direction of the UCDH Anatomic Pathology Chair, a Digital Pathology focus group was created. Five lead attending pathologists were selected to initially review slide scan quality of surgical pathology biopsies scanned by the GT450. A Microsoft Teams channel was created so that each focus group member could record slides with image quality issues or instances when a pathologist had difficulty achieving a timely diagnosis. The Teams channel included a tracking spreadsheet for a pathologist to record the case number, slide ID, image quality issue, and additional notes. The AP Department Chair met weekly with the focus group to discuss findings, while comparing physical and digital images to determine if slide preparation had led to poor image quality.

Feedback was given to the AP lab manager and lab supervisor to make various process improvements to slide preparation in order to improve digital image quality. Moreover, several of the validation studies reviewed suggested pathologist efficiency and comfort with reading digitally would improve overtime. Therefore, it is recommended that the UCDH Digital Pathology focus group conduct quarterly pathologist training workshops. Another possibility is that the workshop could review a complex case that was difficult to be signed-out digitally. The workshop could thus serve as a forum to discuss ways to mitigate issues related to why the case was difficult to read digitally. Determinations could be made as to whether the issue related to improved slide preparation or utilization of different slide staining protocols. Moreover, if the complex case could be properly viewed with image adjustment within the Aperio WebViewer, the workshop could demonstrate proper use of the image calibration tools to achieve a timely and accurate diagnosis.

Display Color Calibration

Several of the reviewed validation studies found that the display used to read WSI did not emulate the color balance of viewing glass slides under conventional microscopy. Although, a display's color balance did not lead to diagnostic discordance, it contributed to slower read times, either due to difficulty identifying certain cell structures or differentiating tissue types. Since UCDH did not purchase an FDA-approved WSI system and procuring self-calibrating displays was significantly cost prohibitive, UCDH Pathology requested additional quality assurance controls than the standardized 4k diagnostic display selected for DP workstations.

Prior research has also suggested that ambient room lighting can diminish the digital slide image, reducing the effective contrast. This can be problematic if the display is placed in a room with natural light, as natural lighting changes throughout the day. However, the effect of color accuracy on diagnostic accuracy in digital pathology is not known (Wright et al., 2020). Therefore, there is a need to optimize digital pathology display screen environments for making reliable observations. The University of Leeds has developed the point-of-use quality assurance (POUQA) tool for remote assessment of viewing conditions for reporting digital pathology slides. A software for ensuring quality assurance, standardization, and error detection in interpretation of digital pathology images, POUQA was rapidly developed in response to the need for pathologists to sign-out cases remotely during the COVID-19 pandemic. The University of Leeds and Ohio State University used POUQA to test and ensure image quality of the pathologists' displays at their homes (Lujan et al., 2021). The POUQA tool is a software with the purpose of ensuring quality assurance, standardization, and error detection in the interpretation of digital pathology images. UCDH Pathology intends to use the following five components of the POUQA by implementing the following:

1. Assessment Tools: The POUQA tool encompasses various assessment tools to evaluate WSI quality. The tools will allow each attending pathology to check focus, resolution, color accuracy, and presence of artifacts or errors. By systematically examining these aspects of a digital image, pathologists can identify potential issues that may affect the accuracy of interpretation.
2. Standardization: The POUQA tool helps maintain standardized image quality across different digital pathology systems. It provides adjustments and corrections that pathologists can apply to align the images with predefined quality standards or guidelines. These adjustments may involve optimizing brightness, contrast, color balance, and other image settings to ensure consistency and comparability.
3. Error Detection: The POUQA tool aids in the detection of errors or artifacts that may be present in digital pathology images. It assists pathologists in identifying issues like blurriness, inadequate focus, compression artifacts, or color inaccuracies. By flagging or highlighting these problems, the tool enables pathologists to take corrective actions or seek further investigation to improve image quality.
4. Documentation and Reporting: The POUQA tool facilitates the documentation and reporting of image quality assessments. Pathologists can record their findings, observations, and detected errors within the tool. This documentation serves as a reference for quality control purposes and allows for comprehensive reporting of the quality assurance process.
5. Compliance and Quality Control: The POUQA tool helps pathologists comply with regulatory requirements and adhere to quality control protocols in digital pathology. It provides a systematic approach to assess and maintain image quality, ensuring that

images meet specific standards and guidelines. This contributes to the overall accuracy and reliability of digital pathology diagnoses.

At the time of writing, the POUQA tool has not been implemented. In order for the UCDH Pathology to begin using the POUQA tool, the software must be reviewed by the UCDH I.T. Evaluation Committee. The committee will evaluate the POUQA tool to ensure it meets UCDH I.T. security policies and infrastructure standards. The POUQA tool is a web based application, but is hosted on servers in country outside the United States. Therefore, the I.T. Evaluation Committee will request additional information from the developer to ensure data security and cybersecurity controls. Once the POUQA tool is approved, UCDH I.T. will work with the AP Pathology and Pathology Informatics Chair to develop a protocol for use of the POUQA tool. However, we'll describe the fundamental framework of the protocol while it's still being developed (see Appendix G).

Each attending surgical pathologist will be provided with a POUQA Profiler account, they will login to the system and proceed to the POUQA Pathology system.

Part 1: The Test

Pathologist will be required to read four letters displayed in colored boxes, the letters should be barely visually discernable. The Pathologist will then type these letters the corresponding input boxes. The Pathologist will check two toggles to indicate if they are working clinically and at home. The pathologist will click to submit their answers, for the tool to determine if the display passed the test.

Part 2: The Result

Once the test is complete, the Pathologist will be presented with either a success or failure message. A successful result will generate an access token and an option to copy test information

to the computer's clipboard. The Pathologist will paste the test information to a Microsoft Teams SharePoint repository for auditing purposes. However, if the pathologist receives a failed result, they will be asked to reattempt the POUQA test. Moreover, the POUQA tool precents the Pathologist from taking the test more than three times in a row. The pathologist will have to wait 20 minutes to retake the test, during this time the Pathologist should make the necessary adjustments to improve ambient lighting in the room. Whether that be closing outside window shades, dimming overhead lights, or removing artificial lighting directly reflecting on the displays.

Future Implementation and Suggested Enhancements

LIS Integration

During the completion of this paper, UCDH Pathology requested UCDH I.T. to begin implementing an LIS integration with Aperio eSlide Manager (eSM). An LIS integration with the Image Management System (in this case Aperio eSM) will allow the pathologist to launch digital slide images directly from the EMR. Therefore, the pathologist will no longer need to manually search for the surgical pathology case with Aperio eSM. By eliminating these steps, it will result in fewer clicks and navigation to retrieve digital slide images, improving pathologist efficiency and ease of use. The integration will require significant planning amongst clinical stakeholders, because the project includes UCDH's Dermatology Lab, as they share the same LIS and Aperio eSM instance with UCDH's Surgical Pathology Lab. Moreover, the integration project will require several interdisciplinary UCDH I.T. teams to carefully plan, design, build, and test a proof-of-concept to ensure all workflows are accounted for. Significant user-acceptance-testing will also be required, to ensure the integration functions accurately and it

meets the needs of the clinical stakeholders. The LIS integration project is tentatively scheduled to go-live at the end of 2023.

Increasing Throughput

As mentioned previously in the digital pathology workflow section, UCDH Pathology prefers to present the complete surgical pathology case to the assigned attending pathologist. Meaning, once the pathologist is assigned to a case, they are provided with all the prepared glass slides associated to the case. However, since UCDH Pathology only possess one WSI scanner (GT450) it is near impossible to scan an entire resection case with its corresponding biopsy slides. Moreover, possessing a single GT450 adds strain to Histology and IHC workflows and staffing schedules. Surgical Pathology cases requiring IHC special stains require various processing times based on staining protocols ordered. Histology staff may finish preparing IHC slides when the GT450 is fully loaded H&E biopsy slides. Leading to delays with the attending pathologist waiting for digital slides to become available, or potentially forcing the pathologist to complete their diagnostic analysis using both glass and digital slides. Therefore, in order to increase scanning throughput, it is recommended UCDH procure at least one additional GT450 for the Surgical Pathology Lab. Procuring an additional GT450 will not only increase scanning capacity, but it also offers redundancy in the event the primary GT450 is offline for maintenance or repair. When the scanner is offline for a significant amount of time, the entire laboratory team must failback to a traditional microscopy workflow. Switching back isn't easy, because histology and slide room staff need to perform additional job duties to assemble slide trays and track physical slides. Furthermore, attending pathologist may lose trust and buy-in with the digital pathology system, if their digital reading workflow is routinely disrupted.

Image Analysis Tools

In the introduction, it was mentioned sophisticated deep learning methods are being developed and implemented to automate routine analysis of digital pathology images. These tools will either assist the pathologist in identifying areas of interest within the tissue, or fully automate the diagnostic analysis by taking the pathologist out of the equation. It is a goal of UCDH Pathology to explore these image analysis technologies, so the team can increase efficiency and reduce pathologist caseload. As of March 2023, Paige and Leica Biosystems announced expanding their existing partnership, Paige has chosen Leica Biosystems as it preferred digital pathology system provider. Moreover, the enhanced partnership's vision is to integrate Paige's automated image analysis tools with Leica's all-inclusive GT450 digital pathology system. As details of the partnership unfold, there is anticipated costs to enable Paige's automated images analysis tools with UCDH's existing Aperio GT450 digital pathology system. Therefore, based on university policies, Paige AI and competitor image analysis tools will need to be evaluated to ensure it meets UCDH's standards and UCDH's Pathology's diagnostic needs. UCDH Pathology plans to engage with these discussions shortly after the LIS integration project is completed.

Future Discussion

With the initial phase of UCDH's implementation of its DP system complete and LIS integration project underway. The UCDH clinical pathology digital library will continue grow, while users become more proficient using the DP system. With that said, UCDH is in a very good position to upscale its DP system to enable primary diagnosis sign-outs. With the decision of procuring advanced digital pathology workstations and an implementing an IMS from a vendor that manufactures a WSI acquisition device currently under FDA validation. UCDH

could easily implement a fully validated IVR digital pathology system in a short amount of time. However, from a clinical perspective, additional consideration is needed to address workflows to transition to a fully digital sign-out model.

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Appendices

Appendix A

Example – Post-Validation Survey Example (Hanna et al., 2019)

Post Validation Survey Example

1. Approximately how many years have you been practicing pathology?

2. How many years of experience do you have using digital pathology? (in any capacity)

3. Rate the digital pathology slide viewer.

4. Rate your satisfaction with the launching of slides from within the laboratory information system.

5. Rate the quality of the digital slides.

6. Rate your satisfaction with the performance in navigating the digital slides.

7. Would you be interested in testing different input devices (i.e., other than a mouse) to navigate digital slides?

8. How would you rate your overall digital signout experience?

9. How comfortable would you feel signing out digitally, for routine clinical practice?

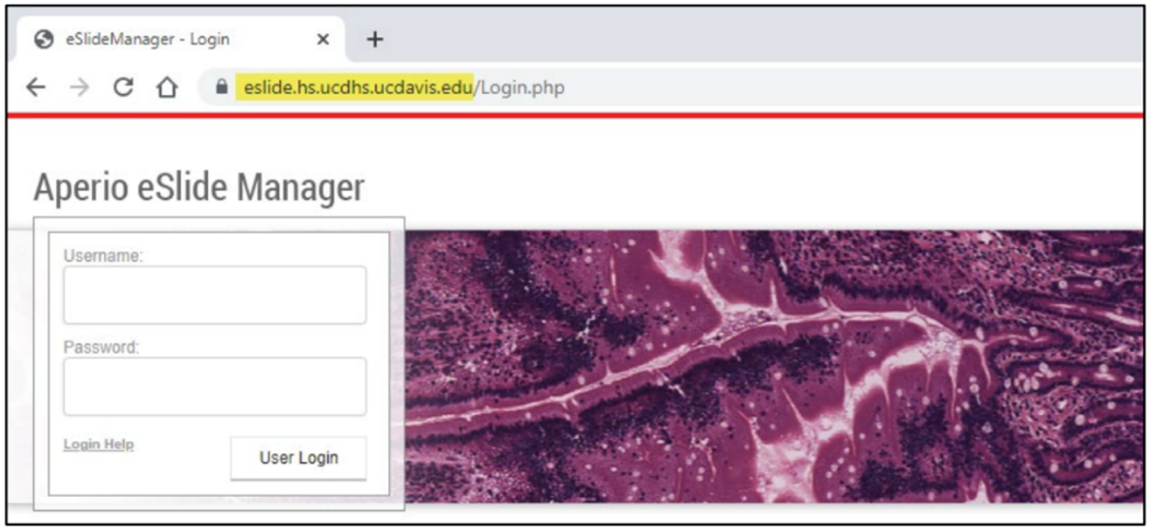
Appendix B

Aperio eSlide Manager Basics

APERIO ESLIDE MANAGER (CLINPATH) HOW-TO'S

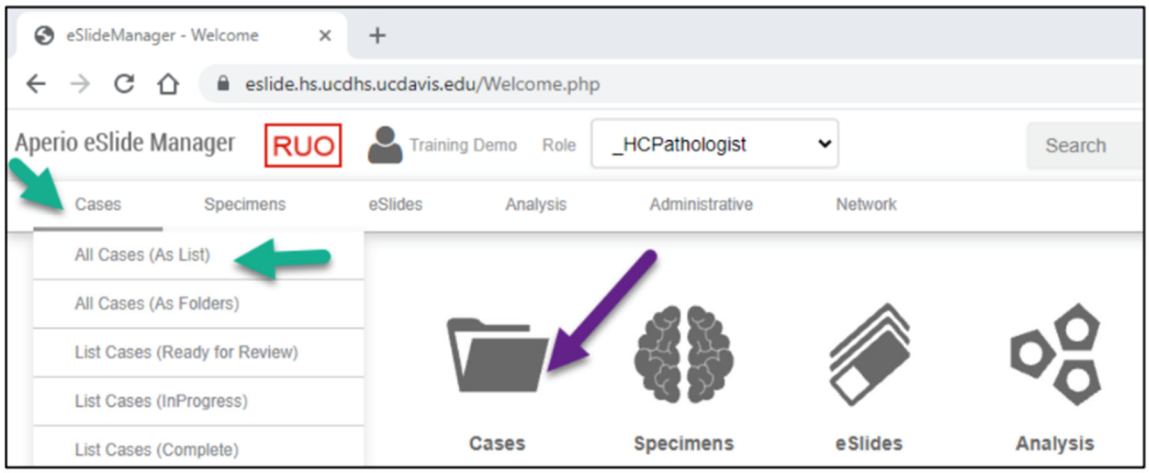
HOW TO LOG IN:

1. Navigate to: https://eslide.hs.ucdhs.ucdavis.edu/
2. Type your Health System (HS) credentials to login (Windows/Citrix/HS Apps)
3. Click "User Login"
4. Click "Continue" for Research Use Only prompt



HOW TO SEARCH FOR A CASE:

1. Click "Clinical"
2. ➔Click "Cases" ***-or-*** ➔Click "Cases" then> "All Cases (As List)"

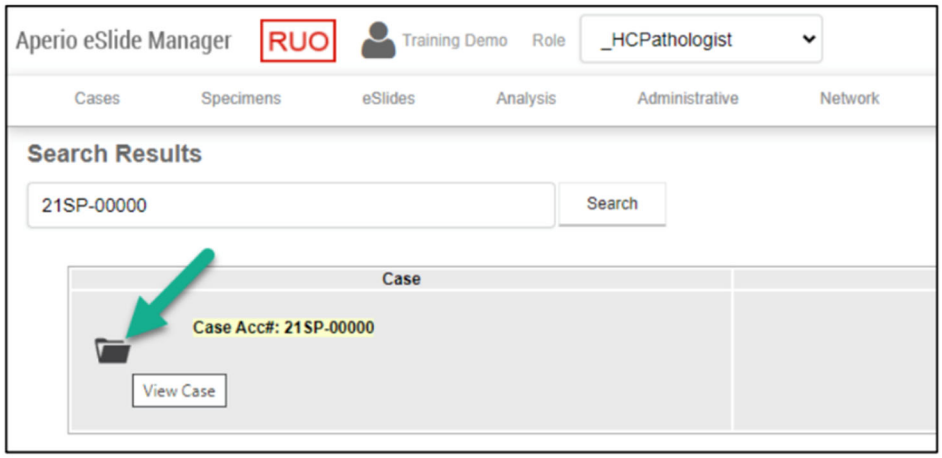


HOW TO SEARCH FOR A CASE (CONT):

3. Find the Search box near the upper left corner of the screen

4. Searching for case by typing the exact case ID found in Beaker, *e.g. 21SP-00000*
5. Hit "Enter" **-or-** Click on the magnifying glass icon

6. Search Results Appear… Click on the folder icon underneath Case column



7. Case Details appear… Upper left corner of screen, click on the eye icon to view the slide images

Appendix C

Aperio eSlide Tumor Board Assignment Training Tipsheet

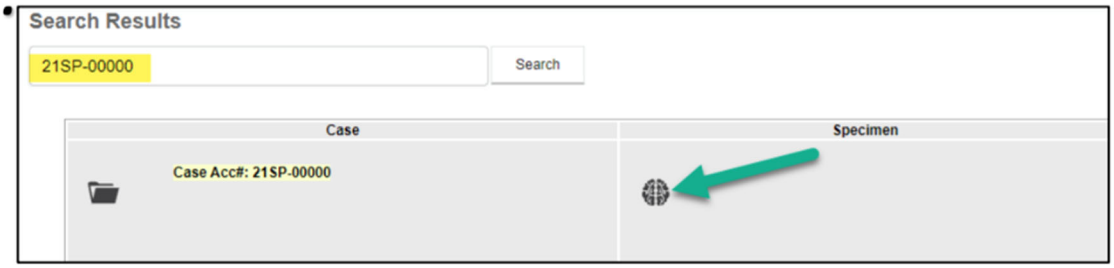
APERIO ESLIDE MANAGER (CLINPATH) HOW-TO'S

HOW TO ASSIGN A SLIDE TO A TUMOR BOARD:

*For Clinical Aperio eSM Instance: https://eslide.hs.ucdhs.ucdavis.edu/

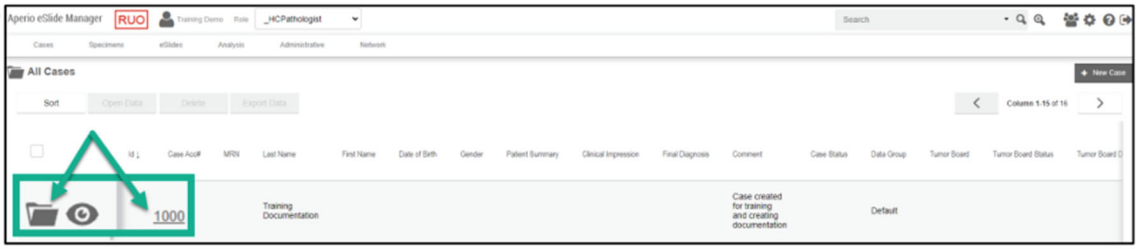
1. Locate the case to be assigned to a Tumor Board either:
   a. Via typing the case/assession ID in to the Search box *(e.g. 21SP-00000)*
      [See tip sheet "HOW TO SEARCH FOR A CASE:"]
   b. *Via the All Cases (As or List)*
2. Via the Search Results, click on the Brain icon under Specimen

a.

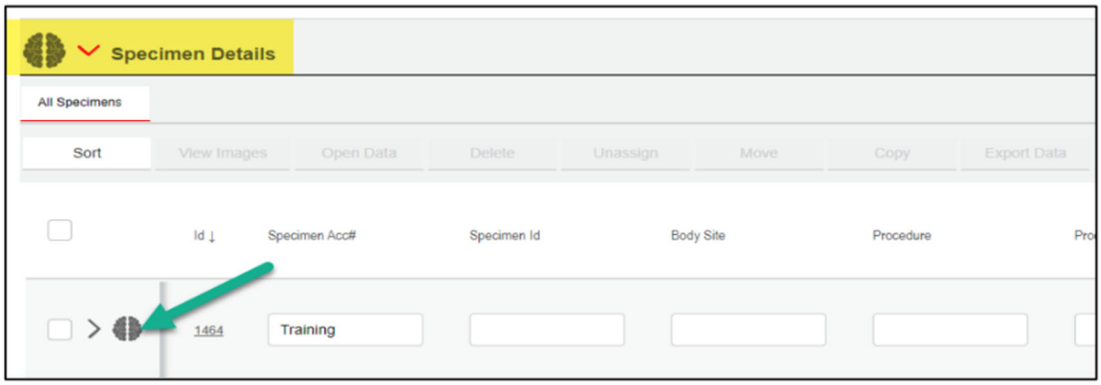


-OR-

b. Via the All Cases (As or List), click the Folder icon, or the case ID hyperlink

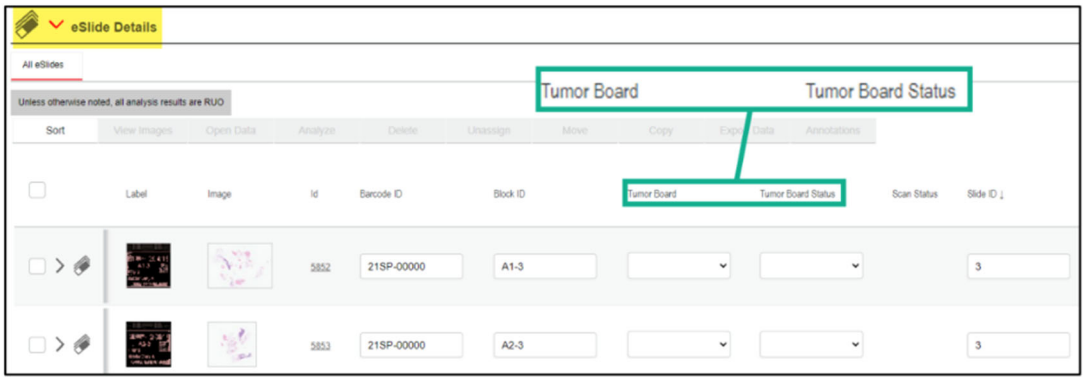


Within the Case, scroll down to Specimen Details, click on the Brain icon under Specimen Details



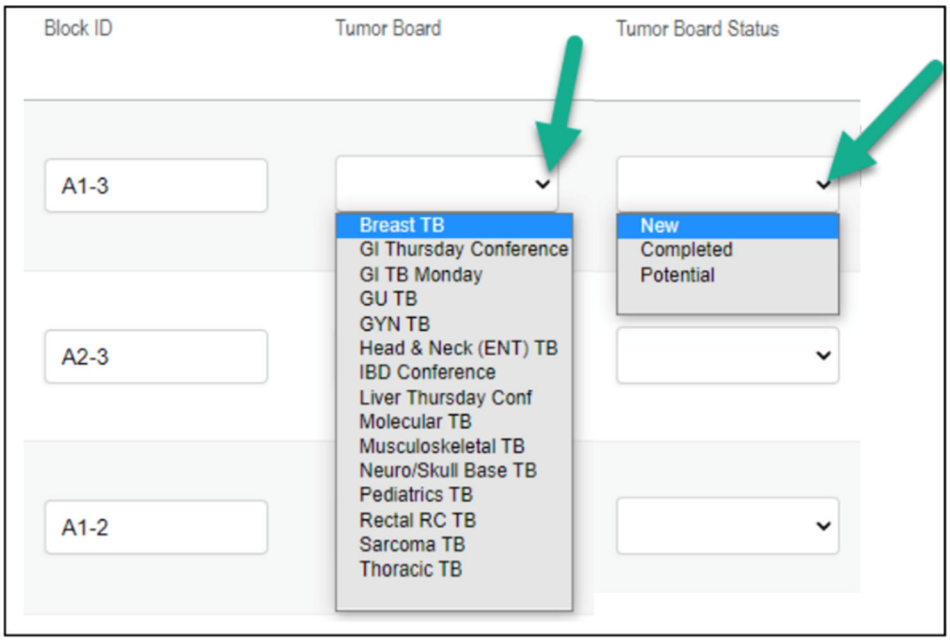
HOW TO ASSIGN A SLIDE TO A TUMOR BOARD (CONT):

3. Scroll down to eSlide Details
4. Locate the Tumor Board and Tumor Board Status columns

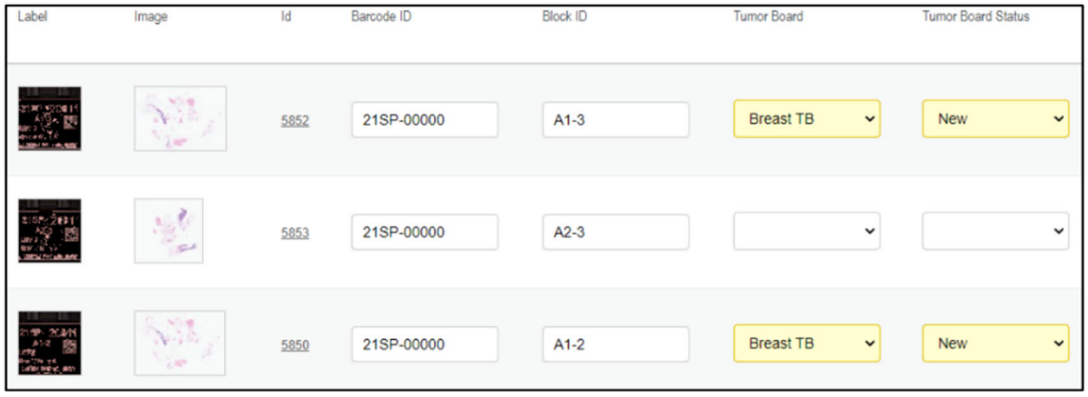


5. Select the appropriate Tumor Board name using the Tumor Board dropdown
6. Select "New" in the Tumor Board dropdown

** Do this for each slide being presented at the Tumor Board…

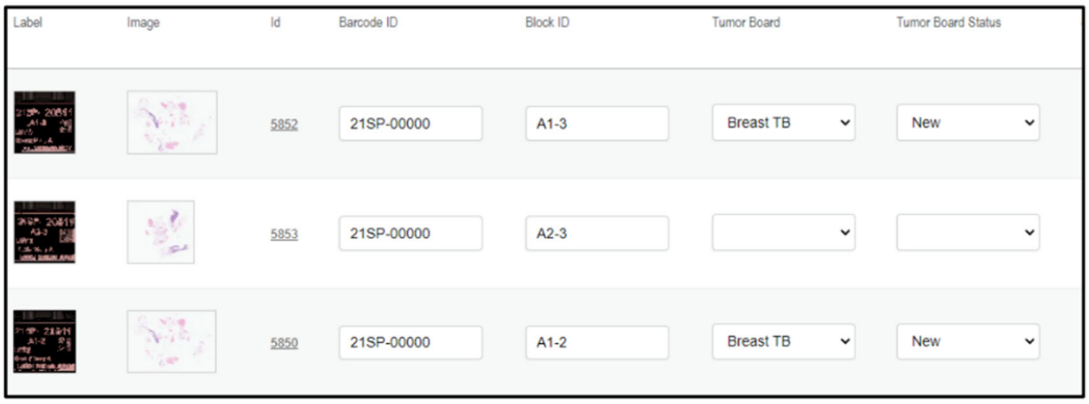


HOW TO ASSIGN A SLIDE TO A TUMOR BOARD (CONT):



7. Save you changes! Bottom right corner of screen, click "Save" to 'You have unsaved changes'

Tip: After you click "Save", fields you made changes to will no longer be highlighted



8. Use the Search field to locate your next case, or return to the All Cases (As List)

Note: Retrieval of Tumor Board slides will be covered in HOW TO USE ADVANCED SEARCH tip sheet

Appendix D

Aperio eSlide Manager Advanced Search

APERIO ESLIDE MANAGER (CLINPATH) HOW-TO'S

HOW TO USE ADVANCED SEARCH:

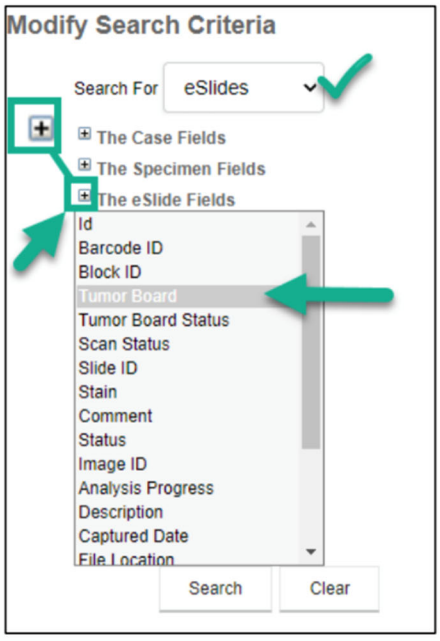
*For Clinical Aperio eSM Instance: https://eslide.hs.ucdhs.ucdavis.edu/

Example: Using Advanced Search to locate slides for assigned to a Tumor Board

1. Login into eSlide Manager
2. Click Clinical Icon *(if prompted)*
3. Click Cases Icon

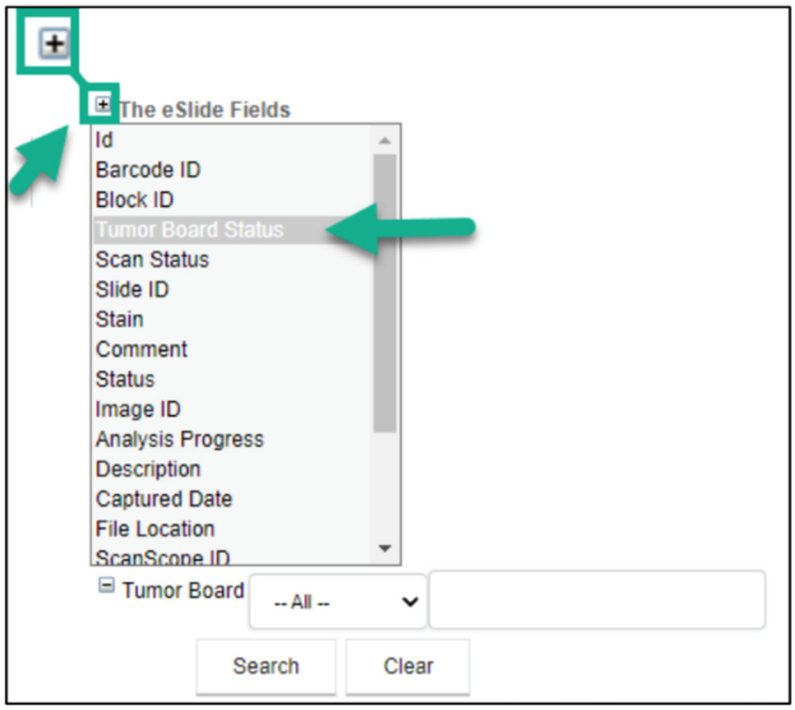
4. In the upper left portion of screen, find the Magnifying Glass Icon with the Plus.

5. Under Modify Search Criteria, confirm **eSlides** is selected in the 'Search For' dropdown
6. Click the Plus Sign next to 'The eSlide Fields' to expand the field/column chooser
7. Select the **Tumor Board** field/column

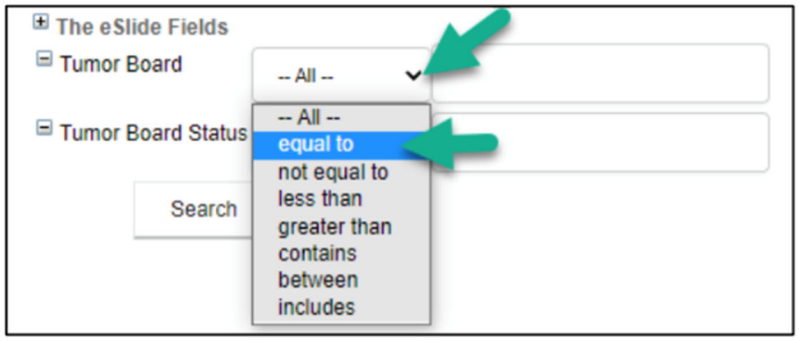


HOW TO USE ADVANCED SEARCH (CONT):

8. Click the Plus Sign next to 'The eSlide Fields' to expand the field/column chooser again
9. Select the **Tumor Board Status** field/column

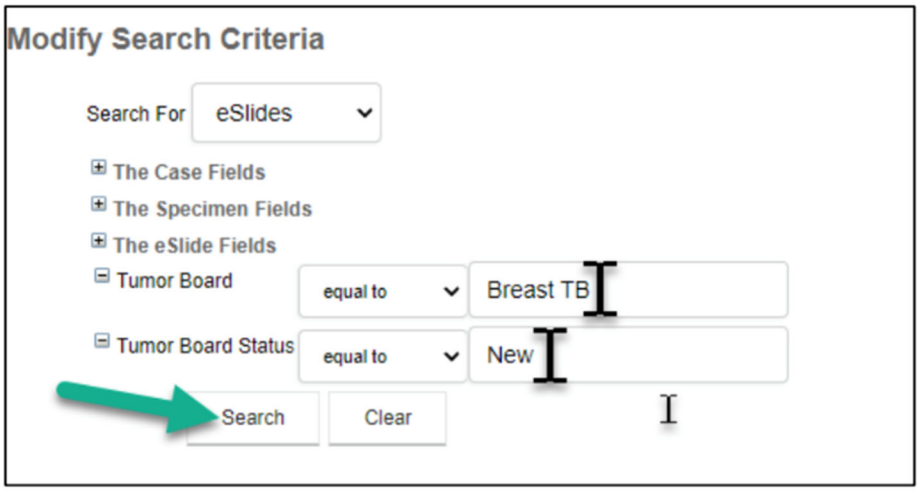


10. In the dropdown next to both fields, select equal to

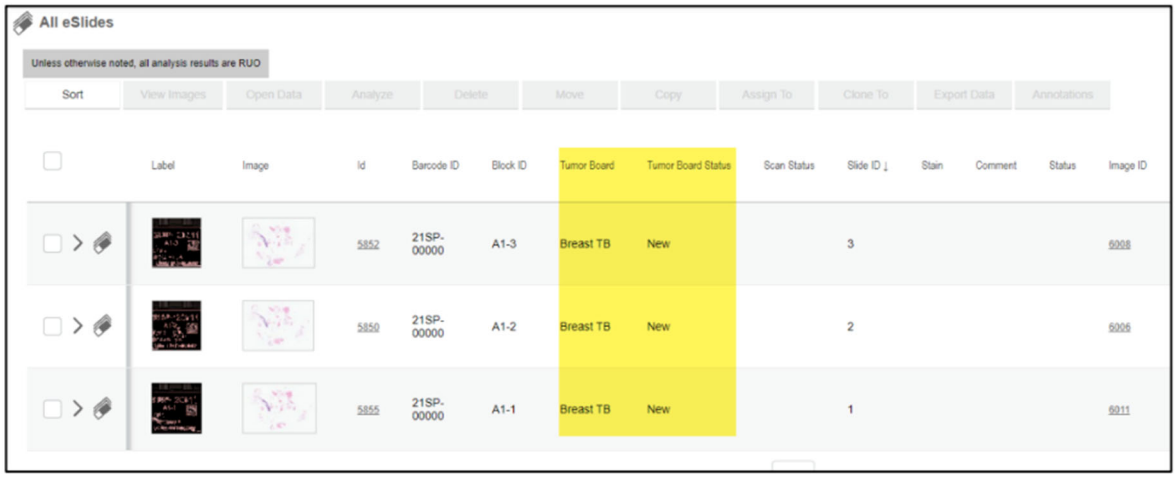


11. In the text field next to each field/column, type:
    a. Tumor Board equal to: Tumor Board name, for this example **Breast TB**
    b. Tumor Board Status equal to: **New**
       ***Helper text will appear to select the correct name*
    c. Click Search

HOW TO USE ADVANCED SEARCH (CONT):



The Advanced Search will return All eSlides that are flagged as: Tumor Board = Breast TB -and- Tumor Board Status = New…



12. Now you've tested your Advanced Search, **before exiting**, let's save the search!
    (See the next section for steps)

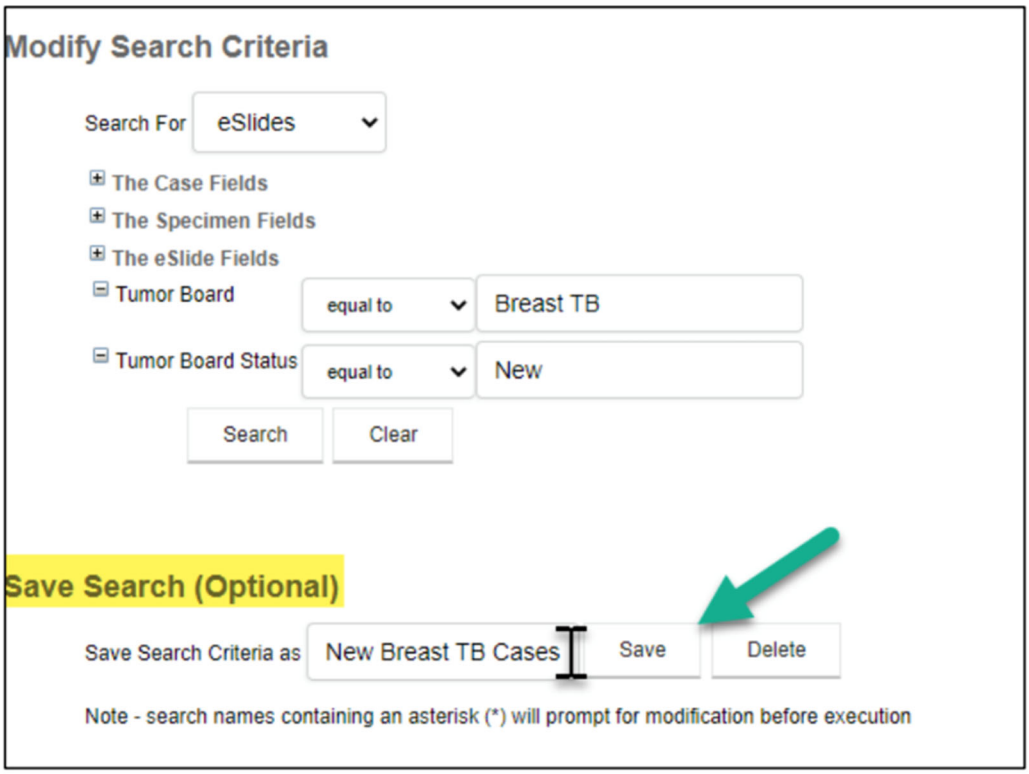
HOW TO SAVE A ADVANCED SEARCH

1. In the upper left portion of screen, find the Magnifying Glass Icon with the Plus.

2. The application will retain your previous search criteria, if you do not navigate away from All eSlides list. However, if you don't see your criteria, you'll need to rebuild it.

3. Save your search by naming it by something easy to identify… Under the Save Search (Optional) header, type your chosen search name in the field next to 'Save Search Criteria as' for this example **New Breast TB Cases**

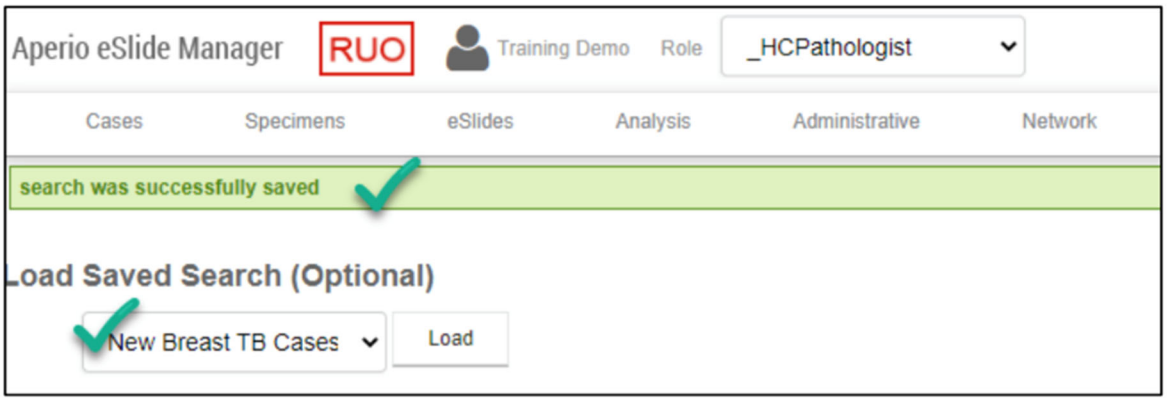
4. Click Save



Pro Tip: You can create a new saved search using one of your existing saved searches… Select a saved search with the similar criteria, make your criteria adjustments, and save it with a new name.

HOW TO SAVE A ADVANCED SEARCH (CONT)

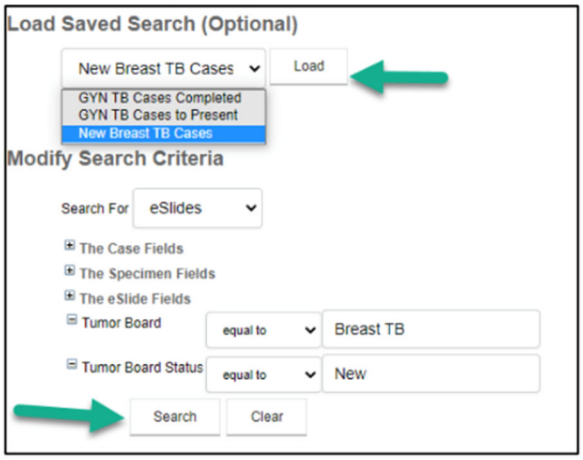
5. The application will confirm the search save successfully…
   You'll see a green banner indicating "search was successfully saved" and your saved search in the dropdown under the Load Saved Search (Optional) header.



HOW TO LOAD A ADVANCED SEARCH

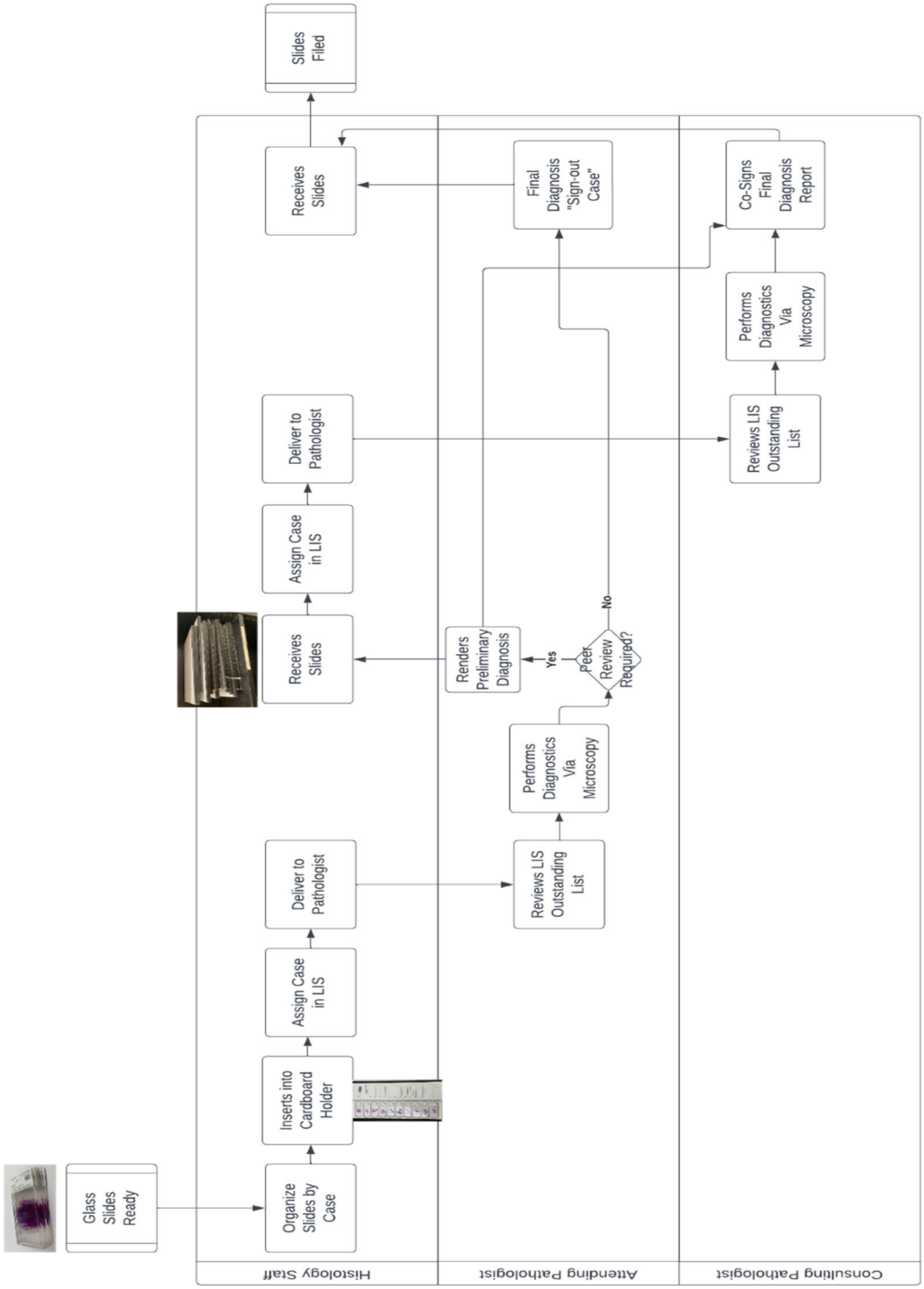
1. To load a previously saved search…
   Click on the Magnifying Glass Icon with the Plus (upper corner of screen)

2. Under the Load Saved Search (Optional) header…
   Select the saves search in the dropdown, click Load
3. Click Search



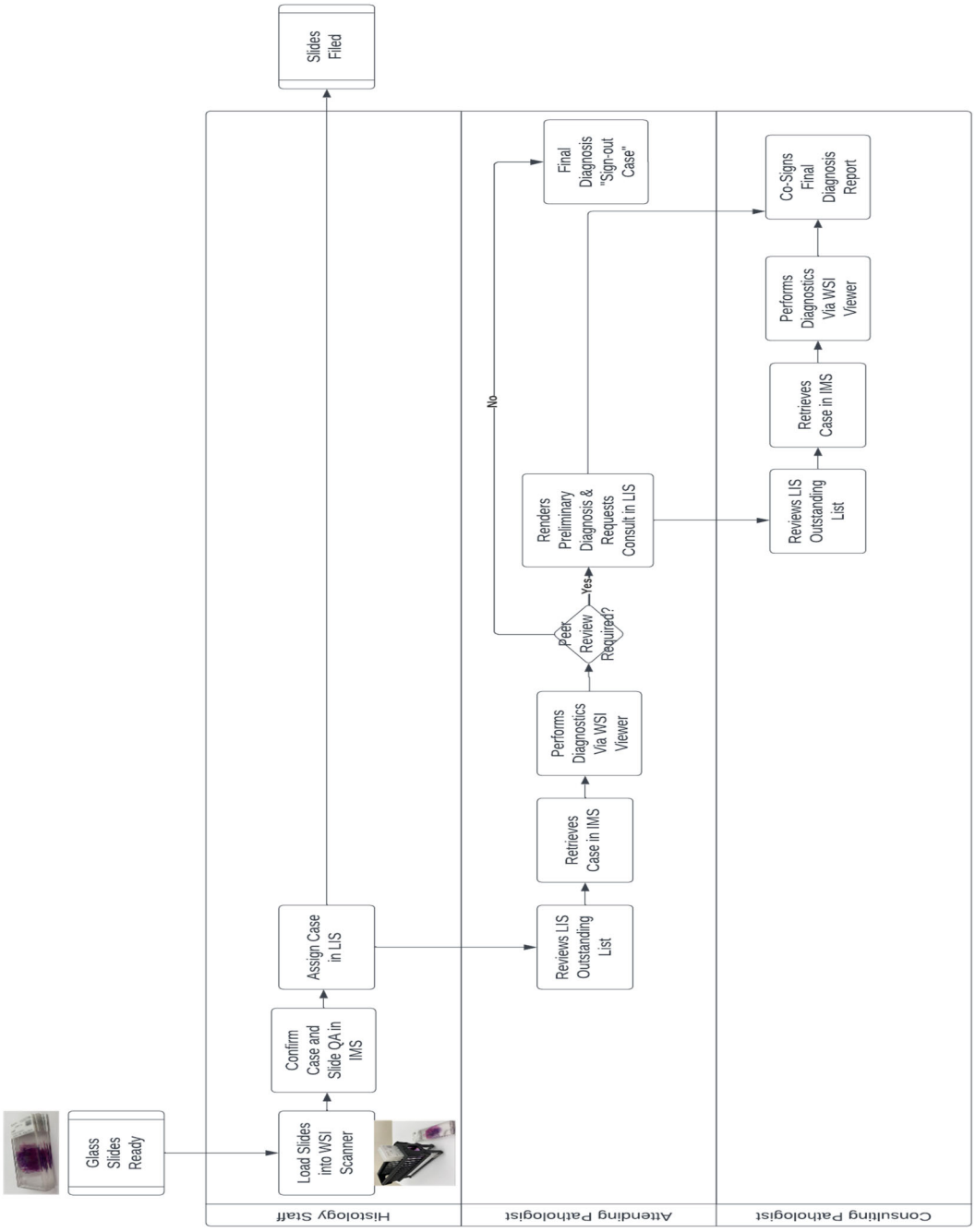
Appendix B

Swim Lane Workflow Diagram Prior to Digital Pathology Implementation



Appendix C

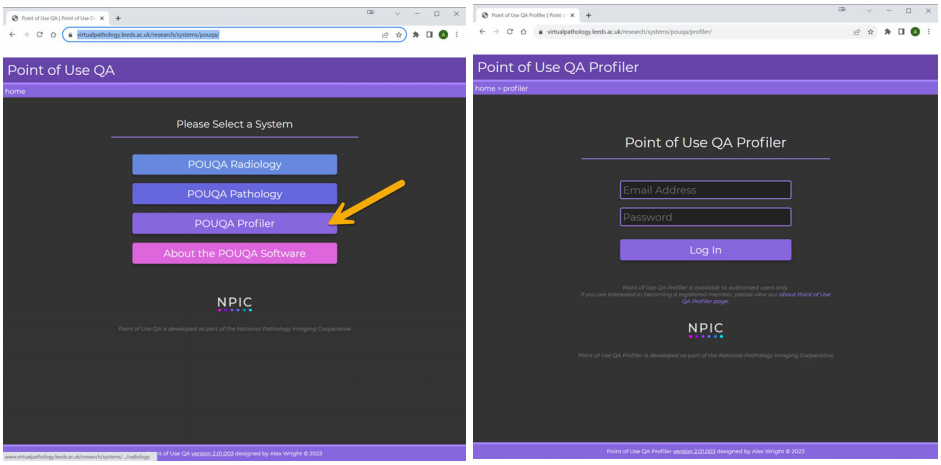
Swim Lane Workflow Diagram Post Digital Pathology Implementation



Appendix F

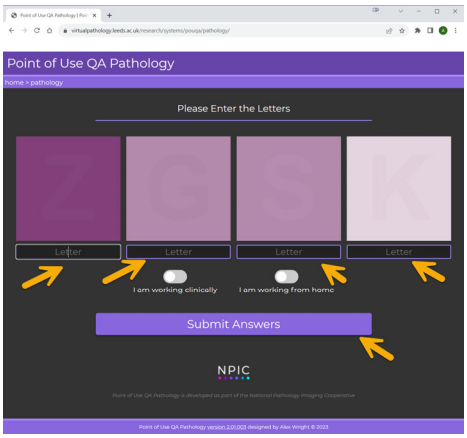
POUQA Display Calibration Protocol

Each attending surgical pathologist will be provided with a POUQA Profiler account, they will login to the system using the following URL: https://www.virtualpathology.leeds.ac.uk/research/systems/pouqa/ and proceed to the POUQA Pathology system.



Part 1: The Test

Pathologist will be required to read four letters displayed in colored boxes, the letters should be barely visually discernable. The Pathologist will then type these letters the corresponding input boxes. The Pathologist will check two toggles to indicate if they are working clinically and at home. The pathologist will click to submit their answers, for the tool to determine if the display passed the test (see figure).

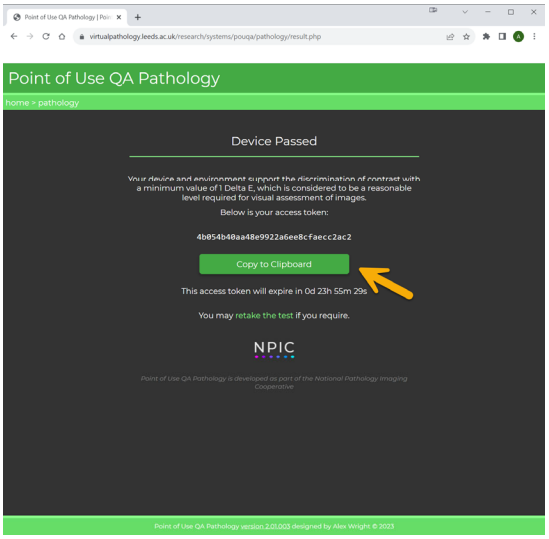


Part 2: The Result

Once the test is complete, the Pathologist will be presented with either a success or failure message. A successful result will generate an access token and an option to copy test information to the computer's clipboard. The Pathologist will paste the test information to a Microsoft Teams SharePoint repository for auditing purposes. However, if the pathologist receives a failed result, they will be asked to reattempt

the POUQA test. Moreover, the POUQA tool precents the Pathologist from taking the test more than three times in a row. The pathologist will have to wait 20 minutes to retake the test, during this time the Pathologist should make the necessary adjustments to improve ambient lighting in the room. Whether that be closing outside window shades, dimming overhead lights, or removing artificial lighting directly reflecting on the displays.

Example of Successful Result:



Token Example:

University of Leeds Point of Use QA tool | Version: 2.01.003 | Date: 2023-08-24 | Time: 18:01:36 | Token: 4b054b40aa48e9922a6ee8cfaecc2ac2 | Valid Until: 2023-08-25 18:01:35 | IP address: undefined | Display Height: 1440 | Display Width: 2560 | Display Colour Depth: 24 | Display Pixel Ratio: 1.5.

Example of Failure Result: