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The California Telepathology Service: UCLA's Experience in Deploying a Regional Digital Pathology Subspecialty Consultation Network

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Abstract

Background: The need for extending pathology diagnostic expertise to more areas is now being met by the maturation of technology that can effectively deliver this level of care. The experience and lessons learned from our successfully deployed International Telepathology Service (ITS) to a hospital system in China guided us in starting a domestic telepathology network, the California Telepathology Service (CTS). Many of the lessons learned from the ITS project informed our decision-making for the CTS. New challenges were recognized and overcome, such as addressing the complexity and cost–benefit tradeoffs involved in setting up a digital consultation system that competes with an established conventional glass slide delivery system. **Methods:** The CTS is based on a hub-and-spoke telepathology network using Leica Biosystems whole-slide image scanners and the eSlide Manager (eSM Version 12.3.3.7055, Leica Biosystems) digital image management software solution. The service currently comprises six spoke sites (UC San Diego [UCSD], UC Irvine [UCI], UC Davis, Northridge Hospital Medical Center [NHMC], Olive View Medical Center [OVMC], and Children's Hospital Los Angeles) and one central hub site (UCLA Medical Center). So far, five sites have been validated for telepathology case consultations following established practice guidelines, and four sites (UCI, UCSD, NHMC, and OVMC) have activated the service. **Results:** For the active spoke sites, we reviewed the volume, turnaround time (TAT), and case types and evaluated for utility and value. From May 2017 to July 2018, a total of 165 cases were submitted. Of note, digital consultations were particularly advantageous for preliminary kidney biopsy diagnoses (avg TAT 0.7 day). **Conclusion:** For spoke sites, telepathology provided shortened TAT and significant financial savings over hiring faculty with expertise to support a potentially low-volume service. For the hub site, the value includes exposure to educationally valuable cases, additional caseload volume to support specialized services, and improved communication with referring facilities over traditional carrier mail. The creation of a hub-and-spoke telepathology network is an expensive undertaking, and careful consideration needs to be given to support the needs of the clinical services, acquisition and effective deployment of the appropriate equipment, network requirements, and laboratory workflows to ensure a successful and cost-effective system.

Keywords: Digital pathology, telemedicine, telepathology, whole slide imaging

INTRODUCTION

The need for specialist pathology expertise in more areas around the world is now being matched by the maturation of technology that can effectively and reliably deliver this level of care.[1-12] Our group has successfully deployed an International Telepathology Service (ITS) in collaboration with the Second Affiliated Hospital of Zhejiang University in Hangzhou, China.[13] This collaboration began in 2010 and

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has since resulted in the sharing of over 2500 telepathology cases. The institutional experience and lessons learned gained from this enterprise guided us in the development of a new domestic telepathology network, the California Telepathology Service (CTS). This service, funded by the state of California stimulus bond initiative Prop. 1D, was designed to bring specialized pathology care to hospitals lacking specific areas of pathology expertise or underserved areas in the state of California.[14,15]

The CTS utilizes a hub-and-spoke telepathology network using Leica Biosystems whole-slide image (WSI) scanners and the Leica Biosystems eSlide Manager (eSM) digital image management software. The service currently comprises six spoke sites (UC San Diego [UCSD], UC Irvine [UCI], UC Davis [UCD], Northridge Hospital Medical Center [NHMC], Olive View Medical Center [OVMC], and Children's Hospital Los Angeles) and one central hub site (UCLA Medical Center). As of the date of this writing, five sites were fully validated for telepathology case consultations following established practice guidelines,[16-18] and four sites have commenced the service.

Many of the technical and cultural challenges that were learned and overcome with our ITS project informed our decision-making for the CTS. However, novel issues were also discovered and addressed. For example, the justification for an international collaboration is much easier to understand versus the costs and complexity involved in setting up a domestic telepathology system which competes with an established glass slide transportation system using conventional mail delivery and only offers 24 h (or less) of improved turnaround time (TAT). However, some clinical services, such as transplant nephrology which requires same-day TAT for optimal patient care, can experience meaningful benefits with improvements in TAT for preliminary diagnoses.

The CTS workflow begins when the glass slides are scanned in the spoke site WSI scanner and finishes when the pathology report is finalized in the hub site pathologist's office. By mirroring an in-house intradepartmental workflow, this system enables improved communication between the spoke-based laboratory technicians and the hub-based pathologists to do tasks such as request additional stains or discuss aspects of specimen handling even before the case is signed out.[1] This communication saves time and does not usually happen with conventional outside case consults.

The challenges and value of establishing a domestic multihospital telepathology service must be considered from the viewpoint of both the hub site and spoke sites, and the cost–benefit analysis of deployment needs to be considered for both entities.[19,20] For the spoke sites, telepathology offers shortened TAT versus carrier mail consultations and significant financial savings over hiring faculty with expertise to support a potentially low-volume service. For hub sites, the value includes exposure to educationally valuable rare cases, additional caseload volume to support specialized services,

and improved referring laboratory communication versus traditional carrier mail.

It is critical to partner with a vendor who is committed to working through the entire development process which includes novel problem-solving and the ability to accommodate the different needs of each spoke site and the hub site. The vendor is expected to install the necessary equipment at each site, train the appropriate personnel, conduct regular maintenance, and offer 24/7 technical support for this clinical service. This included the willingness to swap out originally purchased equipment with more service-appropriate hardware when appropriate. During these episodes, it was very helpful for the vendor to offer accommodating solutions that enabled us to move forward and complete site setup.

METHODS

Each of the six spoke sites received a 5-slide capacity WSI scanner (Leica Aperio CS2) and a local server to store the images generated at the time of scanning. Each site is connected to the central hub server via a 325 Mbps business-to-business virtual private network connection using encryption hardware (Cisco ASA5540, Cisco Systems, San Jose, California).[21]

The system uses data groups to organize images for each site, including the hub site. Each user is assigned a specific role that determines access permissions at a group and individual level. Permissions for each role to access data groups are restricted to prevent users from different sites from accessing another site's images or case metadata.

The diagnostic consultation workflow starts when a spoke site pathologist submits a case to the CTS hub for a second opinion. A trained technician who has the user role of "Dispatcher" scans the slides on the local WSI scanner and submits the case for consultation to the hub data group. The hub site can access the spoke site case only after the hub data group is assigned the consultation. At that point, the data group association changes from a site-specific data group to a shared data group with the UCLA staff who then have access to the case and the associated WSIs. The WSIs are then replicated to the central hub and available for viewing at UCLA shortly after the scanning is complete. Importantly, cases can also be sent from the hub to any spoke site for consultative purpose.

When a case is received at the hub, eSM generates an email addressed to the outreach case accessioners at the hub site. This email notifies the accessioners who can access the case directly through a hyperlink in the email. The case is accessioned, per standard (glass slide) outside case accessioning protocol, and assigned to the appropriate pathology service. However, *in lieu* of glass slides, the case is distributed to the service via an email notification, and the case will also appear in the pathologists' case assignment queue in the hub Laboratory Information System (LIS) (Epic Beaker at UCLA). The WSIs are also available through a case hyperlink in the LIS [Figure 1]. The WSIs are manually added to the case in Beaker at the time
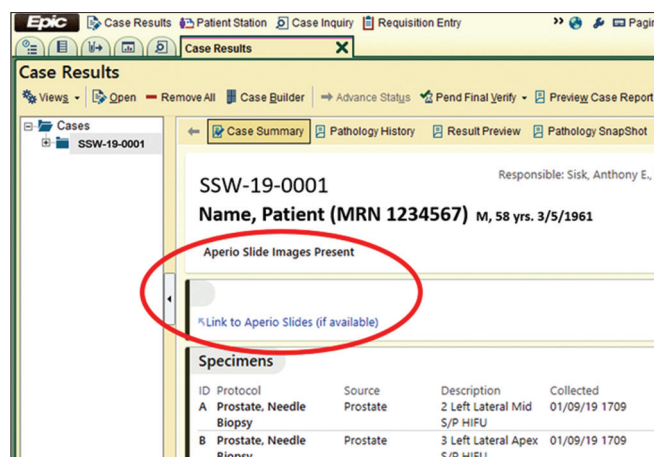
Figure 1: Hyperlink to digital case slide images in Laboratory Information System

Figure 2: Adding digital consultation case in eSlide Manager at the hub site

of case accessioning simply by entering the full pathology case accession number into the hub site accession number box in the eSM [Figure 2]. The case metadata, including clinical information and physician contact information, are entered into appropriate fields in the eSM by the submitting technician at the spoke site. This information is viewable by the hub pathologist and is transferred to the LIS case by the hub accessioner.

After the equipment and eSM software were deployed at the sites, each spoke site was connected to the CTS network, and the full eSM to LIS workflow was developed. Each site was validated based on the CAP Digital Pathology validation guidelines.[17,22] Briefly, each site submitted twenty cases, and four sites submitted five additional cases containing immunohistochemistry (IHC) stains until at least sixty cases and at least twenty IHC cases had been reviewed. The validation cases, including full clinical information and all necessary WSIs, were reviewed first by specialist service pathologists, followed at least 2 weeks later by review of the glass slides received by the conventional carrier mail. The interpretations were reviewed by one pathologist and assessed as "concordant," "minor discordance," or "major discordance." Concordance was defined as "essentially identical," minor discordance as "alternative diagnosis without clinical significance," and major discordance as "alternative diagnosis with clinical significance." Based on internal goals and the use of specialist pathologist for each case type, we defined successful validation as >95% concordant or minor discordant only.

The four sites that have activated the CTS system are UCI, UCSD, OVMC, and NHMC. All cases, except UCSD kidney cases, were first reviewed by a pathologist before scanning and transferring to UCLA. This ensures that the cases are secondary interpretations. At UCSD, the kidney cases are not reviewed by a pathologist, so the glass slides are shipped to UCLA after they had been scanned and uploaded to the hub site. Scanning the cases enables the pathologists to deliver a
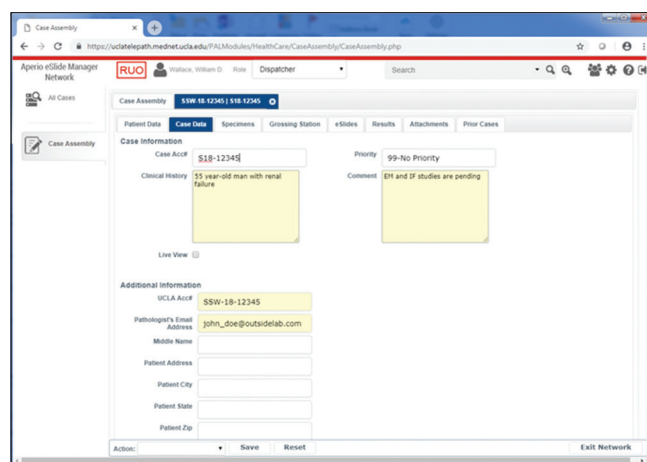
preliminary diagnosis to clinicians in time-sensitive cases.

After each spoke site went live, we reviewed the volume, TAT, and case types for each site and evaluated for overall utility.

RESULTS

Successful deployment of hardware and software followed by validation has been completed on five spoke sites, namely UCSD, UCI, UCD, OVMC, and NHMC. In total, 119 validation cases were reviewed, of which 50 were gastrointestinal (GI)/liver cases, 17 were gynecological pathology cases, 11 were bone/soft-tissue cases, 10 were heart/lung cases, 7 were head/neck cases, 6 were breast cases, 5 were nonneoplastic kidney cases, 4 were dermatopathology cases, 4 were placenta cases, 3 were genitourinary cases, and 2 were neuropathology cases. Of the 119 cases reviewed, three had minor discordances and the remaining 116 were concordant (97.5% concordance; 0% major discordance).

The CTS went live in May 2017. Cases have been submitted from UCI, UCSD, OVMC, and NHMC. Between May 2017 and July 2018, a total of 186 cases were submitted to the service, of which 124 were nonneoplastic kidney biopsies [Table 1]. Eighty-five cases were submitted from UCI, 44 cases from UCSD, 36 cases from OVMC, and 21 cases from NHMC [Figure 3]. NHMC telepathology cases were reviewed as intradepartmental consultations only.

The TAT for final sign out for all case types from all institutions, except NHMC, was 7.8 days. Eighty-one cases (all kidney biopsies) had preliminary diagnoses provided at an average of 0.7 days after accessioning at the hub site. There were a total of ten weekend biopsy reads that were provided to the treating nephrologists after the case had been assigned to the hub site but before the case had been accessioned into the LIS. The largest telepathology service was the UCI pathology service which submitted 85 cases, of which 57 were native kidney biopsies, 23 were transplant kidney biopsies, and five were liver electron microscopy (EM) cases. Preliminary diagnoses were provided for 65 cases on an average of 0.6 days after

Case type	# of cases
Kidney (native) biopsy	86
Kidney (transplant) biopsy	38
Skin biopsy	26
GI biopsy	9
Liver biopsy	6
Lung and thymus biopsy	6
Bone and soft tissue	5
Gynecologic	4
Genitourinary	2
Breast, mastectomy	1
Head and neck	1
Lymph node	1
Pancreas mass FNA	1
Total cases	186

GI: Gastrointestinal, FNA: Fine-needle aspiration

Figure 3: Digital consultation cases to UCLA from Northridge Hospital Medical Center, Olive View Medical Center, UC Irvine, and UC San Diego, June 2017 to November 2018

accessioning at the hub site, and the final diagnosis was provided 4.9 days after accessioning. The final diagnosis incorporated EM studies in the vast majority of cases. The average TAT for final sign out of the OVMC cases was 8.7 days. The NHMC Pathology Department is a satellite department of UCLA, and all telepathology consultations are received as intradepartmental consultations only. Cases are not finalized at the UCLA main campus, and there is no comparable TAT data.

The average number of slides varied based on spoke site and biopsy type. At UCI, the vast majority of cases were kidney biopsies and averaged 14.5 slides/case, including toluidine blue stains for EM. At least four slides were scanned at ×40 in most cases, and the average case size, including all WSIs and EM JPEG images, was 5670 MB. At UCSD, all case submissions were kidney biopsies and averaged 10.5 slides, including toluidine blue stains. The slides were always scanned at ×20, and the average case size was 1759 MB. At OVMC, 26 of the 36 total cases were skin biopsies; the other case types included soft tissue, bone, breast, liver, lung, GI, and pancreas. Each case averaged 3.0 slides and 724 MB in file size.

The speed of transmission varied based on the type of network utilized to transfer the image files. The CENIC network, a high-capacity fiber-optic broadband network developed in California to support California schools and universities, was used as the connection with UCI.[23] The average transmission speed was near constant at 3.3 MB/s. The network connecting to UCSD employed a dedicated high-speed channel used to back up the entire UCLA electronic health record database with San Diego-based servers. This is a high-performance network which delivered an average of 11.7 MB/s data transmission. Based on the average case size and average transmission rate, it takes an average of 28 min to transfer a complete case from UCI. The average transfer time for UCSD cases was 2 min and 30 s.
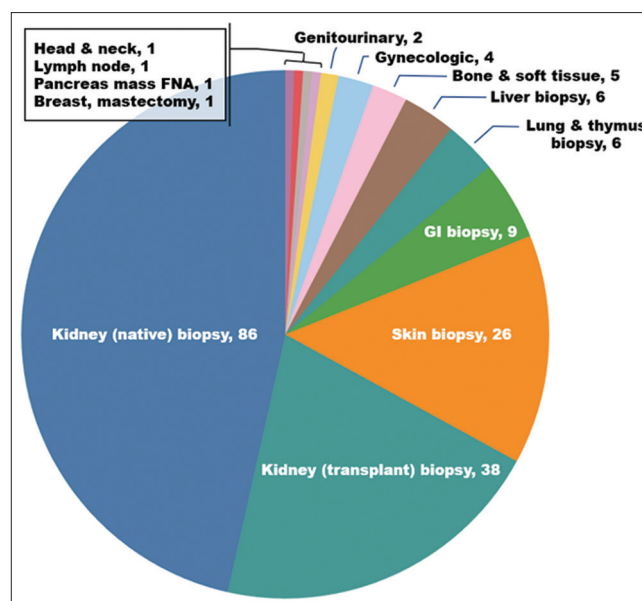
It is important to note that this includes two transmission events: the initial transfer of light microscopy slides and a second transfer step of EM material 2 or 3 days later. The OVMC data transfer rate averaged 13.5 MB/s, and it took on an average of 54 s to transfer an entire case.

In some cases, the pathologists requested review of the glass slides before final sign out. Three of the eighty kidney biopsies from UCI required review of the glass slides before final sign out. Because the kidney service for UCSD was a "primary read" diagnosis, glass slide review was required for all UCSD cases; rapid preliminary diagnoses were provided via a digital review. From OVMC, 11 of the 36 total cases required review of the glass slides before final sign out.

DISCUSSION

The creation of a hub-and-spoke telepathology network is an expensive undertaking, and careful consideration needs to be given to the appropriate equipment, network requirements, scanner locations, and pathology workflows to ensure an effective and cost-efficient system.

The first consideration before the deployment of a telepathology system is supporting the needs of the clinical services. For example, if a spoke site's clinical service needs frozen section coverage, that will impact the telepathology equipment choices and the hub site pathology workflows. For the CTS, we found that the highest case volumes were from the UCI and UCSD kidney pathology services. Kidney pathology has several unique demands. The vast majority of kidney biopsies utilize three diagnostic modalities, namely light microscopy, EM, and immunofluorescence (IF) microscopy. The TAT demands for preliminary kidney pathology interpretations can

be quite onerous and frequently require same-day or weekend diagnoses. Finally, as a service model, a telepathology service should not be considered equivalent to a conventional glass slide delivery consultation service. Telepathology technology offers the ability to facilitate improved communications with real-time WSI conferencing between remote pathologists and more sophisticated conferencing functionality. For example, the nephrology services at UCI and UCSD require monthly or quarterly multidepartmental biopsy review conferences for clinical management decision-making and educational support for their nephrology trainees. For the CTS to be an effective component of the nephrology services for UCI and UCSD, the hub kidney pathology service needed to meet these requirements by taking advantage of the conferencing solution available with telepathology. Without these accommodations, the CTS would likely be unsuccessful.

On an average, it took 28 min to transfer a case from UCI to UCLA and under 3 min to transfer a case from UCSD to UCLA. The speed of transmission enabled the kidney pathologists at the hub site to review the case and contact the treating nephrologist with a rapid preliminary diagnosis. The hub outreach accessioning staff prioritized accessioning of these telepathology cases which enabled an average preliminary diagnosis TAT of 0.7 days. On weekends, accessioning staff was not available at the hub site to accession cases; therefore, all kidney pathologists at the hub site were provided additional "Administrator" roles so that they could see cases that were submitted over the weekend and access the WSIs. This process was aided by the treating nephrologists who understood the need to inform the hub-site kidney pathologists that a weekend biopsy was imminent. During the first 12 months of the CTS, a total of ten weekend biopsies were received and preliminary diagnoses were provided. Providing preliminary weekend diagnoses with our carrier mail consultation service would require additional costs of extra weekend staffing.

EM images were easily transferred as JPEG files that were added as attachments to the original spoke-site case in the eSM. For the five liver EM-only cases, toluidine blue slides were scanned as WSIs, and the JPEG images were added as an attachment. It was important for the pathologists at the hub sites and the EM technicians at the spoke sites to have quick and easy direct communication. This was necessary for the pathologists to provide EM scoping direction in some cases and for the technicians to notify the pathologists when a delay or issue in EM processing was expected. For IF studies, carrier mail delivery of glass slides was used. The original goal of the telepathology service included scanning of IF slides; however, the throughput of the original equipment, the Leica Ariol scanner (Leica Biosystems), was insufficiently matched to the demands of our clinical service where fast TAT was required. Therefore, we worked with the vendor to trade that model for a more telepathology workflow-friendly CS2 which does not perform IF scanning. Other commercial solutions for IF scanning were considered but ultimately determined not to be cost effective or practical for our purposes.

The UCSD and UCI kidney biopsy teleconferences are a necessary clinical activity, which provide useful feedback for the hub pathologists but are time-consuming to prepare. Consideration must be given to the enthusiasm of the hub-site pathologists for participating in the telepathology service. To facilitate teleconferencing with remote sites, numerous applications are available including WebEx, Zoom Meeting, and GoToMeeting. We deployed a Cisco H.323/SIP video conferencing system that has successfully enabled multicampus participation. Monthly biopsy review conferences can be a burdensome activity; however, digital distribution and review of all cases significantly reduced conference preparation time for the hub-site pathologists.

The OVMC spoke site primarily utilized the CTS for secondary dermatopathology consultations. In these cases, the consultation question was always the diagnosis of the underlying pathologic process and not the extent of disease or lymph node status; therefore, most cases consisted of a few representative slides only. In addition, in most cases, the consult diagnosis was not time sensitive, and the complex or rare nature of the cases was challenging for the hub-site pathologists. Therefore, the average TAT was much longer than the preliminary TAT for the kidney biopsies from UCI and UCSD. Furthermore, 11 of the 36 cases required review of the original glass slides before final sign out.

The NHMC spoke site is a satellite department of UCLA and uses the same LIS. This allows the slides scanned at the NHMC to be immediately accessible through the LIS by hub-site pathologists due to the Epic Beaker/Leica Aperio interface that has been implemented at UCLA. This workflow bypasses the need to enter metadata into the eSM and the creation of a new case in the pathology LIS. The hub-site pathologists enter their intradepartmental consultation comments into the "Case Info – Notes" field in Beaker. The hub-site pathologists are notified of consult by standard communication between colleagues (e.g., phone call or secure email). The time between initial contact or hub-site response is not recorded in this workflow. However, the savings against couriering between sites is $24/trip for a total savings of $504 since implementation.

CONCLUSION

We have successfully deployed a hub-and-spoke model telepathology network in California. The deployment required considerable planning (that included spoke-site needs and hub-site workflows/capabilities), financial support from a state of California Proposition (1D), multi-institutional IT support, and an effective working relationship with the digital pathology vendor support teams. The state grant made the 2016 purchase of six WSI scanner systems and the development of an interconnected hub-and-spoke network possible. In addition to the significant initial hardware expense, the installation and setup took approximately 60 nonvendor IT person-hours at the hub and 16 to 24 nonvendor IT person-hours at each spoke site.

Given the current low total case volume received from spoke sites, the consultation revenue to the UCLA hub is not expected to recompense system costs in the short term. The per-case benefit to the hub, at minimum, is the regional Medicare rate of $93.56 for HCPCS code 88321 for a consultation and report on referred slides prepared elsewhere.[24] The benefits for the spoke sites are more significant and include considerable cost savings in salary for a specialized pathologist who would otherwise be needed to support a relatively low-volume service and savings in courier costs. The hub-site benefits include exposure to educationally valuable rare cases and an increase in case volume to support lower volume services such as kidney pathology.

Conflicts of interest

There are no conflicts of interest.

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