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## Practical Successes in Telepathology Experiences in Africa

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### Keywords

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## INTRODUCTION

Across much of Africa, there is a critical shortage of pathology services. A survey from 2016 estimated that there are more than 500,000 people per pathologist in much of the continent, with this ratio exceeding 5 million to 1 in some countries.<sup>1</sup> In large part, lack of diagnostic pathology mirrors access to other medical services. However, even in settings where specialty-level clinical care, such as medical oncology, is available, access to anatomic pathology services has often lagged behind.<sup>1–3</sup>

Cancer registries from the region reflect this problem. For instance, fewer than 20% of cancer cases were pathologically confirmed in the most recent registry from Malawi.<sup>4</sup> This discrepancy creates an untenable scenario where treating clinicians and their patients are often forced to make medical decisions without the benefit of a tissue diagnosis.<sup>2</sup> Even where pathologists are available, they often work in relative isolation with large case volumes and difficult case material. In our experience, cytology, dermatopathology, hematopathology, and pediatric pathology, all of which may require subspecialty training beyond residency in the United States, often represent a disproportionate percentage of cases.

Digital telepathology has been touted as a tool to help overcome the pathologist shortage in Africa, and some successful examples have been reported in the literature.<sup>5–10</sup> Such

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programs are generally supported by international collaborations between hospitals or medical schools in Africa and institutions in the United States or Europe.

In broad terms, there are four basic platforms for telepathology: (1) static images, (2) whole-slide scanning, (3) dynamic nonrobotic telemicroscopy, and (4) dynamic robotic telemicroscopy.<sup>11</sup> These approaches vary dramatically in terms of instrumentation cost, information technology (IT) support, and need for local pathology expertise (Table 1). For instance, static images have the benefit of requiring limited technical infrastructure (only a microscope, digital camera, and Internet connection) but depend on appropriate selection of diagnostic fields. With appropriate training of technologists, this approach has proven effective in some centers. A particularly successful example of this approach has been reported from the Butaro Cancer Center of Excellence in Rwanda, where a static-image telepathology system was established in collaboration with Partners in Health and the Dana-Farber Brigham and Women's Cancer Center.<sup>12</sup> After an intensive training period, static-image telepathology diagnoses were 97% concordant with subsequent glass slide review. These results highlight the potential for remarkable accuracy when applying this approach to appropriately selected cases. In the published Butaro experience, hematoxylin-eosin stained slides were available for all cases, and carcinomas represented nearly 90% of all malignant diagnoses. Field selection may be more challenging when applied to cytologic preparations and hematologic malignancies.

By comparison, whole-slide imaging systems allow the consulting pathologist to see the entire specimen at a range of magnifications. However, these advantages come at considerable cost, including purchase of slide scanning equipment, increased IT support, and server space to allow data storage. Both dynamic nonrobotic and robotic telemicroscopy systems allow consulting pathologists to review slides in real-time from a remote microscope. Dynamic nonrobotic telemicroscopy is technically much simpler and involves transmission of video images across any of several Internet-based teleconference systems, such as Skype or Zoom Video Communications.<sup>13</sup> Similarly to static-imaging systems, dynamic nonrobotic telemicroscopy works best when a skilled local pathologist is available to "drive" the microscope. Although dependent on image resolution/camera quality and Internet speed, this system provides the benefit of whole-slide review at much lower cost than whole-slide imaging systems. Finally, robotic telemicroscopy, a system that allows the consulting pathologist to control the stage and objectives of a microscope remotely, has been less frequently used in low-income countries because of cost and technical challenges. However, all of these approaches have been implemented with reported success in Africa.<sup>5–10</sup>

Herein, we describe successful implementation of telepathology services to support local pathologists and clinical care, with an emphasis on our experience at Kamuzu Central Hospital (KCH) in Lilongwe, Malawi.

## **ROLE OF TELEPATHOLOGY IN OUR CLINICAL PRACTICE**

The KCH Pathology Laboratory opened in 2011 as a collaborative effort between KCH, the Malawi Ministry of Health, and the University of North Carolina at Chapel Hill (UNC).<sup>2,3</sup>

Two years later, we initiated a telepathology program using whole-slide imaging on the Aperio Digital Pathology System (Leica Biosystems, Buffalo Grove, IL) to support local pathologists, clinical care, and research efforts. Technical details of this system are outlined in the next section.

At KCH, biopsies and cytology specimens are submitted to the pathology laboratory, which is directed by a Malawian pathologist and provides basic cytology and histology processing, and a limited panel of manual immunohistochemical (IHC) stains.<sup>3,10</sup> Cases are initially reviewed by local pathologists, who generally communicate an initial impression to clinicians, often after ordering supporting IHC stains.

In difficult cases, and before enrollment in UNC-affiliated research studies, slides are then scanned and loaded to a secure server, which collaborating US pathologists access via a virtual private network connection. Once each week, Malawi-based clinicians and pathologists present these patients at a telepathology conference, which is attended by local providers and their counterparts in the United States (Fig. 1). After discussion and frequently after additional rounds of IHC stains, a consensus diagnosis is rendered by the pathologist in Malawi. This framework has provided critical support to the ongoing Kamuzu Central Hospital Lymphoma study. As part of that study, biopsies from all enrolled patients are shipped to the United States for final pathology review, typically after a much larger panel of IHC stains is performed. Even after incorporating additional immunophenotypic data, we have demonstrated that diagnoses rendered at the weekly telepathology conference are highly accurate (only ~5% major discordance) for guiding clinical care under local conditions.<sup>10</sup>

From inception, incorporation of telepathology into the clinical workflow at KCH has been modeled after internal multidisciplinary tumor boards, with an emphasis on consensus diagnoses reached after conversations between local clinicians, local pathologists, and US pathologists. To this end, US-based participants are viewed as collaborators, not consultants. This model is intentionally in contrast to consultative pathology services popular in the United States, where diagnoses are rendered at a remote site by an expert pathologist often without direct communication with the submitting provider.

In light of this ethos, more recently, our group has begun to experiment with alternative teleconferencing solutions, primarily using the online Zoom Video Conferencing system (Zoom Video Communications, San Jose, CA). When coupled to a microscope-mounted digital camera, this system allows dynamic telemicroscopy driven not by the US-based collaborating pathologist (as would be the case in robotic telemicroscopy) but by local pathologists in Malawi. Although of this system is in its infancy in our program, potential advantages include a primary role for local pathologists in the conference, and lower up-front capital costs (mostly limited to the cost of a digital camera).

## TECHNICAL INFRASTRUCTURE

The success of the UNC Project Malawi weekly telepathology conferences largely relies on a thoughtfully developed technical infrastructure and a dependable Internet connection. The

KCH Pathology Laboratory houses the complete Aperio Digital Pathology System on site, which includes a ScanScope CS slide scanner, workstation CPU, and image server. The images of the scanned slides are stored on the image server, accessible for pathologists anywhere internationally once granted access through a username and password-protected virtual private network within our own server network.

Approximately 10 to 15 cases with 5 to 10 distinct slides are reviewed weekly. For histologic sections and immunohistochemical stains, the slides are scanned at  $\times 20$  magnification, whereas selected areas of cytology preparations and peripheral blood smears are scanned at  $\times 40$ . The 0.75-TB server can store approximately 2000 images in a .sis file format, which can be deleted as necessary to preserve storage space for conference. Unless specifically requested to remain accessible on the server, the 600 oldest slides are deleted from the server whenever space becomes limited. Requested images can also be stored on an external hard drive, but all slides are archived and can be rescanned at any time.

Proprietary software (Spectrum Plus, Buffalo Grove, IL) installed on the image server is used to organize cases and slide information, and viewing software (Imagescope, Buffalo Grove, IL) is freely available and necessary to open stored images. The Image-scope viewing software also allows access to a Digital Slide Conferencing feature and provides a mechanism to control and annotate the image in real time. This allows either US or Malawian pathologists to identify relevant cells or fields for discussion and control the conference as need be.

The UNC Project–Malawi employs a four-person IT team on site, with a single IT member assigned to all pathology-related work. This pathology-dedicated IT specialist typically serves as the point of contact. IT support is provided either via email to a support email address or by calling the IT support office extension. The Project uses last mile fiber for its Internet connectivity. All internal connections within the building are either through a CAT 5e or 6 ethernet cable capable of a 100 Mps–1 Gbps connection. We are currently receiving 8 MB on a ratio of 1:1. In addition, we use networking tools that allow control of bandwidth usage, primarily a Barracuda Web Filter 410 (Campbell, CA) that allows the IT team to prioritize bandwidth based on work-related Internet traffic. This Internet connection is sufficient to support clear voice calls through online messaging applications and the remote conferencing system described previously (Zoom Video Communications).

## EXAMPLES OF OTHER PROGRAMS

Established telepathology systems between resource-limited settings and resource-rich academic centers have been described.<sup>5–7,9,14–25</sup> Although workflow design and specifics of implementation vary, these collaborations seem consistently effective. Representative examples of such programs are described next.

Wamala and colleagues<sup>7</sup> describe their experience with a telepathology platform between a hospital in Uganda and academic hospital in Germany. The collaborators used an Internet browser–based dynamic imaging system that provided clinical information, gross pathologic description, and a digitized microscopy platform. The remote pathologist had control of the

microscope focus, brightness, magnification, and field selection. The authors report progress from the first year of their efforts, which included the random prospective selection of 96 surgical pathology cases for review by the remote pathologist following diagnosis by the local institution. Concordant diagnosis was made for 92 of the 96 cases (97%). The average time for transmission of the images and review by remote pathologist was 10 minutes per case, and the robotic microscope controls were easy to learn by the consultants, making this platform a feasible tool for remote consultation on challenging cases.

A static-image teledermatopathology system between four hospitals in Kenya and Tanzania and Massachusetts General Hospital is reported by Gimbel and colleagues.<sup>9</sup> The local pathologists would make an initial diagnosis based on hematoxylin-eosin-stained slides alone, with the option of referring difficult cases for second-opinion review at Massachusetts General Hospital. Representative images were taken by the referring pathologists and uploaded to an online World Wide Web platform. The authors report the first 29 cases referred for telepathologic consultation. A diagnosis was made by evaluation of the static images in 22 of 29 cases (76%), with the remaining seven cases partially or nondiagnostic because of lack of IHC staining or clinical information, and inadequate image quality. Glass slides from the 22 evaluable cases were then sent to the United States to blindly assess diagnoses made by static-image examination compared with the gold standard of traditional microscopy. A comparable diagnosis was made in 91% of these cases. Their experience demonstrates that a telepathology service for providing second opinions on challenging dermatologic cases is effective using a less-expensive telepathology imaging modality.

In settings with even less capacity, telepathology may provide the only access to pathology services. Pagni and colleagues<sup>6</sup> reported on a telepathology collaboration between their institution in Italy and a hospital in Zambia that previously did not have a pathology service. This system used whole-slide imaging to allow the Italian pathologists to make remote histologic and cytologic diagnoses on a variety of anatomic pathology specimens. Following 7 months of operation, the original glass slides were shipped to Italy to establish a true diagnosis, and these results were compared with those made via telepathology. Similar to our experience in Malawi, more than 85% of final diagnoses were either unchanged or had only minor differences on final review, and in only 3% of cases did a change in diagnosis occur that would have resulted in different treatment in Zambia. Agreement was even higher for cytology cases in this series, with no treatment-relevant differences between telepathology and final diagnoses.

Although programs like this one can overcome some resource limitations, infrastructure investments are still necessary, and local technical expertise remains essential even to process specimens before scanning. To this end, the Italian program supported the training of two Zambian technologists and provided the satellite server needed for transmission of the images. This study emphasizes the potential of telepathology to provide a much-needed service to health care centers without pathology capabilities, provided that resources exist to train personnel and establish and maintain equipment and servers.

Lastly, the American Society for Clinical Pathology (ASCP) has created an initiative, Partners for Cancer Diagnosis and Treatment in Africa, bringing together a large number of

partners from academia, industry, governments, and NGOs to provide telepathology solutions that can meet the pathologist shortage in Africa today while training for future pathologists is ongoing.<sup>26</sup> The program began in 2015 with Butaro District Hospital receiving the first installation. With the advent of Food and Drug Administration approval of the first system in the United States for primary diagnosis of histology by telepathology, the role of telepathology in settings with few or no pathologists is likely to increase sharply and programs like the ASCP initiative, our Malawi program, and the previous described examples should flourish and expand to fill this major diagnostic need.

## COMMON THEMES OF SUCCESSFUL PROGRAMS

In our experience, the main common ingredients of successful programs are strong commitments by participating pathologists, clinicians, and IT collaborators.<sup>2,3,10</sup> Rendering accurate diagnoses for complex diseases in real-time across continents and time zones will inevitably encounter logistical challenges. However, these are usually surmountable, provided that participating members value the activity sufficiently to find work-around solutions. Commitments to regular real-time conferences also serve to improve communication and build rapport between team members, thereby adding incremental value to the conferences over time as they become an integral and important vehicle for improving patient care and the overall academic environment. This is not dissimilar to ubiquitous tumor boards that take place in cancer centers worldwide in higher resource settings. Other key components for successful programs include minimum computing and image capture technologies, although these can be modest and low-tech while still serving as valuable and effective conference platforms. A reasonably stable source of funding is also important to maintain and replace equipment over time as required. Finally, for our group telepathology has become vitally important as an instrument for collaboration and mentorship even beyond service provision alone. Our program's success reflects significant engagement by team members in the activity as a key local resource for bilateral scientific engagement, capacity building, and career development for junior Malawian and US pathologists.

## CHALLENGES AND OBSTACLES

Although the current system has met the need to support clinical trials at KCH, including studies sponsored by National Cancer Institute cooperative groups, there are notable challenges and limitations. Importantly, development and continued operation of the laboratory at KCH have been and remain heavily dependent on research grants. Initial renovation and equipment costs for the laboratory totaled approximately \$200,000 USD, most of which was provided through funding from the US National Institutes of Health Medical Education Partnership Initiative, AIDS Malignancy Consortium, and Division of AIDS. This initial investment included the \$85,000 USD purchase of the Aperio ScanScope system.

Annual operating costs for the KCH laboratory total approximately \$170,000 USD. Much of the laboratory's budget is devoted to salary support for employees. Equipment maintenance fees are approximately \$16,000 USD per year, including a \$4500 USD service contract for the Aperio system. Although KCH provides some support for consumable supplies in the

laboratory, all other expenses are covered by external grant sources, which are often used to cover costs of routine pathology services in the Malawi public sector even outside research studies. To ensure sustainability of our program, we are actively diversifying funding sources beyond faculty research grants, to include revenue generated by the laboratory using locally appropriate fee schedules, philanthropic and foundation sources, and development partners. Other potential funding models include the ASCP Partners for Cancer Diagnosis and Treatment in Africa, which aims to increase access to telepathology resources.<sup>26</sup>

Beyond funding concerns, technologic limitations also create obstacles for our program. Despite efforts to manage traffic, bandwidth is occasionally insufficient for smooth communication and timely loading of scanned slides. Internet service provider outages are unpredictable in the region, leading to conference rescheduling approximately every other month. Conference interruptions and inconsistencies can result in delayed patient care and treatment.

Sufficient space is available for temporary image storage, but regular purging of stored images is nonetheless necessary because of the large size of whole-slide imaging files. This can be overcome with additional hardware upgrades and purchases but financial resources are not available at this time. This limitation does lead to the unfortunate loss of a potentially valuable educational resource for local trainees and pathologists. Smaller image files, such as static photographs of representative diagnostic fields, might be more easily adapted for generation of such educational resources.

The current cost of Internet service is \$3300 USD/month for 8 MB contention at 1:1 ratio. Additional costs include the router license, the switch, and the wireless access point hardware used in the pathology building to provide access.

The Project faces extensive delays when sourcing materials is required to address repairs to the Aperio server. As with other technical skills, there are few personnel with the adequate skill set who are able to make repairs and adjustments to equipment and hardware. These challenges result in prolonged delays when maintenance is required.

We find that the magnification and image quality is sufficient to effectively and consistently evaluate histologic sections and immunohistochemical stains. However, cytologic evaluation of peripheral blood, bone marrow, and fine-needle aspirate smears can be limited with a maximum effective objective magnification of  $\times 40$ . Moreover, identifying a plane of focus is challenging for the slide-scanning instrument, particularly for bone marrow aspirate preparations.

Finally, when working in a setting with substantial technologic limitations, we find that it is imperative to take full advantage of those resources that do exist, most importantly, local clinical expertise. In our experience, the thoughtful impressions of a skilled clinician can help to overcome many resource limitations. Such observations emphasize the need for clinical context in telepathology programs and remind us to be cautious when making interpretations that counter clinical impression.

## SUMMARY

Despite limitations and challenges, the telepathology conferences have had a dramatic impact on diagnostic accuracy for direct patient care and have supported successful implementation of clinical trials.<sup>10</sup> These systems provide referral and educational opportunities for pathologists worldwide, and additionally can support quality control and improvement initiatives previously impossible in some regions of Africa. Furthermore, telepathology can make possible collaborative relationships and significant scientific opportunities for hospitals and academic institutions in sub-Saharan Africa. Groups interested in developing related processes in resource-limited settings have many options with respect to whole-slide imaging systems, digital microscopy, and conference format. However, we have found that the flexibility to deal with technical challenges and inclusion of clinicians and pathologists in weekly conferences is absolutely critical to program success.

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**KEY POINTS**

- Anatomic pathology services are lacking in much of Africa.
- Telepathology infrastructure can help support local pathology services, clinical care, and research in this setting.
- The most important features of a successful program include consistent participation of team members and reliable Internet service.

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**Fig. 1.** Pathologists, laboratory technicians, and clinicians at UNC Project-Malawi review digital slides with their US collaborators in a telepathology conference using the Aperio system. Approximately 10 to 15 cases are reviewed at these weekly conferences.

**Table 1**

Telepathology platform overview

Method	Relative Cost	Local Support	Published Examples
Static images	Low Specimen processing Microscope Digital camera Internet connection Minimal IT support	Local technical expertise: Essential: Necessary for specimen processing Local pathology expertise: Essential: Local pathologic expertise necessary for selection of diagnostic fields	Gimbel et al, <sup>9</sup> 2012
Whole-slide imaging	High Specimen processing Slide scanning equipment Internet connection Server space Substantial IT support	Local technical expertise: Essential: Necessary for specimen processing Local pathology expertise: Not essential: Local pathology less critical given whole slide scanning	Pagni et al, <sup>6</sup> 2011; Montgomery et al, <sup>10</sup> 2016
Dynamic nonrobotic teleradiology	Low Specimen processing Microscope Digital camera Internet connection Moderate IT support	Local technical expertise: Essential: Necessary for specimen processing Local pathology expertise: Essential: Local pathologic expertise necessary for selection of diagnostic fields	UNC Project Malawi (unpublished work, Robert Krystiak, MS, 2017)
Dynamic robotic teleradiology	High Specimen processing Microscope Digital camera Internet connection Robotic microscopy unit Substantial IT support	Local technical expertise: Essential: Necessary for specimen processing Local pathology expertise: Not essential: Local pathologic less critical as microscope controlled remotely	Wamala et al, <sup>7</sup> 2011

Abbreviation: IT, information technology.