International Telepathology: Promises and Pitfalls

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Key Words

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Abstract

Innovative technologies for digital imaging and telecommunications are changing the way we deliver health care. Telepathology collaborations are one example of how delivering remote pathology services to patients can benefit from leveraging this change. Over the years, several academic and commercial teleconsultation networks have been established. Herein, we review the landscape of these international telepathology efforts and highlight key supportive factors and potential barriers to successful cross-border collaborations. Important features of successful international telepathology programs include efficient workflows, dedicated information technology staff, continuous maintenance, financial incentives, ensuring that all involved stakeholders are satisfied, and value-added clinical benefit to patient care. Factors that plague such telepathology operations include legal/regulatory issues, sustainability, and cultural and environmental issues. Pathologists, vendors and laboratory accreditation agencies will need to embrace and capitalize on this new paradigm of international telepathology accordingly.

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Introduction

Significant technological gains continue to fuel the process of globalization, with direct effects on the health care industry [1]. For example, it is often easier to move images across geographic borders and across continents than it is to send biological material (e.g. tissue slides and/or blocks) or transport pathologists or patients. Thus, telepathology, which facilitates access to pathology experts around the world, continues to demonstrate considerable growth. Telepathology is of great benefit to underserved and rural areas where there is a significant shortage of pathologists. In these areas, not only is there a high demand for diagnostic consultation, but also a need for continuing education and guidance on patient management. Telemedicine in Africa has proven to be a very useful conduit of health care [2]. A review of telepathology consultation between the University of Pittsburgh Medicine (UPMC) in the USA and KingMed Laboratories in China revealed that in many cases patient management was significantly impacted as a result of expert diagnoses [3]. In recent years, international teleconsultation has grown and provided a novel source of revenue.

Over the years, there has been a plethora of international telepathology ventures. Table 1 lists several of these collaborations [4]. One of the earliest of these undertakings was iPATH, developed by the University of Basel in

Table 1. Examples of international telepathology solutions, services and collaborations

Solution/service/collaboration ('vendor')	Brief description	Website (URL)
SIMIAGIS Live Digital Pathology (smart imaging technologies)	Digital slide management software, WSI analysis applications and cloud hosting services	http://web-pathology.net/
PathForce ^{dx}	Consultation service for establishing digital pathology including slide scanner acquisition, networking and data storage	http://pathforcedx.com/
CuePath platform (InvitroCue)	Web-based platform for uploading, viewing, sharing, managing and analyzing virtual slides	http://www.invitrocue.com/en/cuepath/services/
DP3 platform (Corista)	Manages patient cases and digital images from acquisition through archiving	http://www.corista.com/
Core + console (Proscia)	Cloud-based platform for WSI	http://proscia.co/
TeleSlide TeleMedecine (TRIBVN)	Web 2.0-based platform for medical image management	http://www.tribvn.com/
ProNet (Xifin)	Online information exchange and global digital consultation network	http://www.xifin.com/pronet
Aperio ePathology Solutions (Leica Biosystems)	Hardware and software services that support sharing whole-slide images	http://www.leicabiosystems.com/pathology-imaging/aperio-epathology/
Precision digital pathology platform (Omnyx)	Hardware and software services that support sharing whole-slide images	http://www.omnyx.com/precision-platform-2/overview/
iPath	Open source multipurpose communication platform for telemedicine, distance teaching and medical knowledge management	http://www.openclinical.org/os_iPath.html
UPMC Pathology Consultation Services	US-based academic digital pathology consultation service	http://www.upmc.com/healthcare-professionals/physicians/pathology-consultation/Pages/default.aspx
Réseau en Afrique Francophone pour la Télémédecine	Teleconsultations for use in rural areas	http://www.who.int/workforcealliance/members_partners/member_list/hugraft/en/
Medical Electronic Consultation Expert System & Virtual International Pathology Institute (DiagnomX GmbH)	Medical communication platform/forum for remote telepathology, education and training using Web 2.0 technology	http://www.diagnomx.eu/portal/home.php

2001 [5, 6]. iPATH was built using open source software to service over 150 user groups around the world. This global network has enabled the examination of over 15,000 telepathology cases. MECES (the Medical Electronic Consultation Expert System), a similar international telepathology platform, exploits Web 2.0 and whole-slide imaging (WSI) technologies [7]. VIPI (the Virtual International Pathology Institute), which utilizes MECES for both data input and output, is an international, electronically based institute of pathology, which provides expert consultation, 'liable' diagnoses, and numerous additional features like automated access to reference libraries, automated measurement of images and automated language translation [1, 8]. More recently, several international telepathology networks have been established by large academic institutions (e.g. the University

Health Network in Canada, UPMC, MD Anderson in Texas and the Massachusetts General Hospital in Boston). Commercial vendors have also begun offering collaborative telepathology portables, cloud services and established business partnerships with several pathology groups (e.g. PathCentral, AccelPath, Aperio ePathAccess, Corista and XIFIN).

Technologies utilized to practice international telepathology have evolved since their inception in the late 1980s [9]. Initial efforts relied on store-and-forward systems where static images were the mainstay of image exchange. By 2001, the transplant pathology service at UPMC had accumulated experience with teleconsultation for over 3,000 static images. Digital consultation for these cases demonstrated acceptable diagnostic concordance between digital and glass diagnoses [10]. More

contemporary telepathology platforms have adopted WSI. WSI enables remote viewing in one of two ways: digital files can either be accessed on a remotely shared server owned by the host facility (or third party), or transmitted and uploaded (e.g. via a web portal) to a server that is owned by the consultant group [10, 11]. The former arrangement requires strong cooperation between medical, administrative and information technology (IT) divisions on both ends, in addition to permission to access foreign servers. The latter arrangement may result in time delays due to image transmission; however, image viewing is less likely to suffer from network delays or firewall issues. Newer platforms to support telepathology have begun using diagnostic viewers, cloud services, more open access platforms, plug-in technology and even mobile cellular devices.

Evaluation of international telemedicine collaborations in general has revealed several factors deemed vital to success [12]. These include low operating costs, utilization of simple technologies, bidirectional communication, incentive-based programs, locally responsive services, strong team leadership, appropriate training and user acceptance. Barriers to international telemedicine include legal/regulatory issues (e.g. ensuring that all parties adhere to applicable laws and international safe harbor regulations), sustainability factors (e.g. costs, inconsistent use and poor scalability), cultural factors (e.g. language, trust and limited resources) and environmental factors (e.g. IT infrastructure, network limitations and time zones). It is anticipated that many of the current obstacles will likely be addressed as technology advances and standardization of international contracts become more commonplace [13]. Eventually, geographic borders will hopefully no longer serve as a barrier to the remote delivery of pathology services.

Technology

Over the last two decades, there has been a significant shift in the types of technologies deployed in the practice of telepathology. The Weinstein Telepathology System Classification describes 12 distinct classes of telepathology systems [14]. For simplicity, these modes can be divided into static (store-and-forward), dynamic (aka real-time) or hybrid systems that combine elements of both static and dynamic imaging.

Early international telepathology efforts relied heavily on static (snapshot) imaging platforms. These systems captured, stored and forwarded galleries of digital images

for remote diagnosis. In order to be effective, such platforms had to link digital images with metadata such as patient identifiers, and, if necessary, relevant clinical, laboratory and radiological information. For static image telepathology, the individual who selects representative microscopic fields at the sending site must possess basic knowledge in order to determine which regions of interest need to be imaged. The major advantages of static image telepathology include relatively low start-up costs and minimal equipment maintenance. Moreover, image files are small and hence often easier to manage and store. These are all-important factors when dealing with resource-poor countries. However, there are numerous disadvantages (e.g. sampling errors, limited fields of view and focus problems) to this method that likely account for its low diagnostic accuracy when compared with dynamic telepathology [15, 16].

Dynamic telepathology platforms enable pathologists to view entire glass slides by remotely controlling motorized microscope functions, including slide navigation (in the x- and y-axes) and focusing (along the z-axis). By the 1990s, this particular method of robotic telepathology was very popular [17–19]. However, these dynamic telepathology platforms were more expensive, required the use of proprietary hardware/software by both sending and receiving sites, and hence lacked interoperability. Robotic telepathology systems have been infrequently used to share images across international borders. In addition to the disadvantages alluded to above, their use for real-time telemicroscopy is often impractical when dealing with time zones and in countries with limited telecommunication infrastructure. With robotic microscopy capability recently being incorporated into whole-slide scanners, it is likely that this form of telepathology may be better exploited in the near future.

WSI has been used not only for international telepathology, but also heavily employed to foster educational and research collaborations among international parties. WSI systems produce large, high-resolution digital images of entire glass slides that can be stored on web-accessible servers or in the cloud to be viewed over the Internet. WSI permits access to an entire glass slide or a set of slides at various magnifications [20, 21]. Contemporary WSI scanners can potentially capture a 1.5×1.5 cm tissue section at $\times 20$ magnification in under 1 min. For international telepathology, this facilitates the scanning of large volumes of slides. Certain WSI scanners offer z-scanning, which permits slides to be digitized with multiple focal planes. Such z-stacked digital slides are better suited for interpreting cytology teleconsultations. Viewing whole-

slide images is usually faster than using dynamic telepathology, especially when using a powerful computer and high-speed network connection [22]. The primary disadvantages of WSI telepathology include the expensive costs of the equipment, image archiving demands for large digital files and image viewer compatibility for different file formats. OpenSlide provides an interface to read virtual slides in many (e.g. .svs, .svslide, .tif, .bif, .ndpi and .scn) but not all formats [23].

Collaboration Benefits

Telepathology, international and domestic efforts alike, facilitate remote access to specialist expertise, which in turn results in better and often more efficient patient care [19–22]. Successful telepathology practice is directly related to advances in computing technology and the Internet (e.g. web 2.0 tools). One of the primary strengths offered by telepathology is the potential to improve operational efficiency. It is often easier to move an image than it is to move a pathologist or patient. A recent study by Ho et al. [24] projected millions of dollars in cost saving for their health care system that could be realized from the adoption of digital pathology due to improved productivity (e.g. consolidated histology operations and workload balancing) and more accurate diagnoses (e.g. facilitation of teleconsultation). Telepathology eliminates the costly, inefficient and time-consuming process of having to manually transport delicate glass slides via third-party courier services. For certain countries (e.g. China), human tissues may not be allowed to cross international borders, making telepathology the only means of obtaining a second opinion. For institutions that lack in-house specialty expertise, teleconsultation is critical [25]. In these instances, telepathology capabilities may be deemed invaluable, especially by patients, who can reap the benefits of remote expert consultation [2]. Telepathology collaborations have proven to be beneficial for developing countries because such partnerships have also offered a mechanism for sharing of best practices for laboratories, providing education and creating the opportunity for research. In some cases, broad institutional telemedicine efforts have combined telepathology with other services, such as teledermatology. For pathologists, travel to remote locations to provide care can be avoided. By being able to work anywhere and at any time, pathologists' experience enhanced job satisfaction, and they feel less isolated when working in remote regions and retain access to educational activities [22].

Keys to Success

Successful international telepathology depends on several factors. The key stakeholders include pathologists, as well as administrative and IT personnel. Pathologists, the primary users of telepathology systems, are arguably the most critical stakeholders. Hence, any telepathology platform under consideration must be reliable, intuitive and flexible enough to meet their needs. One concern is that digital pathology disrupts their existing workflow. Telepathology platforms should not only be easy to use, but pathologists will also need to be well trained to use them. This is especially true for those professionals who are reluctant to switch to digital pathology or may be technophobic. For administrative stakeholders, it is important that telepathology improves patient care while concurrently improving operations and return on investment. IT buy-in and support is critical to successful telepathology practice to ensure that storage needs, system compatibility, network capabilities and security are not overlooked. Despite lowered costs and recent advances in digital storage infrastructure, large-scale use of WSI can easily deplete server capacity. Several vendors now offer cloud-hosting services. However, there are still concerns related to security and cloud computing. Threats related to cloud security include reports of prior corporate data breaches, data loss, account or service traffic hijacking, public-facing application programming interfaces and shared technology.

In recent years, major steps have been undertaken to improve and encourage the adoption of telepathology by the pathology community. In 1999, the American Telemedicine Association put forth telepathology guidelines, which were subsequently updated in 2014 [26]. Additional telepathology guidelines using WSI were provided by the College of American Pathologists, Royal College of Pathologists in Britain and the Canadian Association of Pathologists [27–30]. These guidelines not only address the varying technologies available and different clinical applications, but also discuss important issues related to maintenance, quality assurance, security and regulations.

Barriers

Apart from financial and technology barriers (e.g. electricity supply and reliable telecommunication bandwidth in rural or underserved areas), there are also regulatory and cultural factors that may impede international telepathology [31]. There is some degree of uncertainty

regarding the liability of health professionals when delivering care across borders [32]. While there are no specific provisions set forth in the European Union legislation, in the United States physician licenses are not portable. There is a draft bill currently before the US Congress to facilitate telemedicine endeavors by addressing such legal barriers [33–35]. Apart from these regulatory concerns, uncertainty regarding medicolegal implications poses another barrier. The adoption of explicit and/or implied consent should be included during telepathology contract negotiations. This can be especially challenging in countries with high rates of illiteracy and limited familiarity with the technologies used to share information across borders [36]. Additional legal issues associated with telepathology stem from data security concerns regarding the confidentiality of medical information on the Internet [37–40]. Potential solutions for confidentiality include the anonymization of data through a variety of mechanisms (i.e. removal of patient identifiers or limiting user access to stored patient information). Platforms that support secure data transfer and data encryption are an essential element of successful telepathology programs [41, 42].

Other important factors to delivering quality care across borders include local technical support, reliable connectivity, good image quality, quality assurance measures, monitoring timeliness of reporting, database maintenance and the availability of bidirectional communication between parties. Many international laboratories with limited resources encounter difficulties in the production of optimal, high-quality glass slides that have well-stained tissue. Consequently, telepathology consults may be limited due to these poor quality slides. Furthermore, poorly prepared tissues and slides (e.g. tissue present outside the coverslip or tissue folds) may affect optimal scanning and thereby hamper interpretation [3]. Another limiting factor is when experts do not have additional data about the case, such as pertinent clinical information, radiology images or measurements, and the results of ancillary studies (e.g. flow cytometry or molecular information). Lack of these metadata can make it hard for an expert consultant to provide a comprehensive opinion for challenging cases. Sustainability of cross-border telepathology services has been a major problem for several collaborations. Historically, these failed telepathology programs have been small-scale collaborations initiated by individuals or poorly funded nongovernmental organizations. The implementation of international telepathology undertakings can be established using simple, low-cost technologies, with low initiation and main-

tenance costs. Expensive setups, like satellite-based services, are now being replaced by cheaper and more ubiquitous alternatives (e.g. the Internet and cellular devices). For international telepathology, there may also be language and cultural barriers. Therefore, it is important to have a pathologist champion and IT expert on both sides that are familiar with local/regional issues. They need to be able to easily communicate and foster collaboration and trust, and deal with troubleshooting when problems arise. Obtaining patient and public trust also plays an essential role in long-term international telepathology collaborations.

Conclusion

International telepathology efforts have primarily been driven by the need to improve access to specialist pathology services in low- and middle-income countries where there is a shortage of pathologists. To date, telepathology collaborations have mainly offered teleconsultation services (i.e. providing second opinions on challenging cases) and education. Fruitful collaborations highlight the importance of satisfying the needs of all key stakeholders, providing financial incentives and adequate training, employing sustainable and flexible telepathology platforms, adopting WSI and fostering trust between groups. Factors that hinder international telepathology are numerous and include finances, lack of local IT support, legal and regulatory issues, data security and confidentiality concerns, as well as language barriers. Nevertheless, it is anticipated that the practice of international telepathology will continue to grow as more vendors begin to offer practical solutions to support these collaborations, and studies begin to show their positive impact on global patient care.

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