

# Chapter 6

## Teleconsultation

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### Introduction

Digital pathology has been successfully implemented around the world mainly for education, clinical pathological conferences, and research and its integration into clinical diagnostic activities is rapidly increasing. Although its use for primary diagnoses on routine clinical material remains rather limited, certain niches such as consultations between pathologists and frozen sections are clearly expanding. In this century of increasing diagnostic complexity, personalized medicine and molecular pathology, obtaining the opinion of an expert may be critical for patient management. Sharing whole slide images (WSI) instead of glass slides to get an opinion from a remote expert concurs to efficiency gains but digital pathology also offers additional advantages such as the possibility to request opinions from more than one expert and, for experts, to share challenging cases with others abroad. Globally, the patient is the first to benefit from this technology since the improved

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efficiency resulting from teleconsultations leads to faster patient management. This chapter presents the spectrum of current and potential clinical applications of teleconsultations.

## Historical Background of Telepathology and Digital Pathology

The term “telepathology” was introduced into the English language in 1986 by Weinstein [1]. The first recorded event of “telepathology” occurred in the late 1960s, when a real-time “television microscopy” service was established between Massachusetts General Hospital (MGH) and Logan Airport Medical Station in Boston, Massachusetts and black and white real time television images of blood smears and urine specimens were sent from Logan Airport to MGH for interpretation [1]. The first robotic telepathology system was invented and patented by Dr. R. S. Weinstein. The first patent application was submitted in 1987 and granted in 1993.

Since the 1960s, telepathology systems, technology and services have continued to be developed and continue to evolve [2]. Historically, development has been in three broad types of telepathology systems including dynamic, static and hybrid systems. Dynamic systems are essentially remote-controlled microscopes that give the pathologist a live view of the distant microscopic image while allowing him or her to move the stage, focus, and change the magnification, remotely. The clear advantage to dynamic systems is that they give the consultant tremendous flexibility in perusing the entire slide to examine in detail any specific field at any power. Disadvantages to dynamic telepathology systems include the expensive and proprietary nature of the host and client stations and the tremendous bandwidth needed to carry live, full-motion video.

Static (“store-and-forward”) telepathology requires that the referring pathologist capture a collection of still digital images for transmission to the consultant. The major disadvantage is the loss of control experienced by the consulting telepathologist, who must rely on the referring pathologist to capture all of the necessary diagnostic fields to support an adequate examination. On the other hand, static systems can be extremely versatile. Any system that captures images in standard file formats, when coupled with any file transfer protocol program or almost any reasonable E-mail system can be used to perform static telepathology.

The third historical approach used hybrid systems that attempt to combine some of the better features of both static and dynamic systems. Hybrid telepathology systems couple remote-controlled microscopy with high-resolution still image capture and retrieval. This approach requires a significantly lower bandwidth than purely dynamic systems do while providing high-quality static images for diagnostic, reporting, and medical record-keeping purposes.

Virtual slide telepathology also known as whole slide imaging (WSI) is the most recently developed mode of telepathology. WSI has resulted from technical advances during the recent decade which have led to the creation of high-quality,

high-resolution images of entire glass slides known as whole slide imaging (WSI), using innovative, automated, high-speed, high-resolution WSI scanners [3]. WSI scanners incorporate robotic motion, digital camera technology, and high-quality microscope optical components controlled by software to scan and traverse the entire glass slide to acquire a digital image “replica” of the slide. In addition to movements along the X and Y axis of the slide during scanning, as the histology specimen has a variable depth dimension (i.e., Z axis).

Technologies used in telepathology have historically evolved over time. In the 1990s, a large scale study done by Veterans Affairs (VA) hospital demonstrated the wide-scale clinical application of telepathology [4]. These telepathology applications included both anatomical pathology such as for use in frozen sections and for clinical pathology services. The VA group involved in this study used an Apollo dynamic telepathology system. The telepathology study showed a high diagnostic concordance of robotic telepathology with light microscopy. In addition, a decreased turnaround time for surgical pathology cases was reported at the remote sites [4]. By 2009, the VA study had expanded and had reported on their experience with over 11,000 telepathology cases. Pathologist-specific discordance rates using dynamic/robotic telepathology were reported to be in the range of 0.12–0.77 % [5].

In 1993, the Armed Forces Institute of Pathology (AFIP) launched a static imaging consult. This was an attempt to provide expert consult service for difficult anatomical pathology cases and was available for global teleconsultation [6]. By 2001, dynamic telepathology was adopted by the United States Department of Defense (DOD) within the Army Telemedicine Program. In 2005, these systems were converted to a WSI platform. Today, the type and complexity of telepathology platforms continue to evolve and the clinical applications continue to grow. In order to increase their use of telepathology and intent to capitalize on the rapid advances being made in digital pathology, the United States Airforce Medical Services (US AFMS) introduced whole slide imaging-based telepathology to its pathology practice in 2007. As a first step in these efforts, under a congressional appropriations award, a model digital pathology network comprised of WSI systems was built by the AFMS pathology centers with the potential to expand to additional and smaller AFMS pathology centers in the future [7].

Due to globalization of healthcare and the worldwide shortage of pathologist, the last few years has seen an emergence of digital pathology networks. Several vendors have developed products for digital imaging, image transmission, display and image storage. The goal is to provide end users with an increasing range of products to enable telepathology and include products for low cost, rapid scanning platforms and image viewers. Several vendors have started to create international digital pathology networks, providing users and consulting groups with collaborative telepathology portals. These digital pathology networks provide virtual consultant platforms with web-enabled access and some feature a cloud-based solution. The last 5 years has seen rapid development of mobile technologies and the use of smart phone and tablets for telepathology. As mobile health (mHealth) continues to grow, we are likely to witness greater use of telepathology using mobile devices (e.g. tablets, cell phones, wearable glasses such as Google Glass).

Telepathology systems continue to evolve but it is interesting to note that some of the recent applications such as smartphone based telepathology continue to use static images as a method of teleconsultation. A notable advance in the field was the publication of the updated guideline document for telepathology by the American Telemedicine Association in 2014 [8].

## **Teleconsultation Activities**

### ***Intraoperative Consultations Using Digital Pathology Methods***

One of the great utilities for digital pathology methods is in the performance of rapid interpretations to guide intraoperative or intraprocedural patient management. The main benefits of digital pathology in this application are increased expertise at any site and improved productivity. The ability to bring subspecialty expertise to any facility, whether local or remote, means that operators at remote sites, where intraoperative consultations were either not available, or only done through generalist pathologists, will now be able to receive expert consultations in any subspecialty in real time. This system would allow a concentration of subspecialty services in a central location that can consult to multiple remote sites, thereby improving expertise and efficiency. Productivity gains can also be achieved within single centralized facilities by allowing pathologists to optimize time commitment via the performance of consultations in multiple sites within their facilities from a single workstation. Networking between digital pathology workstations adds the additional capability of obtaining interpathologist consultation in particularly challenging cases, all in real time, and all with minimal disruption in the usual workflow of the participating individuals. In addition, the use of digital pathology can increase the “temporal” range of pathology services with night call no longer requiring the long drive in to the hospital for a brief look at a frozen section or cytology specimen. A single pathologist can now provide immediate night call services to many sites from home or from an “on call” facility.

In addition to the consultations themselves, digital intraoperative consultations have the advantage of providing the means for improved quality assurance and continuing education maneuvers. For instance, if WSI are used for the rapid interpretations, archived material can allow after the fact rereview to determine reproducibility parameters, and will allow for the collection of libraries of interesting, important, and challenging cases. Snapshots of important fields of view from dynamic streaming methods can provide similar information, particularly if pathologists document fields which they consider the most important in support of their final interpretations.

The two most common intraoperative/intraprocedural interpretations are for frozen section and rapid cytologic assessments. Both procedures guide the operator in making vital decisions about how to proceed in fluid situations. Frozen section interpretations can provide for a variety of maneuvers including decisions on the proper surgical procedure to perform, the taking of additional tissue or margins,

guiding the acquisition of proper tissue for banking or molecular testing purposes, and informing the surgeon about the etiology of the disease when it was not known prior to the procedure. Rapid cytology interpretations can provide similar information, but its more commonly applied application is in the assessment of an adequate specimen.

Although static images have been used in the past for intraoperative assessments, current procedures are most commonly performed via either dynamic video streaming technology or by the use of WSI. Dynamic video streaming has a number of important features that make it useful in rapid assessments. First, it is relatively inexpensive and hence can be widely available. It requires only a microscope with a high resolution digital camera attached to a computer where the real-time image can be displayed. That computer must have a high speed Internet/network connection which will allow “screen sharing” with other computers. There are a variety of screen sharing software packages available which provide the remote site with an identical digital output as is present at the primary site. The consultant generally connects to the remote site by telephone and then instructs the operator on the movement of the slide, focusing, and magnification. In cytologic specimens, the real-time nature of the procedure with focusing capability can be useful in order to better visualize the three-dimensional groups inherent in these types of specimens. The most prominent disadvantage of this method is that the remote observer may not see the entire specimen and may focus on areas that the on-site operator has preferentially shown; a process which introduces an inherent bias into the procedure. A variety of studies have shown the utility of using real time telepathology for rapid cytology interpretations [9–16]. Some studies have shown no, or only minimal differences between rapid and final interpretations. These studies have brought to light issues of work flow important to telecytology and the rapid interpretation process [14]. With the rise in the use of fine needle aspiration biopsy, more biopsies are being performed in more places, and overall optimization will require more attention from the cytologist. The use of telecytology is a less disruptive method of delivering that service, because small numbers of trained cytologists will be able to cover many sites of biopsy performance from a single “connected” office. As experience has been gained there have been cases noted where distinctions between subtle morphologic changes may be necessary for reliable interpretations, and as such in person on-site evaluation may sometimes be a more appropriate solution. Therefore in many laboratories a rule has been introduced that if the consultant has any difficulty arriving at a rapid interpretation within the first several minutes of viewing the case remotely, they should revert to on-site evaluation. In most operators’ experience the number requiring on-site assessments has been only a small minority of cases. To date there has been only limited use of whole slide imaging for cytologic interpretation [17]. Expense of the scanning devices, the time necessary to scan a smeared slide containing a large area of cellular material, and the inability to focus through three-dimensional groups have all been detriments to adoption.

The use of digital methods for frozen section histopathologic interpretations has been more widely accepted than for cytology rapid interpretations. Methods used for frozen section studies have included static imagery, dynamic video streaming,

robotic telepathology, and whole slide imaging. Static image telepathology has been utilized for many years at the University of Pittsburgh primarily for transplant pathology interpretations [18] and has been in use for a number of years in Japan for general frozen section coverage to remote sites [19]. It is simple, image format neutral and rapid, but it is limited by the bias of appropriate field of view selection. Dynamic robotic interpretation allows for the advantage of real time telepathology with the addition of remote control, minimizing the inherent bias of sender bias as noted above. This methodology has been used for many years and has been shown to be robust in terms of accuracy and efficiency in applications ranging from dermatopathology margin analysis, and with thoracic and neuropathology specimens [4, 18, 20]. The need for expensive equipment at the site and the time-consuming nature of the robotic interaction has limited the use of this technology going forward and has largely been replaced by dynamic video streaming applications and whole slide imaging. Video streaming applications (similar to those noted above for cytology) have been shown to be effective in Mohs surgery application [21] and are a commonly used method for institutions performing frozen section night call from home. Whole slide imaging is seeing an expanding role in frozen section evaluation. Neuropathology applications have been most widely cited primarily because of the need for centralization of neuropathologic subspecialty expertise [22–25]. In Toronto at University Health Network, neuropathology frozen sections transitioned from robotic dynamic systems to WSI in 2006 and the authors reported a decrease in turnaround time, a low (5 %) deferral rate, and similar diagnostic accuracy when compared to light microscopic examination [26]. Another study indicated good success with frozen section interpretation in ovarian frozen sections, noting that the overall correlation between benign and malignant/borderline entities was 96 %. Similar to reports of secondary permanent section consultations by WSI, interpretations requiring high magnification detail examination presented the most risk of error [27]. In another review of a broad group of frozen sections by WSI from multiple anatomic sites, diagnostic discrepancies were reported in only 1.4 % of cases [28].

Other issues reported to effect WSI in frozen section analysis have been technical, and have included the need for excellent histologic preparations, scanning process image quality control which includes making sure that all tissue has been scanned and is in optimal focus, and insuring optimal coverslipping technique which includes coverslip placement and limiting mounting media to avoid contamination of the delicate transport mechanism of the scanning device [26].

Guidelines for the implementation of systems for intraoperative digital pathology have been put forth by the Canadian Association of Pathologists [29]. In their document, the Association stresses the need for adequate training of support personnel, particularly when no pathologist is present on site—specifically in procedures related to the grossing of the specimen, including orientation, adequate identification of the margins, and appropriate tissue sampling. In addition, information technology support staff must be available for maintenance and intraprocedural troubleshooting of the scanner and telepathology infrastructure. Similar guidelines recently established by the American Telemedicine Association stressed, in addition, the availability of gross images of the specimen at the time of frozen section

examination to complement the overall evaluation [8]. These guidelines also note that pathologists performing frozen section interpretations must adhere to licensure and regulatory restrictions which are known to vary across individual countries and states.

In summary, intraoperative consultations for both histologic frozen sections and rapid cytology are one of the first widely utilized applications for digital telepathology. Results to date indicate excellent correlation to the current standard of routine light microscopy, and offer significant advantages in terms of productivity enhancement and “projection” of subspecialty expertise to remote sites. Use of relatively low cost dynamic video streaming has advantages for cytology where specimens may be three-dimensional or cellular areas may be poorly defined and widespread on slides; while WSI may be the best technology for “flat” histologic specimens. As costs decline and expertise and acceptance increases, the use of digital telepathology will undoubtedly grow and will be paralleled by improved patient outcomes in the future.

### ***Telecytology***

Telecytology involves the transmission of cytology images for remote evaluation. Telecytology can be utilized for diagnostic purposes (e.g., rapid on-site evaluation, consultation, reviewing intraoperative smears), education (teleconferences), and quality assurance (e.g., proficiency testing) [30, 31]. With advances in digital imaging there has been increased interest in telecytology. Early telecytology efforts focused mainly on gynecological cytology [32]. More recently, as shown above, telecytology has been employed for rapid on-site evaluations of fine needle aspirations (FNA) [33, 34]. For immediate FNA assessments, pathologists are usually required to travel to a distant site where the aspiration biopsy is being performed. Telecytology allows the pathologist to view these slides remotely, which is less disruptive and more cost effective. For consultation purposes, telecytology avoids the potential for unique and irreplaceable glass slides to get lost or broken.

Telecytology can be accomplished using static (store and forward), dynamic (real time), and/or hybrid systems. Most early publications about telecytology used static photos [35, 36]. Static images can be readily acquired using microscope-mounted cameras, and today even with mobile phone cameras. The advantage of using static images is that these systems are generally cheap, easy to use, and readily available. These digital files also tend to be small and easy to transmit (e.g. via email). However, this manual method is labor intensive and relies on an individual that is knowledgeable about cytology to photograph representative material. Moreover, the images only capture a small field of view without the ability to focus. As a result, many cytology laboratories currently rely more on live telemicroscopy using a microscope-mounted camera [18]. In this instance, the host driving the glass slide continuously streams an image in real-time to the pathologist’s remote workstation. If necessary, a pathologist can also remotely access the computer attached to the

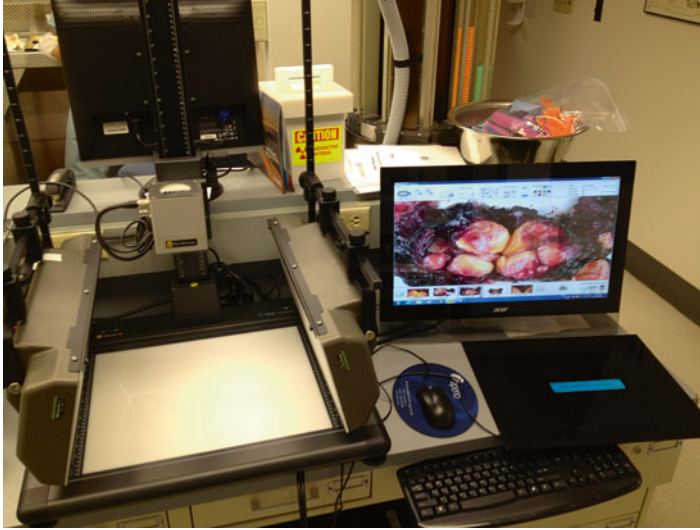
microscope with the camera via desktop sharing software. While this streaming method overcomes focus problems, the interpretation is still dependent on the expertise of the host navigating the slide [37].

With advances in technology, telecytology has shifted to using more sophisticated technology such as whole slide imaging (WSI) devices that incorporate robotic microscopes [38]. Stand-alone robotic microscopes have been used most successfully with intraoperative consultations (e.g., frozen sections), and less so for telecytology [39]. By remotely controlling the robotic microscope, pathologists are able to perform live navigation and focusing of an entire glass slide. WSI also allows an entire glass slide to be rapidly digitized that can then be remotely viewed. Both of these methods minimize the need for an experienced on-site operator for appropriate field selection, but are more expensive solutions. For telecytology, the main limitations of WSI are the inability of some scanners to accept slides without coverslips (which is important when rapidly preparing slides for on-site evaluation) and problems with resolution or fine focusing of thick cytology smears and three dimensional cell groups. Some WSI scanners offer Z-stacking to produce multiplane images, but this generally takes long to scan slides. As a result, for telecytology WSI tends to be more useful for seeking second opinion consultation than for use during on-site evaluations. Given that multiple different stains (e.g. Diff Quik, Papanicolaou, H&E and other special stains) are often used in cytology, it is important to note that there may be a larger number of slides to digitize compared to surgical pathology. Telecytology validation studies should accordingly utilize cytology cases [40].

### ***Macroscopy Supervision***

Telepathology for macroscopy (gross pathology) is infrequently used compared to telemicroscopy. This may explain why there is a paucity of literature on macroscopic telepathology [41–43]. Gross telepathology may be employed to remotely supervise trainees or pathology assistants who have specific questions regarding a pathology specimen, to share specimen resections with surgeons during intraoperative consultation (e.g. for orientation and/or areas to be sampled for frozen section), and less often for education purposes. Gross telepathology can be performed using a sophisticated system including a grossing station, videoconferencing device and a drawing tablet [43] but it can also be performed using an inexpensive commercial webcam or with a dedicated, high-resolution digital camera (Fig. 6.1) that is part of a gross imaging workstation/platform [44]. The software provided with stand-alone gross imaging stations may not always include functionality to share images. In such cases, laboratories may need to rely on a separate teleconferencing or desktop sharing application (e.g. TeamViewer). When sharing gross images it is important to incorporate a mechanism for the host and consultant to discuss relevant information about the case (e.g. clinical history). Such bidirectional communication can be accomplished using a telephone or the Internet (e.g. chat function, annotation tools).





**Fig. 6.1** Stand-alone contemporary macro imaging station (SPOT pathStation2) that can facilitate telepathology of large gross pathology specimens

The digital camera used should ideally be able to accommodate samples of varying size and there needs to be adequate lighting. It may not always be necessary to capture and save shared images. Gross imaging systems typically do not permit remote control of the camera (e.g., focus, zoom); this function is usually handled by the individual handling and showing the specimen. The utility of mobile devices including Google glass (GLASS™) for sharing gross images is promising, but remains to be validated for routine clinical use [45].

### ***Tele-Autopsy***

Teleautopsy represents a potentially new and attractive digital pathology application. Teleautopsy allows the pathologist to perform the external and organ macroscopic examination without having to either move to the remote site or to transfer the body to the pathology laboratory. This is particularly attractive for autopsies requiring specific expertise and in a context of increased workload and shortage of pathologists reported in different parts of the world and for which any time spent at moving from one place to the other results in reduced efficiency. Furthermore, recent literature confirms that autopsy rates are declining everywhere around the world. This decline is attributed in part to the increased precision of modern radiological tools and the poor reputation and decreased interest at performing autopsies [46]. One of the rare examples of teleautopsy network reported in the literature

is the Veterans Integrated Service Network (VISN) connecting 8 hospital-based laboratories. The VISN extends across portions of three states and uses digitized images generated using hand-held digital cameras or gross tissue imaging workstations [47]. In Switzerland, the VIRTOPSY virtual autopsy project uses radiologic imaging facilities and was initiated in 2000 and has been using high-technology imaging techniques applied to forensic autopsies [48, 49]. More recently, the same clinical team launched the VIRTOBOT, a multifunctional robotic system that allows the pathologist to obtain distant automated surface scanning of the body and to remotely take selective biopsies [49, 50]. In Canada, the Eastern Québec Telepathology Network which shares diagnostic pathology services among 21 hospitals [51], is currently experimenting teleautopsies using a videoconferencing device with remote control of the focus and orientation of a high-definition camera. To be efficient and to insure a high level of confidence, a teleautopsy setting requires the support of well-trained and reliable technologists or pathologist's assistants.

## International Teleconsultation Networks

It is often easier to move images across borders than it is to send biological material (slides and/or blocks) or transport patients. Telepathology has thereby facilitated access to pathology experts around the world. This is of great benefit to underserved and rural areas where there is a shortage of pathologists. In these areas not only is there a high demand for diagnostic consultation, but education and guidance on patient management as well. Telemedicine in Africa, for example, has proven to be a very useful conduit of healthcare [52]. A review of telepathology consultation between the University of Pittsburgh Medicine (UPMC) in the USA and KingMed laboratories in China for a 2 year period revealed that in many (approximately 75 %) of cases patient management was impacted as a result of expert diagnoses [53]. In recent years, teleconsultation has become a highway to competition of services and a novel source of international trade. Digital consults offer a new means to insource pathology services.

Over the years there has been a plethora of international telepathology ventures (Table 6.1) [54]. iPATH, developed by the University of Basel, was one of the most successful telepathology platforms [55, 56]. iPATH served over 150 user groups around the world and allowed over 15,000 telepathology cases to be examined. Because the iPATH system used open source software, local server installations were located all over the world. The contemporary telepathology forum called Medical Electronic Consultation Expert System (MECES) exploited Web 2.0 and whole slide imaging technologies [57]. More recently, international telepathology networks have increasingly been established by large academic centers (e.g. UPMC, MD Anderson) and commercial vendors offering collaborative portables, cloud services and business partnerships (e.g. PathCentral, AccelPath, ePathAccess, Corista, Xifin).

**Table 6.1** List of some international telepathology projects

– Réseau International de Télémedecine (RESINTEL) and TRANSPATH network
– Fundamentals of Modern Telemedicine in Africa (FOMTA) project
– Réseau Afrique Francophone de Télémedecine (RAFT) project
– Telepathology Services of the Armed Forces Institute of Pathology (AFIP)
– Pathologie, Cytologie, Développement (PCD) telepathology service
– Telepathology consultation centre of the Union International against Cancer (UICC-TPCC)
– Arizona International Telemedicine Network
– iPath telepathology platform
– Medical Electronic Consultation Expert System (MECES)

Technologies employed to support international telepathology have advanced over the years [18]. Early efforts relied on store-and-forward systems where static images were the mainstay of image exchange. The transplant pathology service at UPMC reviewed over 3000 static digital consultation cases with acceptable diagnostic concordance between digital and glass diagnoses [58]. More recently, whole slide imaging has been used. WSI can be remotely viewed in two ways: WSI 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 owned by the consultant group [59]. The former arrangement requires strong cooperation between IT groups of all parties, and permission to access foreign servers. Although the latter system may result in time delays due to image transmission, viewing images is less likely to suffer from network delays. Newer platforms to support telepathology have begun using agnostic viewers, cloud services, more open access platforms and plug-in technology.

Evaluation of general international telemedicine collaborations has revealed several factors that are key to success [60]. These include low cost, use of simple technologies and bi-directional communication. Also important are incentive-based programs, locally responsive services, strong team leadership, training, and user acceptance. Of course, there are also several barriers to cross-border telemedicine. These obstacles include cultural factors (e.g. language, trust), limited resources (e.g. finances, trained staff, availability of ancillary tests), IT infrastructure (e.g. network limitations, firewalls), time zones, regulatory issues, sustainability factors (e.g. cost, inconsistent use, poor scalability), and top-down (e.g. contracts, formal agreements) versus a bottom-up approach (e.g. empowered by end-users). When dealing with international business collaborations it is imperative to ensure that all parties involved adhere to applicable laws. This includes international safe harbor regulations which refer to a process for companies (and institutions) in the USA to comply with the European Union (EU) directive related to personal data protection.

The Foreign Corrupt Practices Act (FCPA) is another federal law in the USA, concerned with the bribery of foreign officials, which is important to be aware of when dealing with international trade.

## Future Direction

It is expected that the virtual slide technology with its overwhelming advantages will be called to progressively supplant the conventional microscope, more particularly for teleconsultations which are usually requested in cases requiring rapid management and treatment decisions. In addition to clearly improving efficiency, virtual slides offer many more advantages. To name only a few of them, contrary to conventional glass slides, the color quality of virtual slides persists, regardless of the duration of storage and the number of copies performed is unlimited. Furthermore, contrary to the microscope, virtual slides do not require constant resetting of the focus plane and brightness. Virtual slides also offer the possibility of viewing several stains of the same case simultaneously. Finally, virtual slides allow annotation, for teaching or discussion, and quantitative evaluation of objects and structures [61]. Computer-assisted diagnostic systems with imaging and learning algorithms have already been developed. For example, algorithms aimed at grading astrocytomas [62] and predicting prognosis [63] have been tested using digital images. In the future, systems that will recognize certain tumor types and analyze markers in specific tumor compartments are called to expand. For health care organizations and managers, telepathology has been implemented to prevent interruption of frozen section activities in case of the absence of an on-site pathologist [43].

However, despite all those overwhelming advantages, the implementation of virtual microscopy in the daily practice of pathologists is generally slower than expected in most jurisdictions around the world. Part of the barriers to a wider adoption is technological, more specifically with regard to software application ergonomics, of which the speed of user interfaces is felt by many users as inadequate today to support high-volume practice [26, 64]. However, human factors remain among the most important barriers [65]. Despite many advances and clear evidence of the accuracy of clinical diagnoses by telepathology for routine pathology cases [66–68], many pathologists are reluctant to abandon their comfort zone as glass slides are still available with current technologies. The maintenance of both glass slides and virtual images also implies the duplication of storage facilities. This parallel storage system is one of the major differences with teleradiology. However, ongoing research efforts let us believe that the replacement of glass slides by some form of direct microscopy on unprocessed and unstained sections using imaging technologies such as multiphoton microscopy (MPM) [69, 70], optical coherence tomography (OCT) [71], full-field optical coherence tomography (FFOCT) [72] or Raman spectroscopy [73] is expectable in a foreseeable future. Finally, besides these technological and human factors, a number of legal and regulatory issues are being addressed in different parts of the world. For instance, the

liability risk is clearly increased for international experts receiving worldwide consultation requests. Multi-jurisdictional licensure is already a major issue in federal countries such as the United States and Canada and in unions of independent countries such as the European Union where pathologists may be required to obtain different licenses. In that respect, when both the health care professional and the patient are in two different jurisdictions, it is critical to determine the type of licensure required to insure liability coverage [74]. Digital solution licensure, which is the case in Canada and the European Union where several companies were granted Licensure for using digital whole-slide images for routine pathology use, is also critical for a wider adoption of the technology for diagnostic work because it is directly bound with liability [75]. Finally, the fast expansion of telepathology around the world is fostering international collaborations to standardize information parameters for digital pathology, health terminology and standardization of automatic image analysis [76].

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