Telepathology - An Update

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Abstract

Telepathology is a practice of pathology over a long distance. It has been first demonstrated in space by NASA (National Air and Space Administration) since 1960s. After few decades of development, the growth of telepathology is accelerating. Today, its technical development has matured, and it is used in multiple fields such as in clinical practice, intraoperative consultation and medical education. These functions can be performed with the use of all three types of telepathology system (static telepathology, dynamic telepathology and hybrid telepathology).

Telepathology brings advantages in terms of personnel, operational and quality of service. This brings it to be the solution for problems arise in the today's medical field. However, its disadvantages and challenges have restricted it from being widely used. The main problems are the high cost fee of the software, set-up components and maintenance, high complexity of the system, security issues and inconvenient in slide selection.

Therefore, to integrate telepathology into the mainstream diagnostic, immediate finding of solutions are urgently needed.

Key words: Digital imaging; Frozen section; Images; Internet; Pathology; Remote microscopy; Telemedicine; Telepathology; Virtual slide; Whole slide image

Introduction

Pathology plays an important role in identifying the characteristics as well as a cause of a disease in the medical field. Together with current technological advances in medicine, pathology continues to play a role in providing information to medical professionals as well as researchers for further investigation in the form of telepathology.

Telepathology, as the name suggests, is an application of pathology under the specialty in which the study itself is conveyed to a distance with the use of images in

an electronic format rather than view from a glass slide. However, WHO (World Health Organization) defines telemedicine as "The delivery of healthcare services, where distance is a critical factor, by all healthcare professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation and for the continuing education of healthcare providers, all in the interests of advancing the health of individuals and their communities."[1] The full integration of telemedicine is important for establishing a meaningful use of computerized medical records. Electronic medical records increase administrative efficiencies. Besides that, it is not only increases the quality of healthcare and accessibility but also reduces medical cost.

Telepathology is under a subtype of telemedicine and it is used conveniently among medical personnel.[2] Rather than using images of glass slides through the light microscope, pathological samples are being sent under electronic images and it can be stored effortlessly. Today, telepathology is widely used in consultation, diagnosis and medical education. It helps to overcome the problem of the non-availability of immediate pathologist in some areas.

Definition of Telepathology

The term, telepathology was first defined by Ronald Weinstein et al as the "practice of pathology over a long distance".[3] John Sinard defined it as "the use of any of the telemicroscopy technologies to make the primary diagnosis for the specimen from a remote site". [3]

At present, these definitions still hold true. However, it has expanded as taking into account of the development of modern telecommunication and technology nowadays. Telepathology is no longer the practice of pathology by extracting information from a histological slide but also from other sources. These sources include the sex, age, patient's history, clinical finding, or live image and function. [4]

History of Telepathology

Telepathology was first demonstrated in space by National Air and Space Administration (NASA) in 1960s.[5] However, the earliest formal trial was done in April of 1968 when a B&W (Black and White) photo of blood smear sent from Logan Airport to Massachusetts General Hospital, Boston, USA.

In 1990s, a hybrid dynamic-robotic telepathology system was invented in northern Norway in 1990s. [6]After a ten years time, virtual microscopy was marketed.[6]

Classification of Telepathology

Telepathology is classified into 3 modes: static (or store-and-forward), dynamic (or real time) and hybrid (or virtual).[3, 7]

Static Telepathology (or store-and-forward)

Static telepathology is the simplest mode of telepathology. It involves the process of pre-selection and digitization of representative image by sender pathologist. Thereafter, these images are transmitted to a remote telepathologist via e-mail or the Internet.[6] One of the benefits of static telepathology is the low building up fees. It is due to no special software is required to view the images and it requires only some basic components for setting up such as microscope, camera and internet.[3,7] However, there are some disadvantages such as the possibility of missing a potential diagnostic importance area with a glass slide, lack of clarity at low power magnification, lack of focus in still images, labour intensive and the sampling errors may occur.[7]

Dynamic Telepathology (or real time)

Another system, dynamic telepathology system is the most appropriate system for frozen-section telepathology and for understaffed area.[8, 15] It involves the transmission of microscopic slide images to recipient in real time via live telecommunication.[8, 16] With the implementation of remote robotic microscope recipients can completely control the magnification and slide. However, this sophisticated system is expensive and not easy to maintain. It is fitted with charge coupled device (CCD) video camera, high-resolution video monitors, proprietary software and dedicated, high performance hardware (computer).[5] Besides that, it needs a stable and broad-bandwidth telecommunication link between the sender and the recipient.[8]

Hybrid Telepathology (or virtual)

Hybrid telepathology combined both static and dynamic telepathology system; having the advantages of both systems.[3]A series of images are automatically stitched together in software, compressed to a single file form and transmitted once the dynamic telepathology session start.[3] This fastens the consultation process of recipient as less time is required to control the robotic microscope.

As shown in Table 1, each type of telepathology has their potential applications.

Model Set-up

Figure 1 is the set-up of telepathology system. It is complex. It involves many components as shown in Table 2.

Applications of Telepathology

Once installed, a telepathology system can be used for clinical practice, intra-operative consultations and education.[9-13]

Clinical practice

Static telepathology is the oldest form of telepathology. It is used for the transmission of cytopathology images from areas with limited cytology resources or by speeding up routine consult processes.[9] However, this method can easily lead to misdiagnose as a small fraction of information on the glass slides is taken and the diagnosis is based on these few representative images. Thus, the judgment of sender pathologist is important.

The innovation of dynamic telepathology has overcome the weakness of static telepathology. It enables the remote telepathologist to remotely control and rapidly view the entire slides in real-time. It was used in Mohs surgery to solve the problem of the lack of dermatopathologist during a frozen section assessment.[14] A study regarding to the reliability of dynamic telepathology was done in Mohs surgery. 110 slides were being assessed with it. Later, these slides were randomly reviewed by a same dermatopathologist by using conventional light microscope. The result shows a complete agreement between telepathology and conventional light microscope.

Besides that, in another study; 40 cases of cytological evaluation of direct smears from FNABs (Fine Needle Aspiration Biopsy) are assessed and the result demonstrates a high concordance rate. (Intraobserver: 92.5-97.5%); (interobserver: 90-92.5%).[15]This shows the reliability of telepathology.

The reliability of dynamic telepathology enables the reading of the same slide by multiple observers to be taking place simultaneously. This allows the interactive discussion over difficult cases.

Intraoperative consultation

For intraoperative consultations, dynamic telepathology system is used in surgery for the evaluation of a variety tissue type of frozen section.[16] An assessment of frozen section can be done without pathologist. Telepathology can be used for obtaining consultation from pathologist in another location.[17] Thus, tumor-free margins in a tissue-sparing manner can be achieved even though without pathologist. The unnecessary excision of benign region can be avoided.[16]

Education

Telepathology provides a perspective application in medical education. Now, digital imaging is beginning to replace the traditional classroom which involved the use of glass slides and high quality microscope. Digital imaging offers significant advantages over the traditional method.[18] Cytological glass slide examination is time consuming as it can be viewed by only one person at a time.[18, 27] The colour of stain on the slides will fade as time goes.[18,19] It is fragile and can be lost easily.[18] It is costly to make glass slides with a variety of pathologies.

The introduction of telepathology into the medical education field is beneficial in terms of faster the process of knowledge exchange. This improves teaching and learning practices. For example, the use of WSI (Whole –Slide Imaging) in medical education. The main advantage of WSI (Whole –Slide Imaging) is that the images can be accessed easily. [18]Users can review cytological educational material from web-based virtual slide library in anytime and anywhere.[18] Besides that, due to the high image quality of WSI (Whole –Slide Imaging), pathologist can share images among many other pathologists in the same time during medical conferences.[18]

Cairo University uses WSI (Whole –Slide Imaging) technique to create a digital pathology library for their under graduate and post graduate students as well as for all pathology candidates in Egyptian universities and universities surrounding Arabic countries.[20] With that, they able to communicate with all pathology centres within the Middle East to create a digital pathology network for knowledge exchanging purpose.[20]

Advantages

Telepathology brings advantages in terms of personnel, operational and quality of service.

Personnel

The lack of pathologist has become the major problem in many small pathology departments. As a consequence, many residences in rural areas unable to obtain an even total primary medical care. With telepathology, some of the pathological analysis such as intraoperative frozen section can be performed without pathologist. The laboratory technologist processes the specimen locally while a pathologist examines the gross in another location.[29] At the same time, the pathologist will provide some guidances to technologist via monitor.[29] After that, the pathologist can examine digital images and provide his diagnosis by phone.[18,25,29] By that, pathologists do not need to travel to provide service.

Besides that, the implementation of telepathology enables the discussion of the difficult cases among the pathologists. By that, they will feel more secure with their diagnosis.[29]

Operational

Digital slides can be stored a long time as the colour of stains will not fade over time.[17, 25]On contrary the glass slides can break, fade and lost easily. Besides that, the cost for setting up and maintaining the traditional method will be much more costly.

Quality of service

With the implementation of telepathology, the slide does not need to be sent to thousands of miles to have a consultation from an expert.[9] Automatically, the turnaround time will be decreased and the patient can get a proper treatment earlier. This will increase the recovery rate and survive rate.

Besides that, telepathology can be used in intraoperative consultation for the evaluation of a variety tissue type of frozen section. A tumor-free margins in a tissue-sparing manner can be achieved and the unnecessary excision of benign region can be avoided. [14]

Disadvantages

The disadvantages of telepathology are the high cost of the new technology, inconvenient slide selection and not useful for finding artifacts.[20]

High cost of the new technology

The cost for building a new digitized system has limited the adoption of telepathology.[10,20] The high cost of equipments and the maintenance fee for this complex system are unaffordable by most of the small laboratory. The implementation will ultimately fail if the equipment and system cannot be adequately maintained. Moreover, as the file sizes for WSI (Whole –Slide Imaging) is large; the prices for its image storage is relatively high. According to Guzman and Judkins, they estimated they need abound 8 TB (Terabyte storage) per annual just for the storage of neuropathology.[3] The cost for a TB (Terabyte storage) is around $2600.[3,21,30] In short; a huge amount of money is spent on storages without including back-up storage.

Inconvenient slide selection

However, although the applications of the dynamic telepathology system are fantastic, it is preferable if the sending and receiving stations are in similar time zones.[20] Besides that, in the aspect of slide movement; dynamic telepathology has a higher degree of difficulty compared to conventional light microscopy.[21]

Not useful for finding artifacts

There will be a chance of missing critical diagnostic areas such as early stromal invasion is higher.[21, 29]

Current challenges

High cost and complexity

The high cost and complexity of equipment is the most important challenges of the current telepathology system. To date, developing world is still not giving a full attention to telepathology because of the high local equipment cost, inadequate infrastructure, and lack of trained pathologists.[21] However, with the widespread of technology in these days; the prices for equipments are becoming more affordable. In recent, the revolution of simplified communication has cut down the expenses of installing specialized lines.[29, 31] The innovation of nanotechnology applied into the storage device such as hard disk can help to overcome the problem of storage.[22] They use a small mechanical arm to convert the information signals. Moreover, the use of "smart" storage systems can overcome this.[3] This system can detect that image has not been accessed in a certain period of time and moves them to a less expensive storage location.[3] The image files can be reduced image to approximately one-tenth of original size by using image compression.[9]

Low rate of acceptance

The low rate of acceptance toward this change is another challenge. This attribute by most pathologists do not have a clear understanding of the details of telepathology and the feeling of the unreliability of telepathology system. Besides that, there are many other reasons of causing negative preconceptions on telepathology. This includes the danger of missing significance critical diagnostic areas, its limitation on diagnosis of some cases especially thick smear of cytology specimens and questions of responsibility.

Security issues

Furthermore, issues regarding protecting electronic data should be taken into consideration.[23] The use of internet in dynamic telepathology introduces security problems.[23] However, it can be partially overcome by using Intranets, private networks.[23, 32]

Legal-ethical issues

The implementation of telepathology arise a lot of legal related issues such as physician licensing issues, indemnification issues, insurance issues and other contractual issues.[24]

Since the consultation of telepathology across state borders, it is possible to involve the jurisdiction of two different state status.[24,33,34] The complexity is increased when telepathology served as intraoperative consultation. The telepathologist may need to obtain professional licensing in the state where the patient treated in addition to the licensing in the telepathologist's home town.[24,33,34]

Current Situation of Telepathology in Developing countries

The shortage of pathologists and physicians in rural areas are acute and this has lead to delay in diagnosis.[21] Telepathology has become one of many approaches to overcome this problem. Theoretically, it is much easier to set up telepathology system in these areas than to place hundreds of pathologists and physicians. But, its development is restricted by a number of constraints. These constraints include non-uniform pathology specimens processing standards, the lack of infrastructure and the lack of training among medical personnel.[35]

Non-uniform pathology specimens processing standard technique

The availability of well-processed histology and cytology slides is the most important criteria to determine the success of telepathology.[21,35] Lack of uniform pathology specimens processing standard technique in rural areas contributes to the production of poor quality histology and cytology slides. This has become the major obstruction for the progression of a good telepathology system in rural areas.

Lack of Infrastructure

The procurement of the main components of a telepathology system such as digital camera, computer is difficult in some rural areas. Besides that, telecommunication facilities in these areas may be poorly or not developed yet.[35] These factors cause the transmission of medical cases to become difficult or impossible.

Lack of Training among medical personnel

Trained personnel for handling the telepathology system are essential. Staff must get well known of all those functions of each part of the components as well as the way to operate the whole telepathology system. Besides that, they are also expected to perform multitasking.[35] Most of the trained personnel refuse to work in these areas.

Current Situation of Telepathology in Developing countries

However, the development of telepathology in developed countries is very rapid. In Europe and United State, it is overwhelmingly used in consultations while in Japan; it is used widely for intraoperative rapid diagnosis.[36]

For example, in Japan, the analog telepathology system is disappearing rapidly. It is replaced by a telepathology system which utilizes high-speed broadband Internet connections.[36] This recent, the progression of fiber-optic cable infrastructure is overwhelming and it has enormously increased data transfer rates and volume.[36] Besides that, fiber-optic video telepathology allows the recipient pathologist to do

selection on the viewing field. This very much increases the accuracy of telepathology based diagnosis.[36]

Conclusion

The shortage of trained pathologists has urged the telepathology to improve radically in the past decade. Its future is bright as its applications have covered many fields, from the aspect of diagnosis to continuing postgraduate education (CME). Since telepathology will be integrated into mainstream diagnostic, further studies are required to evaluate the feasibility and effectiveness of this technology.Economic benefits also must be taken into account. However, there are many unresolved current challenges hindering the expansion of telepathology. The immediate finding of solutions is urgently needed.

Future development

The emergent of telepathology is turning pathologist into a 'diagnostic expect'. The pathologist can obtain data from different sources, integrate them and generate a clinically useful disease-based integrative report.[26,31,37] Moreover, the incorporation of new molecular and tissue-based testing might classify the disease into a more specific and detail classification. The recent leukaemia classification is a good example of this.[26]

In future, the artificial intelligence and data mining device will be more advance.[22] In gynaecological cytology, PAPNET is a good example of this technology. This device is capable to identify and rank potentially abnormal cells. Pathologists will do assessments on highlighted areas.

Perhaps in future the artificial intelligence and data mining device decreases the workloads of pathologists as they look at pre-screened digitized slides with the area of interest highlighted by computer scanners.

List of Abbreviations

NASA -National Air and Space Administration
B&W- Black and White
CCD- Charge coupled Device
FNABs- Fine Needle Aspiration Biopsy
WSI- Whole-slide Imaging
TB- Terabyte storage
FTEs- Full time employees
IT-Information Technology
CME- Continuing postgraduate education

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References

1. Dasgupta A, Deb S. Telemedicine: A New Horizon in Public Health in India. *Indian J Community Med*. 2008; 33: 3–8.

2. Al Habeeb AA, Evans AA, Ghazarian DD. Virtual microscopy using whole-slide imaging as an enabler for teledermatopathology: A paired consultant validation study. *Journal of pathology informatics.* 2012; 3:2.

3. Williams S, Henricks WH, Becich MJ, Toscano M, Carter AB. Telepathology for patient care: what am I getting myself into? *AdvAnatPathol.* 2010;17:130-149.

4. Kayser KK, Kayser GG, Radziszowski DD, Oehmann AA. From telepathology to virtual pathology institution: the new world of digital pathology. *Rom J MorpholEmbryol.* 1999;45:3-9.

5. Jukic DM, Bifulco CB. Telepathology and pathology at distance: an overview. *Croat Med J.* 1999; 40:421-424.

6. Sowter C, Wells CA. Telepathology: Assessment of the implications and applications of telepathology for practical diagnostic pathology. *J ClinPathol.* 1998; 51:714-5.

7. Schrader T, Kldiashvili E. Virtual health care centre in Georgia. *DiagnPathol.* 2008; 15:S4.

8. Wolf G, Petersen D, Dietel M, Petersen I. Telemicroscopy via the Internet. *Nature.* 1998; 391:613-4.

9. Gabril MY, Yousef GM. Informatics for practicing anatomical pathologists: marking a new era in pathology practice. *Modern Pathology.*2010; 23:349-58.

10. Donnelly AD, Mukherjee MS, Lyden ER, Radio SJ. Virtual microscopy in cytotechnology education: Application of knowledge from virtual to glass. *Cytojournal.* 2012;9:12.

11. Hersh WR, Hickam DH, Severance SM, Dana TL, Pyle Krages K, Helfand M. Diagnosis, access and outcomes: Update of a systematic review of telemedicine services. *J TelemedTelecare.*2006;12:S3-31.

12. Brignell MR, Wootton R, Gray L. The application of telemedicine to geriatric medicine. *Age Ageing.*2007; 36(4): 369-374.

13. Car J, Huckvale K, Hermens H. Telehealth for long term conditions. *BMJ.* 2012; 344:4201.

14. Sukal SA, Busam KJ, Nehal KS. Clinical application of dynamic telepathology in Mohs surgery. Dermatologic surgery: *Official publication for American Society for Dermatologic Surgery.* 2005;31(12):1700-1703.

15. Cai GG, Teot LAL, Khalbuss WEW, Yu JJ, Monaco SES, Jukic DMD, Parwani AV. Cytologic evaluation of image-guided fine needle aspiration biopsies via robotic microscopy: A validation study. *Journal of pathology informatics.* 2010;1:4.

16. Kaplan KJ, Burgess JR, Sandberg GD, Myers CP, Bigott TR, Greenspan RB. Use of Robotic Telepathology for Frozen-Section Diagnosis: A Retrospective Trial of a Telepathology System for Intraoperative Consultation. *Modern Pathology.* 2002; 15:1197-204.

17. Weinstein RS, Bloom KJ, Rozek LS. Telepathology. Long-distance diagnosis. *Am J ClinPathol.* 1989;91:S39-42.

18. Thrall M, Pantanowitz L, Khalbuss W. Telecytology: Clinical applications, current challenges, and future benefits. *Journal of pathology informatics.* 2011; 2:51.

19. Kim MH, Park Y, Seo D, Lim YJ, Kim D, Kim CW, Kim WH. Virtual microscopy as a practical alternative to conventional microscopy in pathology education. *Basic and Applied Pathology.* 2008; 1:46-48.

20. Ayad E. Virtual telepathology in Egypt, applications of WSI in Cairo University. *Diagnostic Pathology.* 2011;6: S1.

21. Hitchcock CL. The Future of Telepathology for the Developing World. *Arch Pathol Lab Med.* 2011;135:211-4.

22. Cross SS, Dennis T, Start RD. Telepathology: current status and future prospects in diagnostic histopathology. *Histopathology.* 2002; 41:91-109.

23. Nanoscience. New Nanoscience data have been reported by researchers at Korea University. *Nanotechnology Weekly.* 2009; Aug 17:138.

24. Wilbur DCD. Digital cytology: current state of the art and prospects for the future. *ActaCytol.* 2011;55:227-238.

25. Wiley CA, Murdoch G, Parwani A, Cudahy T, Wilson D, Payner T, Springer K, Lewis T. Interinstitutional and interstate teleneuropathology. *Journal of pathology informatics.* 2011; 2:21.

26. Alfaro L, Roca MJ. Portable telepathology: methods and tools. *DiagnPathol.* 2008; 3:S19.

27. Della Mea V, Cataldi P, Boi S, Finato N, Dalla Palma P, Beltrami CA. Image sampling in static telepathology for frozen section diagnosis. *J ClinPathol.* 1999; 52:761-5.

28. Steinberg DM, Ali SZ. Application of virtual microscopy in clinical cytopathology. *DiagnCytopathol.* 2001; 25:389-396.

29. Trudel M, Paré G, Têtu B, Sicotte C. The effects of a regional telepathology project: a study protocol. *BMC Health Services Research.* 2012; 12:64.

30. Baruah M. The practice of telepathology in India. *Journal of Postgraduate Medicine.* 2005; 51: 316-318.

31. Weinstein RS, Graham AR, Richter LC, Barker GP, Krupinski EA, Lopez AM, Erps KA, Bhattacharyya AK, Yagi Y, Gilbertson JR. Overview of telepathology,

virtual microscopy, and whole slide imaging: Prospects for the future. *Human Pathology.* 2009; 40: 1057-1069.

32. Blobel B. Intelligent security and privacy solutions for enabling personalized telepathology. Diagnostic Pathology. 2011; 6: S4.

33. Lateef F. The practice of telemedicine: Medicolegal and ethical issues*. Ethics & Medicine.* 2011; 27:17-24.

34. Kuszler PC. Telemedicine and integrated health care delivery: Compounding malpractice liability. *American Journal of Law and Medicine.* 1999; 25:297-326.

35. Desai S. Telepathology and telecytology in developing countries. In: Richard Wootton, Nivritti G Patil, Richard E Scott and Kendall Ho, eds.*Telehealth in the Developing World,* United KIngdom: Royal Society of Medicine Press Ltd; 2009:149-155

36. Sawai T, Uzuki M, Kamataki A, Tofukuji I. The state of telepathology in Japan.*J Pathol Inform.* 2010; 1: 13.

37. Piette JD, Lun KC, Moura LA, Fraser HSF, Mechael PN, Powell J, Khoja SR. Impacts of e-health on the outcomes of care in low- and middle-income countries: where do we go from here? World Health Organization. *Bulletin of the World Health Organization.* 2012;90:365-72.

Table 1: Types of telepathology and their potential applications. [9]

Type	Applications
Static Telepathology	Consultation Continuing education Second opinion
Dynamic Telepathology	Frozen-section diagnosis Second opinion consultation
Hybrid Telepathology	Continuing education Digital archiving Medical education Second opinion

Table 2: Components to be considered

Digital image capture system
Digital data transfer system
Digital data connection
Digital data receiver system
Digital data display system
Storage and archive system
Patient information system interface

Table 3: Components of the Cost Associated with Implementation of Telepathology [3]

Data storage and server capacity
FTEs (Full time employees) for IT (Information technology) technical support
FTEs for system/ scanner operation
High resolution computer monitors
Internet connectivity and bandwidth
Local network bandwidth
Microscopes with digital video cameras
System interfaces
Virtual microscopy slide viewer software
Whole slide imaging system

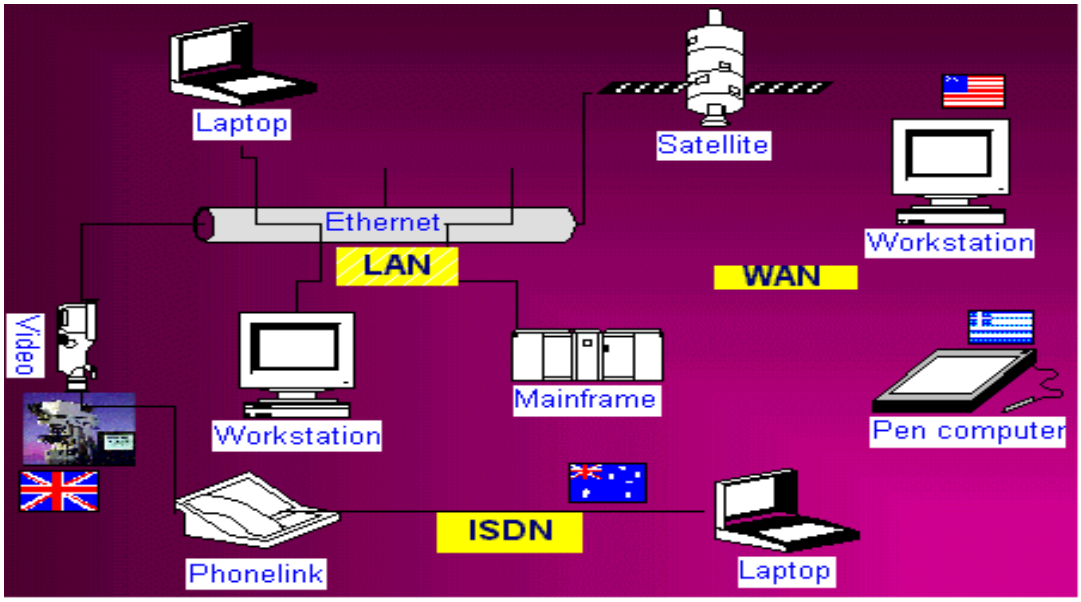

Figure 1: Set-up of Telepathology

Courtesy: http://www.hoslink.com/telepathology.htm