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International Journal of Current Research Vol. 7, Issue, 09, pp.20714-20718, September, 2015 INTERNATIONAL JOURNAL OF CURRENT RESEARCH

REVIEW ARTICLE

TELEPATHOLOGY-A BREAKTHROUGH IN DIAGNOSIS

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ARTICLE INFO	
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ABSTRACT

Article History: Received 22nd June, 2015 Received in revised form 04th July, 2015 Accepted 25th August, 2015 Published online 30th September, 2015

Key words:

Telepathology, Telemedicine, Electronics, Research, Pathologist. Tele medicine is an emerging branch of medicine that eliminates the hurdle of sharing or transfer of data to distant places. Telemedicine uses electronic transmission of data and digital images to distant places for the purpose of diagnosis. There are numerous branches in telemedicine of which this article discusses in detail regarding telepathology. Telepathology is about the practice of pathology at a distance by pathologists. It is already being practiced in developed countries and is being started in developing countries especially India. This review mainly focuses on the types, uses, advantages, disadvantages and the future of telepathology in India and in the developing world.

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Citation: Gudiseva Swetha, Poosarla Chandrasekhar, Ravi Teja Chitturi, Deepika, S. Kattapargi Kiran Kumar and Baddam Venkat Ramana Reddy, 2015. "Telepathology-a breakthrough in diagnosis", *International Journal of Current Research*, 7, (9), 20714-20718.

INTRODUCTION

Tele medicine is an emerging branch of medicine that eliminates the hurdle of sharing or transfer of data to distant places. Apart from the drastic change in the field of communication, there is leap of progress in providing a diagnosis in pathology utilizing the present technology. (Kayser et al., 2011) The usage of telecommunication and informatics helps in accessing the patient's data even from the remote or rural inhabitants. Critical life saving emergencies can be resolved by transmitting the images and the records to the best available health providers by the usage of information technologies. (Weinstein, 1986) Earlier various methods were used just for conversation, but the innovations in telecommunication has lead to transfer and gather information regarding advanced diagnostic systems which facilitate the health providers to offer the best care.Telemedicine uses electronic transmission of data and digital images to distant places for the purpose of diagnosis. It is a suitable form for transferring the data. (Williams et al., 2010) Telemedicine has evolved into various branches like tele-radiology, teledermatology, tele-pathology, tele-neurophystriaty etc. Among the branches of telemedicine the present review focuses on telepathology in detail.

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Department of Oral Pathology, SIBAR Institute of Dental Sciences, Guntur, Andhra Pradesh, India. Telepathology is practicing anatomical or clinical pathology by viewing gross to microscopic images electronically with the help of digital imaging. Transfer of path gnomic images for accurate diagnosis and further research is the crucial aspect of telepathology. The term telepatholgy was coined in 1986 by a pathologist Dr Ronald S. Weinstein, who is also known as "Father of telepathology". (Weinstein, 1986) The updated clinical guidelines for telepathology released in August 2014 by the American Telemedicine Association (ATA) define telepathology as a form of communication between medical professionals that includes the transmission of pathology images and associated clinical information for various clinical applications including, but not limited to, primary diagnoses, rapid cytology interpretation, intra operative and second opinion consultations, ancillary study review, archiving, and quality activities. (Pantanowitz *et al.*, 2014)

It is irrelevant whether telepathology is practiced using static images, virtual slides, whole slide images, or the images generated from a robotically controlled motorized light microscope. Telepathology is about the practice of pathology at a distance by pathologists. It encompasses all of the elements of a pathology and histopathology consultation including the generation of a written report, quality control, and quality assurance of all of the processes of light microscopy, the gathering and interpretation of patient information and where needed, consultation with the patient's other physicians. (Kayser *et al.*, 2005) The system of telepathology plays a crucial role in improving diagnostic pathology for patient care. It was already being practiced in developed countries and is being started in developing countries especially India. This review mainly focuses on the types, uses, advantages, disadvantages and the future of telepatholgy in India and in the World.

Telepathology involves various types of systems:

- 1) Static (store and forward, and live),
- 2) Dynamic,
- 3) Dynamic with a robotic microscope,
- 4) Combination of Static and Dynamic, Hybrid,
- 5) Whole slide imaging (Virtual slide imaging). (Schrader and Kldiashvili, 2008)

Static system

Static telepathology is the simplest approach of viewing the representative site of the pathologic slide. (Sowter and Wells, 1998) Static image telepathology is practiced by capturing microscopic images with a still photo camera, converting them to a digital format and sending them via either wide-area network or local-area network to a recipient. (Weinberg et al., 1996) A conventional static-image system contains a microscope, camera (either a digital camera or an usual photo camera attached with a slide scanner), and a high-speed network connection. The images that are captured in this way are usually of high quality (over 1 megapixel in size) and require extensive storage space and bandwidth. Few images are captured that signify only a portion of the entire histological specimen. (Weinstein et al., 1997) Superior software is not necessary, the usual digital imaging format shall be sufficient. In this system the recipient has no input on the capturing of the image and has to render the diagnosis on the images received. The receiver needs only a high speed network to visualize the images.

These static imaging systems are relatively inexpensive, easy to arrange and maintain, and are more than sufficient if the primary purpose of the telepathology system is to run a consultation service. However, if the originating pathologist (sender) misses an area on the glass slide of potential diagnostic importance, so will the receiving/consulting pathologist. Hence, the diagnosis rendered on a telepathology consult specimen should always include a statute of limitations and the images should be stored and retained in the digital data banks of both the sender and the recipient. (Weinstein et al., 1997) One advantage of static telepathology is, no precise software is necessary to observe the images and it requires only some components such as microscope, camera and internet. It has the major benefits of being the most reasonably priced and usable in the widest range of settings. However, there are some disadvantages such as the possibility of missing a potential diagnostic important area, lack of precision and lack of focus in stagnant images. (Weinberg et al., 1996)

Dynamic system

Dynamic-image telepathology (DIT) captures images from the glass slides and transmits them to recipient continuously in real

time, providing a fulltime control over the images received and allows to visualize the whole slide. For instance, the recipient is the one who decides which magnification and which slide field should be used. A DIT system should include a digital or charge coupled device (CCD) video camera, proprietary software, stable broad-bandwidth connection between originator (sender) and recipient, high-resolution monitors, qualified personnel on both ends and dedicated hardware (computers) capable of handling all the above described requirements (Vidovic and bilalovic, 1997). The DIT captured images are usually of lower resolution than those developed in SIT. As an addition, a robotic microscope used initially will allow the receiving pathologist to actively scan the glass slide and to choose the slide fields, thus reducing the need for a trained pathologist. (Danilovic et al., 1995; Elford, 1997) These systems prove to be high-priced and are effective with enormous samples & scarce personnels. Dynamic telepathology using fully monitored robotic system, has improved the field and a concordance of as high as 95-100% between glass slide and telepathology. (Long, 2000)

Hybrid system

It uses a combination of both static and dynamic systems. In this system of novel hybrid telepathology simultaneous transmission of both real-time microscopy and static imagery at a realistic expenditure is done. It is proficient enough to capture static, true color images at resolution of $1,520 \times 1,144$ pixels and providing a real-time live images of the glass slide in Common Intermediate Format (CIF), which can be viewed at $1,024 \times 768$ pixels or higher. Instant freeze option can be enabled with 4x CIF resolution ($1,408 \times 1,152$ pixels). This system comprises the advantages of real-time communication and high-resolution static metaphors, while straight visuals and audio interactions are maintained at the same time. (Zhou *et al.,* 2000)

Virtual system

Virtual slide systems use automated scanning to capture an overview image of the entire slide, which can be forwarded to another location for the purpose of diagnosis. (Wojcik, 2004) The Virtual Microscope is intended a to be a apart of computer hardware and software system that generates a rational digital analog to light microscopy. The Virtual Microscope system provides the ability to access high power and high resolution digital images of entire histopathology slides, assemble individual image panes into a seamless composite, store the image data into a specially tailored database, and sample the dataset for display onto a local or remote client. ¹⁹ The display systems are designed to evaluate, as much as possible, the actual movement of a slide across a stage, including short latencies between movement and focus or between objective and center of attention. The Virtual Microscope works on a client/server planning. The client software works on an end user's computer, while the database software to store the data. The database software is further decomposed into two parts -a frontend process that accepts queries from clients and one or more *backend* processes that store and retrieve the slide image data required to satisfy a query, and return the data to the client. (Michael Weinstein and Jonathan, 1997)

The main difficulty in providing Virtual Microscope functionality is efficiently dealing with the extremely large quantities of data required to represent a large collection of slides. For example, "using a digitizing microscope available at Johns Hopkins Hospital, the scan of an individual spot reproduces a grid of 1000x1000 pixels, and many examinations are needed to cover the entire slide". In practice, specimen at 200x magnification (real cases will require much higher power) requires approximately 70x50 scans, which amounts to several Giga Bytes of data. (Olsson and Busch, 1995)

Clinical guidelines

Clinical guidelines includes selection of distal imaging systems determined at discretion of medical imaging pathology facility for clinical use. Image may be acquired from variety of devices like cameras, scanners, variety of displays including TV screens and mobile devices may also be used. The judgment of pathologist determines whether or not image is satisfactory for rendering diagnosis. Consistent presentation of images is essential which inturn depends on the software, usage of graphic controlls and few other display devices. When diagonal dimension of display distance is about 80% of viewing distance good visualization of displayed images is obtained. Zoom and Pan function need to be used for the display of image at the originally acquired spatial resolutions. Viewing devices should be color calibrated. Although there is no accepted standard calibration for color medical displays it is important to select one from a variety of options in literature that can readily be implemented and maintained on the display of choice. For the transmission of telepathology images correct band width, proper connectivity and good computing capabilities should be in place. If images used in telepathology are to be checked further, manipulated and to be retrieved adequate storage capacity should be in place. Compression technology may be used as long as it does not compromise the image for clinical use. (Pantanowitz et al., 2014)

Applications of telepathology

Telepathology is currently being used for a wide spectrum of clinical applications including diagnosing frozen section specimens, primary histopathology diagnoses and second opinion diagnoses and research assessments. Advantage of this system include, providing immediate access to off-site pathologists for rapid frozen section diagnoses. (Weinstein et al., 2001) An emergency service in absence of pathologist, case conferences including interdisciplinary summits, quality assurance, education (undergraduate, postgraduate and ongoing professional development) is a must. There is an increasing demand to use 'virtual slides' for certain core diagnostic services in the absence of a local pathologist. This is likely to increase in the near future. (Krupinski et al., 1993)

This diverse applications of telepathology makes the provision of regulation. However, if pathological specimens in one location are being routinely reported at a distant site via a telepathology link without input from a local pathologist, several new and difficult problems will be raised. (Dunn *et al.*, 1997)

Potential benefits of telepathology

Rapid provision of expert opinion

All pathologists from time to time are faced with a case where an expert or second opinion is of value. Telepathology has the potential to allow a pathologist rapidly to seek the opinion of a expertise. This is likely to be significant in smaller departments although, with increasing specialization, even in departments where there are many experts, telepathology would allow deliberations with other professionals. A 'live' telepathology consultation allows the local pathologist and expert to consider the case at the similar time. This significantly improves the learning prospective over that of a conventional consultation.²⁵

Provision of an urgent diagnostic service in absence of local pathologist

Telepathology has been used for many years to provide an intra-operative frozen section service for small hospitals in sparsely colonized areas, where local histopathologist is not avaliable. The consultant pathologist is usually provided with remote control over a local microscope, with the sections and maintenance of equipment being provided by resident technical staff. More recently, the development of virtual slide technology has provided an alternative way to deliver the same type of service.

Provision of an on call service

With increasing specialization, pathologists working in areas where an on-call service is needed (such as transplant pathology) have difficulty in finding a sufficient number of local pathologists. The use of telepathology permits a service, to engage beyond the area in time and obtaining or furnishing the opinion staying at home.

Distant provision of a diagnostic service for the routine workload

With increasing service demands, staff shortages and pressure on costs, new technologies such as 'virtual slides' create the possibility of the complete diagnostic service being provided by pathologists based far from the patient's local hospital. Attempts to use this approach are very inadequate, but are likely to nurture.

Local provision of a diagnostic service for the routine workload

Recent advances in virtual slide technology have led some manufacturers to suggest that, in the future, slides produced in a local laboratory will be digitized and supplied to local pathologists for examination on computer monitors, relatively than using a microscope. This is sometimes described as 'telemicroscopy', to distinguish it from telepathology.

Image analysis and quantification

There are many aspects of routine pathology where semiquantitative evaluation is required, such as severity of inflammation, tumor grading, and degree of dysplasia. These assessments are subjective and poorly reproducible. Some pathologists have attempted to improve reproducibility by applying various techniques of image analysis to digital images. If digital images are routinely produced for diagnosis, the execution of quantitative techniques becomes more practical and may increase reliability of assessment of prognostic and therapeutic biomarkers. (Long, 1999)

Education and training

Telepathology is already quite widely used to support education and training. There are many excellent online resources that have cases or images of very high quality and the breadth of material available provides a valuable adjunct to more traditional journals and books. Streamed video from meetings and case conferences supported bv videoconferencing are becoming part of routine training. Virtual slide technology has the potential to allow many pathologists to view slides and cases as if at their own microscope. Cases and slides are viewed online, significantly reduces the time and cost of travel, can be undertaken at a time that suits the learner. The techniques of telemicroscopy can also be of value in the undergraduate curriculum, with the potential to introduce students the value of microscopy in a structured way, without the need to maintain large numbers of optical microscopes. (James Lowe, 2013)

Difficulties in telepathology

Few complex problems are encountered in the system of telepathology.

Legal issues

Since telepathology is used to send images anywhere in the world for diagnosis, there are several legal issues that arise when a telepathology service is used from outside national boundaries.

Quality issues

At present, there are no defined minimum technical standards in telepathology for capturing image, its retrieval and storage, transmission or observation. Such standards include:

- The image resolution
- The color depth that should be captured
- The speed with which images should be transferred from one site to another
- The essential qualities of any viewing station is to ensure that the captured information is not degraded at the remote site. (Desai *et al.*, 2004)

Defining such principles will be not easy, because they will change with technological developments and with the different uses of telepathology.

Between The Distant Pathologist, Clinical Staff and local laboratory staff

There must be a route by which urgent consultations can be arranged between the pathologist and clinician, to facilitate the transfer of clinical data that is relevant to the pathological diagnosis, and to allow the rapid transmission of information to the clinician who is in urgeny and unexpected laboratory results. The advantage of this in histopathology has been emphasized by the development of multidisciplinary group meetings. It is essential that a pathologist be available to take part in such meetings, even if attendance is by video conference link rather than in person.

Linguistic problems

If telepathology is used to connect pathologists, clinicians, laboratory staff and clerical staff who do not share a familiar language, linguistic problems can be predictable and minimum standards of communication in one common language (usually English) must be assured. (James Lowe, 2013)

Fate of telepathology in developing countries

India, Argentina, Soloman Islands, Cameroon, Ethiopia, Iran, South Africa and Egypt are the developing countries which have started to use the benefits of telepathology. There is an heightened physician scarcity in developing countries where disease burden is greatest and resources for health care are very limited. Lack of pathologists in these countries has lead to delays in diagnosis and misdiagnoses adversely affecting patient care and survival. (Charles L. Hitchcock, 2011) The existing telepathology systems were not designed with budding countries in intellect. Their probable benefits to these nations are still underutilized and largely underexposed. Preliminary studies and demonstration projects have shown that there may be significant socio cultural challenges for integrating telepathology in health care systems of developing countries. Other barriers include insufficient laboratory communications, outdated telecommunication amenities, endowment and sustainability, lack of personnel, poor technical quality of slides, vague legal issues. (Sani Abubakar Malami, 2011)

The practice of telepathology in India

Telepathology in India is still in sprouting stages. Even though much improvement has been made around the world specially in the field of digital imaging and practical slides, the live out of telepathology in India still revolves around static pathology, be it in telelearning or distant learning or in remote diagnosis. (Baruak, 2005) Illustrative of the success of telepathology between institutions is the experience of using static telepathology consultation between a tertiary cancer centre (Tata Memorial Hospital) and a rural cancer hospital (Nargis Dutt Memorial Cancer Hospital) in Barshi, Maharastra. (Desai et al., 2004) This project allowed rapid and timely access to expert opinions and bridged the gap between medically under privileged rural areas and superior centers. It was approved by few pathologists that using tele communication facilities and a 56 k modem it was possible to have first-class telepathology consultation. The project bore fruit after overcoming initial difficulties of unreliable, inconsistent and through perseverance and cooperation among various organizations such as Department of Telecommunications (DOT), Mahanagar Telephone Nigam Limited (MNTL) and Bharath Sanchar Nigam Limited (BSNL). The familiarity gained can serve as a model to make telepathology a working reality in rural India. A quiz page of telepatholgy was opened in patho

india.com e group and interesting cases were put in the form of an interview. Few of these cases were also hosted for conversation at http://ipath.ch, which is a free website offering an open source frame work for building web- and email based telemedicine applications. (Baruak, 2005)

Conclusion

Thus the methods of telepathology have potential to improve several aspects of pathology practice, for the benefit of patient care. The use of telepathology in the developing world must adhere to the chinese proverb : "Give a person a fish, and you feed them for a day. Teach a person how to fish, and you feed them for a lifetime." There is an imperative need to concur accreditation standards for the exploit of telepathology, in relation to its mode of use, image quality, training and communications. These standards may need to be specific to each of the various applications of telepathology. The training and assessment of pathologists needs to incorporate the acquisition, manipulation and use of digital images. Established pathologists also need digital imaging to be incorporated into continuing professional development. The best pathology services are delivered in a context of clinical governance, laboratory accreditation and well-functioning laboratory and clinical teams with good communications.

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