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Review Article

Digital Pathology – From Slides to Screen

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ABSTRACT

The term 'Digital Pathology' (DP) is used to denote digitisation efforts in pathology. DP can be defined as the digitalisation of gross and microscopic tissue specimens. Digital slides are created by scanning glass slides with a scanning device to provide high-resolution digital images that can then be managed, analysed, distributed and stored as digital images. Whole slide imaging helps to get high-resolution digital slides, the pathologist can scan the slides rapidly and focus by zooming in and out on the monitor using the keyboard, mouse, or his/her finger and gather information to make the diagnosis. These images are an accurate representation of the scanned glass slide and in some applications; they may be more valuable than the actual glass slides in terms of image resolution and ease of identification of specific diagnostic features. Digital imaging can be subdivided into two classes, that is, the digital microscopes to create a digital image and diagnosis-aided systems to detect the region of interest and give a presumptive diagnosis. The various benefits of using DP are similar in concordance in diagnosis as with glass slides with rapid access to second opinion, archiving and retrieval of slide images are much easier, and case histories and diagnostic information can be easily shared and retrieved. Another important field is the medical education, for graduates and postgraduate students, where difficult and rare cases can be shared and stored. The integration of clinical, laboratory and radiology data with pathology images, applying artificial intelligence (AI) for correlation is called computational pathology, which is the future of diagnostics. However, DP still has to deal with issues such as large data storage, high initial investment, confidentiality and lack of standardisation. These issues are being dealt with and newer solutions are being discussed. DP has started to expand and there are many well-established DP companies working towards the advanced diagnostic skills for pathologists and building the required business framework to support the development of precision medicine. Few biopharmaceutical companies and top clinical research organisations have adopted the concept of DP to streamline their drug development processes. DP can be relevant with the advent of assays such as markers or multiplex, which are difficult to discern with the human eye. With the increased use of exponential technologies such as AI and machine learning, enhanced translational research, computer-aided diagnosis and personalised medicine is expected to grow in the near future. After a DP system has been successfully deployed and integrated, the possibilities are immense. It is assumed that DP is not meant for taking pathologists out of the picture, infact with the emerging data analytics tools, DP will undoubtedly allow pathologists to make a more accurate and consistent diagnosis in the near future.

Keywords: Digital pathology, Whole slide imaging, Artificial intelligence, Computational pathology

INTRODUCTION

The history of Digital Pathology (DP) goes back to the 1960s, when the concept of telepathology, that is, transmitting microscope images between remote locations was experimented. Later, in the 1990s, concept of virtual microscopy[1] appeared in several life science research areas. The term 'Digital Pathology' to denote digitisation efforts in pathology was introduced at the turn of the century and has been around for nearly 50 years. However, it is in the past decade that

true digital transformation of moving away from analogue into an electronic media has been happening. Over the past 5 years, Whole Slide Imaging (WSI) has been a game changer with affordable scanner technology and mass/cloud storage technologies appearing in the market. The field of radiology has undergone the digital transformation many years ago; however, the same is not true for the haematoxylin and eosin stained routine histological slides. Although virtual microscopy is being used for external quality assurance, continuing medical education programs, teaching purposes, etc., but the replacement of traditional glass slides for routine diagnostics still looks far from being true in most departments of laboratory medicine and pathology.

DP-WHAT AND WHY

DP can clearly be defined as the digitalisation of gross and microscopic tissue specimens, as well as the management, analysis, distribution and storage of clinical data and pathological images. It is a revolutionary idea to make pathology more objective, the routine work of pathologists involves the identification of patterns in gross and microscopic tissue sections to reach a diagnosis that can be rendered to the clinician and to the patient for further investigation or for starting therapy. Pathology has always been a very subjective speciality; with the evidence-based medicine taking precedence, it becomes imperative that we make efforts to objectify pathology, as a subject, too. This can be done by DP to a certain extent. In case of DP, the intellectual process of analysing and interpreting pathology images to provide a final diagnosis is one of the central aspects of the pathologist's work. Therefore, both image and report must always include the name of the consultant pathologist and department where that intellectual work has been performed.

As a teaching tool also DP can be very useful, currently, archival tissue collections and new teaching cases are scanned and converted to static digital images, these images of gross and microscopic pathology specimens are captured by digital cameras, tablets, iPads and smartphones and then downloaded into personal computers or university servers for storage ready for teaching or discussion in the multidisciplinary clinical meetings.

WSI

The introduction of WSI has created some wonderful opportunities for the pathologist by allowing capturing images of the entire pathology slide without the need to select only a few regions of interest.[2,3] A WSI scanner may be considered a digital microscope also known as virtual microscopy, which is fitted with special high-resolution cameras which combined with optics and software serves to produce diagnostic quality images.[4] These images are an accurate representation of the scanned glass slide, and in some applications, they may be more valuable than the actual glass slides in terms of image resolution and ease of identification of specific diagnostic features. Modern WSI scanners can scan from 1 to 400 slides at a time, typically using a microscope lens with magnification of ×20 or ×40. Due to the high-resolution digital slides, the pathologist can scan the slides rapidly and focus by zooming in and out on the monitor using the keyboard, mouse or his/her finger and gather information to make the diagnosis.[5] Digital imaging can be subdivided into two classes according to the aim, the first being digital microscope and the other being diagnosis-aided systems. The digital microscopes aim to create a digital image from an analogic image detected with a light microscope. Conversely, diagnosis-aided systems can detect the region of interest and give a presumptive diagnosis. The robotic microscopic scanner mechanically scans histologic glass slides containing the tissue already processed and stained. A software combines individual scanned fields into a composite digital image. This new technology applied with the WSI can be used for primary diagnosis, for publication of scientific data in peer-reviewed journals, and to capture static images for reporting, archiving or computer-aided analysis and training purposes in the universities and hospitals. At present, multiplane images are feasible, but take very long to scan slides and produce large files. Some pathologist has resorted to video microscopy on cytology material.[6]

ADVANTAGES OF DP

The principal benefits of using DP are as follows:

Service Quality

- Multiple studies have compared WSI glass slides to digital slides and evaluated their concordance. In a study used for FDA market authorisation,[7] a total of 1992 cases were included, resulting in 15,925 reads. The major discordance rate with the reference standard diagnosis was 4.9% for WSI and 4.6% for microscopy, when evaluated ≥4 weeks after initial diagnosis. Authors conclude that WSI is non-inferior to microscopy for the primary diagnosis in surgical pathology, including biopsies and resections stained with hematoxylin and eosin, immunohistochemistry and special stains.
  WSI offers the possibility to view the entire slide which enhances orientation within the specimen. Image analysis software allows precise selection of the structures to be evaluated and notes can be added right on the image and saved.
- Rapid access to second opinions and expert review, thus better and higher quality of diagnosis.

- Convenient recording of cancer staging parameters, including measurements, to improve the outcomes and reproducibility.

Improvements in patient safety

- Use of an integrated DP system allows faster and more secure transfer of digital slides directly to the pathologist
- The glass slides are fragile and prone to breakage which is overcome by portable and transmissible diagnostic image
- Also reducing the turnaround time.

Advanced workflow

- Flexibility for the individual and the departments
- Rapid case tracking, archiving and retrieval of slide images, case histories and diagnostic information
- Fast case transfer times between the laboratory and assigned pathologists, resulting in streamlined turnaround times and defined Standard Operating Procedures (SOPs).

More involved and positive laboratory workforce

- With DP, there is a better balance in individual workload with the option and ease of remote corroboration of any diagnosis
- Choice of working whenever and wherever may help in better productivity. Even those considering retirement can choose to offer their services on more flexible terms, and thus work till longer ages
- Making 'work-life balance' more attainable is likely to appeal to the next generation of pathologists.

In medical education

- The use of 3-dimensional (3D) data to produce physical models, which is entering in education of undergraduate and postgraduate medical students.[8] The benefits being multiple people can examine the 3D gross specimens at one time, at their pace and without being exposed to toxic chemicals such as formaldehyde. There is also the advantage to go back to the sample at any time
- The integration of clinical, laboratory and radiology data with pathology images, applying artificial intelligence (AI) for correlation is called computational pathology, which is the future of diagnostics.

Use of DP and AI in diagnostics

- The use of digital images for building helper tools and diagnostic algorithms for the pathologist as a decision support work flow. The AI-based prognostic or diagnostic algorithms can be used to look for specific features such as the number of mitotic figures, presence of infectious agents such as acid-fast bacilli or even grade cancers.

Telepathology

- It is the practice of pathology at a distance using technologies. Telepathology is an efficient and cost-effective means for inter-professional histopathology consultation, pathology working groups and peer review, facilitating collaboration and sound science and economic benefits by enabling more timely and informed clinical decisions.[9]

LIMITATIONS OF DP

Data storage

Large data storage capacity is required for high-resolution images, which serves to be a challenge.

Non-standardisation

With no standardisation in DP processes, there are limited choices of solutions currently available in the market.

High investments

Significant investments are required to set-up or upgrade DP networks. The ambiguity of potential return on investment is slowing the adoption and growth rate for DP. Introducing DP diagnostics requires a large investment in IT infrastructure, including setting up the hardware and software and additional staff training.[10]

Data safety

Robust networks are required to process data and ensure high-level data confidentiality, as per regulatory guidelines. Instable technology is a major limiting factor.

Computer vision syndrome (CVS)

CVS or digital eye strain is defined as the eye and vision problems associated with the use of long term electronic screens. Between 64% and 90% of computer users experience visual symptoms such as burning eyes, diplopia, dry eyes, headaches, eyestrain and blurred vision due to using (computer) screens.[11]

FUTURE TRENDS IN DP

DP has started to expand and will be providing advanced diagnostic skills for pathologists. Few biopharmaceutical companies and top clinical research organisations have adopted the concept of DP to streamline their drug

Table 1: Companies actively working in digitalising pathology.

Companies	Product	Brief description
Thermo Fisher Scientific	3D HISTECH	It uses various digital pathology instruments and tools for digitalisation of the pathology labs.
PathAI	Concentriq platform-Proscia	This software is dealing with optimising laboratory operations, expert reviews and tumour boards.
Roche	uPath	Fast, customizable platform enhancing the efficiency of the pathology laboratory workflow.
Deep lens	Virtual Imaging for Pathology Education and Research	This cloud-based virtual pathology platform uses artificial intelligence.

development processes. DP can be relevant with the advent of assays such as markers or multiplex, which are difficult to discern with the human eye. Well-established DP companies need to consider building the required business framework to support the development of precision medicine using DP.

Some of the companies, such as Inspirata Inc. and MD Biosciences, have adopted different approaches to increase their foothold in the DP domain. Inspirata offers 'Digital Informatics Solution' that streamlines case management and communication among the entire care team, whereas MD Biosciences offers cutting-edge DP imaging equipment for rapid, high-resolution digitalisation of whole slides for reviewing and assessing through their secure and cloud-based image management system.

Several algorithms are being developed (e.g., pattern recognition algorithms) that improve accuracy, reliability and productivity. Computer-assisted Image Analysis has been used to score certain immunohistochemical stains, this gives all pathologists the same yardstick for scoring immunohistochemistry findings in cancer.

With the increased use of exponential technologies such as AI and Machine Learning, enhanced translational research, computer-aided diagnosis and personalised medicine is expected to grow in the near future. [Table 1] lists some of the companies actively working in digitalising pathology.

CONCLUSION

A variety of digital solutions are already available in the market for migrating the entire workflow of pathologists from manual to digital; these solutions have helped overcome barriers and address associated challenges with the traditional pathology workflow. The requirement now is fundamental change in how tissue is processed, the workflow is standardised and most important is the mindset and the willingness to adapt to this new system. Challenges such as high bandwidth requirements, electronic platforms, the operating systems and data storage have been targeted and are improving enormously. The solution is accelerating data storage, simplifying data management and improving data protection for cloud infrastructure, data analytics, AI-rich content, high scientific computing and numerous other applications that may be considered unconceivable currently. Therefore, it is time that pathology is completely digitalised, and we adapt to these winds of change.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

Dr. Alpana Gupta, Dr. Richa Ranjan and Dr. Abhishek Pathak are on the editorial board of the journal.

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