Original Article

USE OF ARTIFICIAL INTELLIGENCE IN HEALTH DIAGNOSTICS - A VALIDATION STUDY ON CHORIONIC VILLI

Talat Zehra[1], Asma Shaikh[1], Nighat Jamal[2], Asma Shabbir[1], Binish Arif[1], Nausheen Ferozuddin[3]

[1]Jinnah Sindh Medical University, Karachi Pakistan
[2]Bahria University Medical & Dental College, Karachi Pakistan
[3]Fazia Ruth Pfau Medical College, Karachi Pakistan

ABSTRACT

Objective: The aim of the study was to validate chorionic villi identification by artificial intelligent software verses manual diagnosis.

Material and Methods: A Cross sectional study carried out at Yasmeen Syed Lab from 1st September 2020 to 30th October 2020 on samples(n=60) previously diagnosed cases of products of conception. Glass slides were scanned into digital slides using Bes Scope camera at 4x objective (0.1 um pixel). Digital slides were imported into Aiforia Oy software for all subsequent steps, including annotation, training, and analysis of digital slides. The minimum confidence level for diagnosing chorionic villi in software was 50%.

Results: Out of 60 cases, the software was able to diagnose 50 cases correctly. The concordance between glass slide and digital slide was 50 (83.33%). Once the software attained maturity, software showed green color chorionic villi present on digital slide after analyzing.

Conclusion: Artificial intelligent software is a novel technique, as it can overcome the scarcity of pathologists all over the world in general and in the developing world particularly. The results of this study were encouraging. We have certain limitations because of the unavailability of digital microscope or a pathology slide scanner.

Key Words: Digital pathology, Artificial intelligence, Chorionic villi.

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INTRODUCTION

Histopathology is microscopic study of disease cells and tissues. Histopathological analysis is implemented by examining thin slices of tissues embedded on glass slides under light microscope. The microscopic study of histopathology images is commonly regarded as the gold standard for the clinical diagnosis of many diseases. In practice, histopathologists visually examine the irregularities of tissue, architecture, and various cellular features to determine morphological abnormalities benign tumors and malignancy [1]. Manual analysis of tissue slides in present-day still remains to be the primary way to identify malignancy and non-neoplastic pathologies along with ancillary studies, which depends heavily on the expertise and experience of histopathologists. Such manual intervention has the disadvantages of being too much time taking for such a high throughput and high content screening. Sometimes it is also difficult to grade in a reproducible manner due to high intra- and inter-observation variations in the grading process [1].

It has been about more than two decades since the introduction of the whole slide imaging (WSI) scanner. During this time, various WSI devices have transformed the field of pathology [2]. Digital Pathology is a novel technology and is currently being implemented worldwide [3]. Digital and computational pathology, partnered with artificial intelligence software and machine learning, set the stage for a groundbreaking shift in laboratory operations. Digital pathology enables the pathologist to perform most of their work at home. Various validation studies have been conducted and published, indicating that WSI is a reliable tool for routine diagnosis in surgical pathology [4,5].

Digital pathology enables full section ‘‘bird’s-eye” view, contrast of different tissue sections on the same display (especially supportive in valuing interval changes in samples taken at different time or different stains from the same sample [6,7]. Once the slide becomes virtual, tumors can be more accurately measure and also the quantification of much pathology can be reliably done. The second part of digital pathology is tissue image analysis by using image analysis software which help the pathologist work a bit easier by quantifying certain features for example in certain tumors, the presence and no of mitosis play an important role in the grading and staging of tumor [8,9]. Sometime pathologist consumes lots of time and energy for picking up small pathology in a busy slide but with the help of image analysis software, this work can be

Correspondence: Dr Talat Zehra, Assistant Professor, Department of Pathology, Jinnah Sindh Medical University, Karachi, Pakistan

Email: **talat.zehra@jsmu.edu.pk**

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accomplished in span of seconds with reliable and reproducible manner.

Digital pathology, which captures high-resolution images of tissue specimens, has been pivotal in enabling pathologists to maintain operations during the pandemic situation These digital images can be viewed anywhere and easily shared for second opinions and consults or in digital teaching sets, overcoming the limitations of working with physical glass slides and microscopes. The practice of sharing images at a distance is referred to as tele-pathology.

After Covid-19 pandemic, as the world is an adopting new norm, current pathology practice is vastly adopting toward a digital technique, cumulating in applying screens to view scanned histology slides. These screens can be either of computer, smart phones or tablets. The process of digitization of glass slides with the combination of specialized artificial intelligent (AI) software tools to identify and measure different pathologies which were previously observed via light microscope has brought revolution in the competency of pathologists to utilize whole slide image analysis on tissue sections. This will result in the growth of tissue-derived data that are more detailed and highly reproducible as AI based image analysis software [10].

The study will validate the glass slide diagnosis with digital slide made simply by using microscope camera and then analyzed these slides by Aiforia Oy software. The purpose of this study was to validate artificial intelligence diagnosis with manual diagnosis. The study had one limitation, we had not the facility of a slide scanner.

MATERIAL AND METHODS

This was a cross sectional study carried out at Yasmeen Syed Lab from September 2020 to October 2020. Sample size was calculated according to College of American Pathologist (CAP) guidlines15. 60 cases of endometrial curetting labeled as products of conception in women ages between 20-40 years, received at the Yasmeen Syed Lab from January till July 2020 were collected after the approval of Ethical Board Committee. Poorly fixed/autolyzed samples or endometrial curettings send for other purposes were excluded from the study. All slides were made digital on 4x power to get max area. Digital slides were made by using microscope connected camera. Then these slides were trained and analyzed by tissue image analysis software Aiforia Oy. The software was trained for various size and shape of chorionic villi including hyalinized/ghost chorionic villi for about 1000 times. We trained few slides for various sizes and shapes of chorionic villi and feed the software to become green after attaining 50 % confidence level. 50% confidence level was already feed in the image analysis software. The training was supervised by Aiforia customer success manger Dr. Darshan Kumar.

RESULTS

A total of 60 cases were selected according to College of American Pathologist guideline for validating single pathology. Out of 60 cases, software was able to diagnose 50 (83.33 %) cases successfully. The minimum confidence level for diagnosing chorionic villi in software was 50%. We made training regions with gray color and after selecting training region, we applied annotations as green color for various size and shape of chorionic villi and rest of the area was labelled with black colour pencil as shown in Figure-I.The software showed green color chorionic villi after analyzing it as shown in Figure-II. Once the software attained maturity as shown in Figure-III and IV, we did not make annotations, just made training region with gray color as shown and put the digital slide in software and jump on analysis option, the software was able to recognize all the chorionic villi present on digital slide as shown in Figure-IV We use simple percentage method for validation of results. As we use only single pathology so advanced method used for making results were not used in this study.

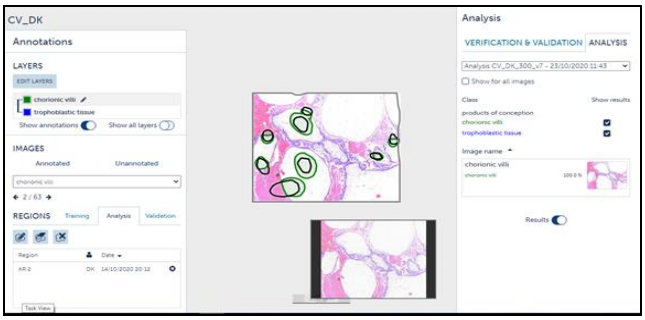

Figure-I: Hematoxylin & eosin stained slide was made digital at 4x. We put the slide in Aiforia Oy software; training regions were made as gray color. Annotations were made as green for various size and shape chorionic villi. The black color denotes as background showing hemorrhage.

Figure-II: The chorionic villi became green in most of the slide where they were present.

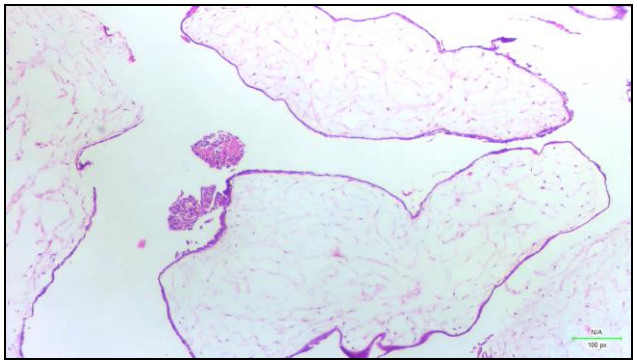

Figure-III: Hematoxylin & eosin stained slide is showing chorionic villi of various size and shape at 4x. This slide was not trained for chorionic villi.

Figure-IV: We made only the training region and put the slide for analysis. The software was able to recognize all the chorionic villi and turned green.

DISCUSSION

Histopathology labs are nowadays under enormous burden to increase their productivity in diagnostic process timing and improving quality. The reasons are many, few of them are due to increased incidence of cancer cases every year but the numbers of histopathologists are decreasing day by day. By making the glass slides digital, pathologists can view their cases from everywhere on their screens surpassing the requirement of a microscope [11,12].

Despite of many above mentioned possible benefits, like other medical device planned for clinical purposes, there is the requirement to monitor certain regulatory necessities so that patient care may not be compromised[13]. Validation of applications for digital whole slide images for routine diagnostic use is a very important step to guarantee that accuracy is at least comparable to the one attained by viewing glass slide through conventional light microscopy [13].

College of American Pathologist (CAP) has already given its recommendation for validating single pathology in glass slide by digital slide [14]. In recent years many researchers/pathologists work with digital pathology and Al solutions and demonstrate the importance of these tools in diagnostic Pathology [15]. The success of these recent studies has showed the improvement in the information management of the patient cases.

Chorionic villi are one of the most common pathology, the histopathologists come across in routine cases, and many times it is very easy to pick up but some time it consumes lots of time of histopathologists to identify chorionic villi in a busy slide showing extensive hemorrhage and deicidal tissue. It is important to document chorionic villi in cases of specimen in abortion or dilatation and curettage cases with history of pregnancy to rule out trophoblastic diseases like choriocarcinoma and other trophoblastic diseases [16]. This study was conducted to validate chorionic villi detection by using tissue image analysis software. We had few limitations in our study. The most important was absence of pathology slide scanner or a digital microscope to make whole slide image of the slide. So, we simply made digital slide by using the camera of microscope. We made slide digital on 4x to get maximum area covered.

More validation studies by using the data of our own patients in terms of whole slide imaging is required before the implementation of digital pathology systems in routine clinical diagnosis, so that the confidence of pathologist can be attained as most of the pathologists working in different parts of the world are still not aware of this novel technique [17].

Tissue image analysis is second part of digital pathology, which when performed correctly, can change the entire horizon of traditional thought process of pathologist which has been unchanged for decades. After that the role of pathologist will not be of reactionary but the pathologist will be on the seat of policy making by making the disease models and predict the disease trend of specific geography through data science and data mining [18].

In 2017, US Food and Drug Administration approved whole slide imaging for primary diagnosis [19,20]. Since then the adoption of digital pathology technique was slow even in the developed part of the world as compare to the field of radiology. The promises of AI embedded digital pathology are undoubtedly beyond the scope of traditional microscopy. Applications like machine learning can provide the opportunity for pathologist to go on smart sign out system for pathology [18].

Since last year, the entire world is on the threat of Covid-19 Pandemic which has taken until now more than 2.8 million human beings across the globe irrespective of geography and financial status. No one can predict how long this pandemic will threat the humanity and for how much time we will have to work from home which is not possible currently in our scenario even after the arrival of vaccination.

Whole slide imaging by using a scanner or a digital microscope is a part of profound and fast technologic expansion with far success and overarching requests in the field of pathology. Regardless of the benefits, the adoption of this novel technique has been slow even in the developed parts of the world as the pathologists were used to of seeing cases under microscope for decades.

The barriers discussed below presently exclude the extensive implementation of whole slide scanning in the low resource organizations of the developing part of the world. Some of these weaknesses can be overcome by teamwork between a reference laboratory equipped with a WSI system and smaller laboratories through a hub-and-spoke model [21].

Along with the technical and cost-related stuffs, regulatory and validation requirements also need to be sufficiently spoken, particularly for the developing nations. Nonetheless, whole slide imaging provides an excellent opportunity for pathologists to guide its development, standardization, and execution by playing a crucial role in defining or refining guidelines. Digital pathology can also offer equal opportunities of learning the post graduate trainees across the country to have uniform and equal learning opportunities irrespective of their station. In this way we can create harmony and satisfaction among the trainees working in different part of country [21,22].

Journey of Digital Pathology has already begun and we as a Pathologist are excited about its implementation on large scale in our countries in future. In Pakistan, the concept of digital pathology and artificial intelligence is still new and not too many pathologists know about this novel technology [23]. The reason may be that the pathologists are not aware of the benefits of these techniques. Due to this reason and issues like regulation in the steps of slide processing, calibration of digital slides, variability in the image quality and technical problems, pathologists may be reluctant to adopt to digital pathology [24].

CONCLUSION

Adaptation of digital cases is now demand of the day particularly in this Covid-19 era and also for remote diagnosis even after the pandemic resolves for more reliable diagnostic approach. This was just a very small effort to go towards digitalization but the results were appreciating. Few larger validation studies are required before the implementation of digital pathology in our part of the world which contains most of the bulk of world diseases but unfortunately less equipped with diagnostic modalities particularly the novel ones! Unavailability of whole slide scanner and digital microscope are expensive and beyond the budget of many low socioeconomic organizations in developing part of the world.

LIMITATIONS

The study was limited by absence of whole slide scanner. So, we used digital slides of the cases not the whole slide image.

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AUTHOR CONTRIBUTION

Talat Zehra: Conceived the idea, designed the study and involved in making digital slides, trained the software and writing.
Asma Shaikh: Idea, methodology, writing & drafting manuscript.
Asma Shabbir: Paper writing, drafting and discussion.
Nighat Jamal, Binish Arif, Nausheen Ferozuddin: Methodology and drafting.

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