Biomedical Science Letters 2023, 29(2): 53~57
https://doi.org/10.15616/BSL.2023.29.2.53
eISSN : 2288-7415

Review

Application of Artificial Intelligence-based Digital Pathology in Biomedical Research

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The main objective of pathologists is to achieve accurate lesion diagnoses, which has become increasingly challenging due to the growing number of pathological slides that need to be examined. However, using digital technology has made it easier to complete this task compared to older methods. Digital pathology is a specialized field that manages data from digitized specimen slides, utilizing image processing technology to automate and improve analysis. It aims to enhance the precision, reproducibility, and standardization of pathology-based researches, preclinical, and clinical trials through the sophisticated techniques it employs. The advent of whole slide imaging (WSI) technology is revolutionizing the pathology field by replacing glass slides as the primary method of pathology evaluation. Image processing technology that utilizes WSI is being implemented to automate and enhance analysis. Artificial intelligence (AI) algorithms are being developed to assist pathologic diagnosis and detection and segmentation of specific objects. Application of AI-based digital pathology in biomedical researches is classified into four areas: diagnosis and rapid peer review, quantification, prognosis prediction, and education. AI-based digital pathology can result in a higher accuracy rate for lesion diagnosis than using either a pathologist or AI alone. Combining AI with pathologists can enhance and standardize pathology-based investigations, reducing the time and cost required for pathologists to screen tissue slides for abnormalities. And AI-based digital pathology can identify and quantify structures in tissues. Lastly, it can help predict and monitor disease progression and response to therapy, contributing to personalized medicine.

Key Words: Digital pathology, Whole slide imaging, Artificial intelligence

INTRODUCTION

The primary objective of tissue examination for pathologists is to achieve accurate diagnoses of lesions. This task is critical for identifying the causes of diseases and developing effective treatments, thereby providing a rational foundation and guidance for these processes.

The explosive growth in the number of pathological slides requiring diagnosis has placed a considerable burden on pathologists. Additionally, differences in the training and experience of researchers have resulted in inconsistencies in diagnostic outcomes.

Despite efforts to establish diagnostic names and criteria, the subjective nature of pathology diagnosis may lead to variations in the names and criteria used (Mazer et al., 2019). Consequently, various diagnosis names and criteria may exist within a single diagnosis, making it necessary to systematize and standardize them (Morton et al., 2010).

Received: April 5, 2023 / Accepted: June 27, 2023

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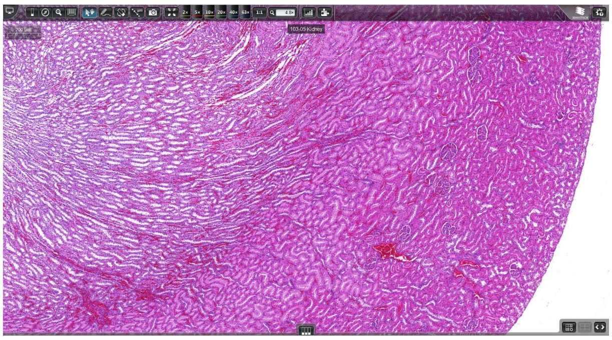

Fig. 1. Representative figure of whole slide imaging in kidney of rat.

Advent of digital pathology

Digital pathology is a specialized area of pathology that emphasizes on managing data generated from digitized specimen slides. Pathological materials are consisted of wet tissue, tissue block, tissue slide and so on. Among them, analogue tissue slide is converted into digital image file, called whole slide image (WSI) using virtual slide scanner. Representative figure of whole slide imaging is presented in Fig. 1.

A virtual slide scanner comprises various components, including an optical microscope, camera, storage system, and computer hardware. The time taken to scan a slide varies based on the tissue's size and the magnification used, but typically ranges between 1 to 10 minutes per slide. WSI technology is used to digitize tissue slides for pathological assessment (Hamilton et al., 2012) and has replaced glass slides as the primary method of pathology evaluation (Bradley and Jacobsen, 2019).

Additionally, image processing technology that utilizes WSI is being implemented to automate and enhance analysis. WSI has advantages over conventional tissue slides because it enables permanent data storage and the analysis of various information through image values stored in pixels. Successful implementation requires collaboration among pathologists, technologists, and executive leadership (Zarella et al., 2019). This approach has been applied to assess the classification of various cells, such as bone marrow hematopoietic lineages (Kozlowski et al., 2018b), and specific tissues, such as collagenous tissue (Liang et al., 2017).

Digital pathology that employs WSI facilitates the utilization of digitized tissue slides for data management, image analysis software for quantitative analysis, and mathematical models for disease prediction. With the availability of WSI of tissue slides, image processing techniques have been employed to automate and optimize analysis. WSI-based digital pathology has been adopted to enhance time efficiency and reduce costs (Farahani et al., 2015) and eliminate potential human bias (Aeffner et al., 2019).

Artificial Intelligence (AI)

Various applications incorporating AI are being developed to assist the process of pathologic diagnosis, and detection and segmentation of specific objects. AI is expected to show breakthrough potential in medical imaging, especially in the field of digital pathology (Tizhoosh and Pantanowitz, 2018).

Several companies are working on developing AI algorithms for screening digital slides to automate the classification of specific tissue lesions often observed in nonclinical and clinical studies. The growing number of AI algorithms is refining the pathology platform and enhancing the accuracy of diagnoses, which is especially beneficial for personalized medicine (Turner et al., 2020). Among them, deep learning has been successful in image classification and is expanding into medical image analysis (Brent and Boucheron, 2018). including CNN-based systems such as VGGNet or ResNet (Hoefling et al., 2021).

Application of AI-based digital pathology in biomedical researches

Application of AI-based digital pathology in biomedical researches is classified into four areas: diagnosis and rapid peer review, quantification, prognosis prediction, and education, as illustrated in Fig. 2.

1) Diagnosis & rapid peer review

AI-based digital pathology can be used for diagnosis & rapid peer review. Combining AI with pathologists can result in a higher accuracy rate for lesion diagnosis than using either a pathologist or AI alone. For instance, AI algorithms have been used to detect cancer and achieve similar accuracy in diagnosing skin cancer biopsies (Esteva et al., 2017) and distinguishing between benign and malignant breast tumors

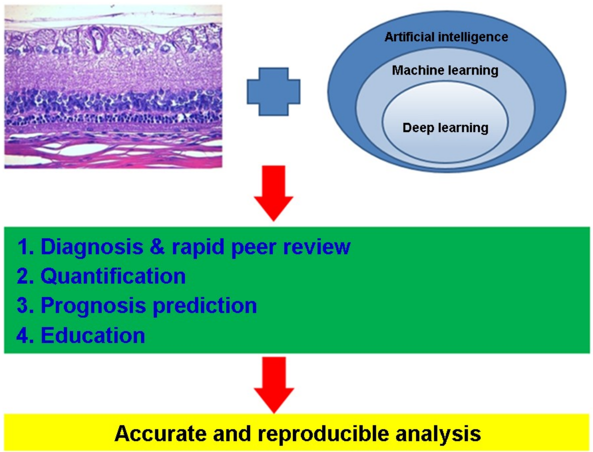

Fig. 2. Application of AI-based digital pathology in biomedical researches.

(Radiya-Dixit et al., 2017). Additionally, AI can perform multiple functions, including identifying nuclear, epithelial, and tubular divisions and finding interrelationships among various pathological parameters that researchers may overlook (Janowczyk and Madabhushi, 2016).

With a substantial amount of WSI and the aid of AI in retrieving similar lesion images, it is anticipated that the duration of slide examination can be shortened and precise pathology diagnosis can be achieved. It can enhance and standardize pathology-based investigations through advanced techniques, including unifying input criteria and improving test endpoint accuracy (Pell et al., 2019).

Additionally, it can reduce the time and cost required for pathologists to screen tissue slides for abnormalities, leading to more efficient diagnosis and potentially increased accuracy (Schaer et al., 2019). For instance, AI can help to shorten the time for differential diagnosis in difficult tumor cases and improve the accuracy and consistency of diagnosis by reducing the differences between individual pathologists and laboratories (Mazer et al., 2019). Furthermore, it decreases inter- and intra-laboratory variability.

Peer reviews conducted through AI can significantly reduce the time required for the process in case of errors or conflicting opinions among pathology experts. Actually, AI can supplement pathology data and evaluations from experienced pathologists to ensure accurate and consistent lesion diagnosis, speeding up the peer review process (Morton et al., 2010).

2) Quantification

Lesions in pathology are graded on a scale, but the subjective nature of human analysis can affect the accuracy of the grading system. To overcome this, AI classifiers are being developed to grade lesions objectively.

AI-based digital pathology using classifiers can accurately and rapidly quantify pathological lesions. It is anticipated that it has the potential to detect differences in cellularity that may be difficult for humans to distinguish, especially when cellularity is less than 10%. In addition, it can isolate and count cells in tissues, such as bone marrow cells, to detect bone marrow decline (Kozlowski et al., 2018a).

Moreover, AI-based digital pathology can identify and quantify structures in tissues. For example, it can automatically count glomeruli in kidneys (Sheehan and Korstanje, 2018) and detect and segment tubules in kidney tissue (Kannan et al., 2019). Collagen can also be quantified through AI analysis, and specific tissue types can be estimated (Liang et al., 2017). AI has also shown efficiency in quantitatively interpreting special stained slides (Segnani et al., 2015) and immunostained slides (Sheikhzadeh et al., 2018).

3) Prognosis prediction

AI-based digital pathology can assist in predicting prognosis by allowing direct analysis of tissue slides, reducing the time needed for genomic analysis. This not only decreases the workload of pathologists but also lowers the cost of diagnostic tests while potentially increasing diagnostic sensitivity. Moreover, it can integrate complex genomic, transcriptomic, and metabolomic data from slide images, enabling molecular-level analysis that can be translated into clinical trials involving blood and urine samples.

AI-based digital pathology can predict genetic mutations and microsatellite instability (MSI) by analyzing images and genetic profiles, improving clinical outcomes. For instance, it can identify and classify subtypes of lung cancer and predict cancer-specific gene mutations (Coudray et al., 2018), and predict MSI in gastrointestinal cancer (Kather et al., 2019). This approach has been found to be effective in identifying cases with molecular alterations.

4) Education

The current education system for pathology in biomedical researches, which requires extensive training and experience, is insufficient to meet the growing demands of this field (Kuo and Leo, 2019). As more substances require pathological analysis, the demand for trained pathologists is increasing. To address this shortage and improve diagnostic accuracy, a new education system incorporating AI technology is needed.

AI-based digital pathology can be used to train pathology trainees, students, and even current pathologists or technical staff. The traditional light microscopy can be replaced with WSI, which produces high-fidelity digital representations of entire histological glass slides, offering numerous educational possibilities (Saco et al., 2016).

With the aid of WSI, trainees can acquire knowledge, practice diagnosis-related tasks, and obtain specialist licenses for precise diagnoses in a shorter time. In addition, the creation of a database using WSI and big data technology, combining data from various tests and generating large datasets for pathological research, is expected to have a significant impact on education.

CONCLUSION

The use of AI-based digital pathology in biomedical researches is gaining popularity in various pathological tasks. When pathologists work alongside AI and combine their knowledge, the accuracy of lesion interpretation can improve and errors can be reduced.

Experts in pathology should actively incorporate AI to advance lesion evaluation technology. It is expected that the collaboration between computer science and pathology will become more common, and an AI-based platform will be necessary to establish diagnostic criteria in pathology.

AI-based digital pathology is a promising approach that can provide accurate diagnosis and rapid peer review, as well as precise quantitative analysis of various tissue structures. Moreover, it enables prognostic prediction and ongoing education through further examination.

ACKNOWLEDGEMENT

Funding for this paper was provided by Namseoul University 2022.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

Aeffner F, Zarella MD, Buchbinder N, Bui MM, Goodman MR, Hartman DJ, Lujan GM, Molani MA, Parwani AV, Lillard K, Turner OC, Vemuri VNP, Yuil-Valdes AG, Bowman D. Introduction to digital image analysis in whole-slide imaging: A white paper from the digital pathology association. J Pathol Inform. 2019. 10: 9.

Bradley A, Jacobsen M. Toxicologic pathology forum*: Opinion on considerations for the use of whole slide images in glp pathology peer review. Toxicol Pathol. 2019. 47: 100-107.

Brent R, Boucheron L. Deep learning to predict microscope images. Nat Methods. 2018. 15: 868-870.

Coudray N, Ocampo PS, Sakellaropoulos T, Narula N, Snuderl M, Fenyo D, Moreira AL, Razavian N, Tsirigos A. Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning. Nat Med. 2018. 24: 1559-1567.

Esteva A, Kuprel B, Novoa RA, Ko J, Swetter SM, Blau HM, Thrun S. Dermatologist-level classification of skin cancer with deep neural networks. Nature. 2017. 542: 115-118.

Farahani N, Parwani AV, Pantanowitz L. Whole slide imaging in pathology: Advantages, limitations, and emerging perspectives. Pathology and Laboratory Medicine International. 2015. 7: 23-33.

Hamilton PW, Wang Y, McCullough SJ. Virtual microscopy and digital pathology in training and education. APMIS. 2012. 120: 305-315.

Hoefling H, Sing T, Hossain I, Boisclair J, Doelemeyer A, Flandre T, Piaia A, Romanet V, Santarossa G, Saravanan C, Sutter E, Turner O, Wuersch K, Moulin P. Histonet: A deep learning-based model of normal histology. Toxicol Pathol. 2021. 49: 784-797.

Janowczyk A, Madabhushi A. Deep learning for digital pathology image analysis: A comprehensive tutorial with selected use cases. J Pathol Inform. 2016. 7: 29.

Kannan S, Morgan LA, Liang B, Cheung MG, Lin CQ, Mun D, Nader RG, Belghasem ME, Henderson JM, Francis JM, Chitalia VC, Kolachalama VB. Segmentation of glomeruli within trichrome images using deep learning. Kidney Int Rep. 2019. 4: 955-962.

Kather JN, Pearson AT, Halama N, Jager D, Krause J, Loosen SH, Marx A, Boor P, Tacke F, Neumann UP, Grabsch HI, Yoshikawa T, Brenner H, Chang-Claude J, Hoffmeister M, Trautwein C, Luedde T. Deep learning can predict microsatellite instability directly from histology in gastrointestinal cancer. Nat Med. 2019. 25: 1054-1056.

Kozlowski C, Brumm J, Cain G. An automated image analysis method to quantify veterinary bone marrow cellularity on h&e sections. Toxicol Pathol. 2018a. 46: 324-335.

Kozlowski C, Fullerton A, Cain G, Katavolos P, Bravo J, Tarrant JM. Proof of concept for an automated image analysis method to quantify rat bone marrow hematopoietic lineages on h&e sections. Toxicol Pathol. 2018b. 46: 336-347.

Kuo KH, Leo JM. Optical versus virtual microscope for medical education: A systematic review. Anat Sci Educ. 2019. 12: 678-685.

Liang L, Liu M, Sun W. A deep learning approach to estimate chemically-treated collagenous tissue nonlinear anisotropic stress-strain responses from microscopy images. Acta Biomater. 2017. 63: 227-235.

Mazer BL, Homer RJ, Rimm DL. False-positive pathology: Improving reproducibility with the next generation of pathologists. Lab Invest. 2019. 99: 1260-1265.

Morton D, Sellers RS, Barale-Thomas E, Bolon B, George C, Hardisty JF, Irizarry A, McKay JS, Odin M, Teranishi M. Recommendations for pathology peer review. Toxicol Pathol. 2010. 38: 1118-1127.

Pell R, Oien K, Robinson M, Pitman H, Rajpoot N, Rittscher J, Snead D, Verrill C. The use of digital pathology and image analysis in clinical trials. J Pathol Clin Res. 2019. 5: 81-90.

Radiya-Dixit E, Zhu D, Beck AH. Automated classification of benign and malignant proliferative breast lesions. Sci Rep. 2017. 7: 9900.

Saco A, Bombi JA, Garcia A, Ramirez J, Ordi J. Current status of whole-slide imaging in education. Pathobiology. 2016. 83: 79-88.

Schaer R, Otalora S, Jimenez-Del-Toro O, Atzori M, Muller H. Deep learning-based retrieval system for gigapixel histopathology cases and the open access literature. J Pathol Inform. 2019. 10: 19.

Segnani C, Ippolito C, Antonioli L, Pellegrini C, Blandizzi C, Dolfi A, Bernardini N. Histochemical detection of collagen fibers by sirius red/fast green is more sensitive than van gieson or sirius red alone in normal and inflamed rat colon. PLoS One. 2015. 10: e0144630.

Sheehan SM, Korstanje R. Automatic glomerular identification and quantification of histological phenotypes using image analysis and machine learning. Am J Physiol Renal Physiol. 2018. 315: F1644-F1651.

Sheikhzadeh F, Ward RK, van Niekerk D, Guillaud M. Automatic labeling of molecular biomarkers of immunohistochemistry images using fully convolutional networks. PLoS One. 2018. 13: e0190783.

Tizhoosh HR, Pantanowitz L. Artificial intelligence and digital pathology: Challenges and opportunities. J Pathol Inform. 2018. 9: 38.

Turner OC, Aeffner F, Bangari DS, High W, Knight B, Forest T, Cossic B, Himmel LE, Rudmann DG, Bawa B, Muthuswamy A, Aina OH, Edmondson EF, Saravanan C, Brown DL, Sing T, Sebastian MM. Society of toxicologic pathology digital pathology and image analysis special interest group article*: Opinion on the application of artificial intelligence and machine learning to digital toxicologic pathology. Toxicol Pathol. 2020. 48: 277-294.

Zarella MD, Bowman D, Aeffner F, Farahani N, Xthona A, Absar SF, Parwani A, Bui M, Hartman DJ. A practical guide to whole slide imaging: A white paper from the digital pathology association. Arch Pathol Lab Med. 2019. 143: 222-234.

https://doi.org/10.15616/BSL.2023.29.2.53

Cite this article as: Kang JS. Application of Artificial Intelligence-based Digital Pathology in Biomedical Research. Biomedical Science Letters. 2023. 29: 53-57.