**TOPIC- INTEGRATION OF ARTIFICIAL INTELLIGENCE & MACHINE LEARNING IN THE FIELD OF CONVENTIONAL PATHOLOGY.**

**DR. SUNEEL KUMAR JAISWAL (MBBS, GMC MUMBAI) ( MD PATHOLOGY, MGMMC INDORE)**

**DR. D. S. GUPTA (MBBS, MD IMS BHU, SENIOR PHYSICIAN JHANSI)**

The current gold standard in histopathology is based on the visualization and analysis of representative two-dimensional tissue sections of three-dimensional specimen. It has been established for many decades and is currently used for most histological examinations. The diagnostic workflow for histology consists of three steps: sample preparation, visualization, and algorithm-based analysis [1].

Tissue are examined grossly and subsequently cut for transfer of relevant tissue into casting molds. The casting molds are then poured with paraffin and prepared for manual cutting of the tissue blocks and transferred onto a glass slide, After that staining with Hematoxylin & Eosin (H&E) stains representative tissue sections are sequentially analyzed by pathologists using light microscopy.  but the main limitation to morphologic diagnosis is diagnostic variability in bearing error among pathologists.

**Immunohistochemistry (IHC)** is a well-established and indispensable assay being consistently performed in Histo-pathology worldwide in order to provide a specific diagnosis and subclassification of neoplasms and prognosis [2,3]. IHC serves at present both as a diagnostic, prognostic, and predictive assay and the results contribute to the final decision for patient treatment. IHC is in its most common application a descriptive, threshold based test to determine if a target protein is present or absent and thus the result, classified as either positive or negative, is used in the final diagnostic work [4,5]. IHC is widely applied in formalin-fixed paraffin embedded (FFPE) histological material and primarily used to identify the origin and subtype of cancers

At present, more than 200 IHC targets such as S-100, HMB-45, NAPSIN-A, WT-1, Thyroid Transcription Factor 1 (TTF1), Cytokeratin’s (CKs), Cluster of differentiation (CD) molecules, etc.

In the last decades, the number of predictive IHC tests have gained increasing acceptance and been widely applied for decision making prior to the administration of targeted therapies. Since the introduction of HercepTest™ (Dako) in 1998 as an IHC assay for the demonstration of human epidermal growth factor receptor 2 (HER-2) protein overexpression in breast cancer and thereby guide the selection of patients to be treated with Herceptin, many similar IHC assays have been developed and now used as Diagnostic assays to stratify patients and predict the response likelihood of a specific drug [6]. Examples of these include IHC analysis of anaplastic lymphoma kinase (ALK) and ROS1 mutations in non-small cell lung cancer (NSCLC) for treatment with tyrosine kinase inhibitors as Crizotinib or Alectinib and more recently introduction of IHC assays to demonstrate the level of PD-L1 in many cancer types such as NSCLC, urothelial carcinoma, triple negative breast carcinoma (TNBC) to predict response with checkpoint inhibitors such as Pembrolizumab, Azetolizumab, and comparable drugs [6,7]

Accurate and timely diagnosis is critical for deciding on the best treatment for the individual patient at the right time. Pathologists have assumed a more central role and are again essential physicians, especially on the oncology care team, because they have specialized knowledge to inform diagnostic test selection, performance, and interpretation at the highest quality level, as well as the communication of results and the implications for subsequent care decisions — a role that pathologists self-confidently owned after the successful implementation of light microscopy about 200 years ago.

**Artificial intelligence (AI)** is the ability of computer software to mimic human judgement. Current AI systems carry out only very specific tasks for which they are designed, but they may integrate large amounts of input data to carry out these tasks quickly and accurately.

It is a powerful technology, but many pathologists do not yet know how AI could be applied in their daily clinical work. Yet, pathologists must participate in the development and clinical use of AI-based solutions to deliver the digital future and guide the generation of diagnostic and predictive algorithms through their existing expert knowledge and visual experience. In order to get a consistent and possibly more accurate diagnosis, it is natural to introduce algorithmic intelligence in the pathology domain, at least in the morphological analysis of tissues and cells. With the help of digital pathology equipment varying from microscopic cameras to whole slide imaging scanners, morphology-based automated pathologic diagnosis has become a reality. In this review, we focus on morphology-based pathology: diagnosis and prognosis based on the qualitative and quantitative assessment of pathology images. Typical digital image analysis tasks in diagnostic pathology involve segmentation, detection, and classification, as well as quantification and grading.

Digital pathology images used in AI are mostly scanned from H&E-stained slides. Pathology specimens undergo multiple processes, Each step of the process and the different devices and software used with the digital imaging scanners can affect aspects of the quality of the digital images, such as color, brightness, contrast, and scale. For the best results, it is strongly recommended to alleviate the effect of these variations before using the images in automated analysis work.

The most important advantage of AI based pathology is to reduce errors in diagnosis and classification. The Camelyon Grand Challenge 2016 (CAMELYON16 challenge) is a worldwide machine learning-based program to evaluate new algorithms for the automated detection of cancer in hematoxylin and eosin (H&E)-stained whole-slide imaging (WSI), has achieved encouraging results with a 92.4% sensitivity in tumor detection rate. In contrast, a pathologist could only achieve 73.2% sensitivity [8]. Computational pathology has the potential to transform the traditional core functions of pathology and not just growing sub-segments such as digital pathology, molecular pathology, and pathology informatics (9,10).

**Machine learning (ML)** is a collection of mathematical and computer science techniques for the extraction of relevant data from large datasets trained and explained by human experts and in this case by expert pathologists. Therefore, ML can support the human factor, mostly in performing difficult, tedious, and repetitive tasks. An automated ML method will read multiplexed immunohistochemistry images always in the same reliable and robust manner, yielding the identical result over and over again. This allows a global comparability of complex and larger datasets without significant inter- and intra-observer variability. ML algorithms may include decision trees, Bayes’s networks, clustering solutions, and regression solutions as well, depending on whether the solution is rather supervised or unsupervised.

In the new era of deep learning-assisted pathology, data banking, integration, and cloud laboratory are becoming an essential part of daily practice of pathology. Furthermore, pathologists, data scientists, and industry are starting to incorporate the genomics, proteomics, bioinformatics, and computer algorithms into a large amount of complex clinical information. Through this process, computational pathology can contribute valuable insights to the diagnosis, prognosis, and treatment of disease.

With the rapid development of digital pathology, Artificial intelligence-based pathology is increasingly involved in many subspecialties such as pulmonary, renal, gastrointestinal, neurology, and gynecology pathology. We believe the initial phase of AI will start with specific tasks such as the diagnosis of a particular cancer and classification of tissue types, which require limited and simple criteria.

Automated Artificial Intelligence (AI) systems will have a hard time increasing their performance to 95% or even 99%. But that might be required to get close to the performance of a pathologist using the right tools. The key problem for automated Artificial Intelligence (AI) systems for pathology are the variations between different patient types. In a disease state, no two patient samples look identical.

Finally, despite the challenges and obstacles, the potential of Artificial intelligence-based pathology which will change and improve the current health care system is promising and exciting.

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