Move from Traditional Histopathology to Digital and Computational Pathology: Are we Ready?

Traditionally, histopathology has largely been a manual and subjective field of pathology and is still so in most parts of the world. In the move toward automation and objective evaluation, histopathology has lagged behind other fields of pathology and laboratory medicine.[1] One of the main reasons for its slow adaptation to automation is the fact that many manual and largely independent steps are involved in the preparation of material for visualization under the microscopes by the pathologists and beyond, which, on a superficial view, seem unfit for automation and digitization. The dawn of digital pathology (DP) has undoubtedly provided a spur for the move of traditional histopathology to fully automated field. Currently, DP has a limited but definite role in histopathology, and it is likely to expand in future. DP is defined as the practice of pathology using digitized images of whole microscopic sections. It has gained considerable momentum in recent years, driven primarily by the development of whole-slide imaging (WSI) systems. The latter enable the acquisition and subsequent evaluation and interpretation of high-resolution digital images of entire histologic sections on computers, which serve as digital microscopes. The overall process of WSI systems involves two steps. In the first step, scanning and imaging are done of the whole microscopic glass slides at high speed and high resolution with the subsequent creation of a single digital file, known as the digital slide. This is done by WSI scanners, of which several different brands with different imaging software programs are available in the market. The WSI scanners essentially consist of a microscope attached with robotic and computer systems. More than 30 commercial WSI scanners are currently available; common brands include Panoramic scan II, Pathscope, TISSUEscope, NanoZoomer, Lamina, Axio, and ScanScope. They have a wide range of appearances and functionality. Most have bright-field imaging mode, while a few have both bright-field and fluorescent imaging modes. The slide loading capacity varies from a few slides to more than 400 slides at a time. The speed also varies depending on bright-field or fluorescent imaging and on the highest magnification level used for image acquisition. Of note, in WSI also, the glass slides are prepared and stained in the same way as in conventional microscopy, but instead of examining the slides on a microscope, these are examined on a computer screen. The second step involves examination of digital slides on computers with a variety of image visualization and management software programs. The digital slides can be efficiently and instantaneously stored, accessed, analyzed, and shared with pathologists or scientists from across the web by using the Internet and the above-mentioned software programs. These can be examined and interpreted in the laboratory, at home, or at remote places via the Internet. The user can navigate the tissue sections, zoom in or zoom out, and annotate or measure any findings. Thus, one of the main advantages and currently the main use of DP relates to the acquisition of objective measurements of morphologic, histochemical, and immunohistochemical (IHC) features of microscopic sections, including particularly the predictive markers, such as ER, PR, HER2neu, and Ki-67, increasing both the quantity and quality of data obtained from histologic assessments by histologic image analysis methods. At present, many histologic image analysis software programs are commercially available. Choosing the appropriate program is dependent on considerations of the investigative question, computer programming and image analysis expertise, and cost. Some of the current applications of WSI include rapid transmission of pathologic data for telepathology and collaborations, standardization and distribution of pathologic materials for education, research, publishing, slide archiving, and image analysis. However, its role in making primary diagnoses in clinical laboratories is still limited but is likely to expand in the future. Recently, a milestone has been achieved as FDA has approved the use of WSI for making primary diagnosis in surgical pathology in the US. WSI has already started to change the workflows of many laboratories in the developed countries.[2-8]

However, DP is a huge and costly undertaking, particularly for resource-constrained settings, requiring a lot more than mere WSI scanners. As a result, its use is limited to hospital and corporate setups, particularly in developing countries. In addition, there are many barriers to its smooth integration with existing infrastructure and workflows in the laboratories, especially in developing countries. Some well-known hurdles include limited background infrastructure, section and image quality, problems with scanning some types of pathology materials (e.g., cytology and immunofluorescence slides), digital slide storage, inability to handle high-throughput routine work, standardization of reporting on DP, regulatory barriers, and last but not the least, the pathologists' reluctance. The scanning and imaging process is also time consuming and tedious for routine day-to-day cases. Despite the above-mentioned hurdles, the fields of DP and histologic image analysis are continuing to evolve at a steady pace and will increasingly transform the practice of pathology, permitting it to mature toward a quantitative science. However, this transition requires that the pathologists should abandon their reluctance and be at the forefront of the process, ensuring their proper application for the validity and accuracy of results, as is done by Gupta *et al*.[9]

In this issue of IJN, Gupta *et al*.[9] analyzed the diagnostic performance of WSI and compared the accuracy of WSI coupled with digital mapping with conventional eye-balling or subjective assessment of one of the chronic renal lesions, that is, tubular atrophy, in 151 adequate native renal biopsies and found that WSI is more accurate and is the way forward in quantifying reliably the chronic changes in renal biopsies in future. The authors need compliments for performing such a study from this region. This study may pave the way for digitization of histopathology in India and other countries in the region. The results of this study will interest not only pathologists but also nephrologists and will ultimately improve the patient outcomes. There are, however, a few caveats in the study. The main caveat is that the authors only studied one morphological feature on renal biopsies, that is, the tubular atrophy, whereas DP and computational pathology (CP) are supposed to offer a total solution, and the chronicity score includes chronic changes in all four compartments of kidney parenchyma.[10] Much more sophisticated image analysis tools are available, which were not used. Obviously, cost, lack of trained personnel, and lack of proper infrastructure were the likely barriers. Adoption of this technology will incur huge costs in the beginning. However, in the long term, the cost-benefit ratio will likely be favorable for DP and CP. Before this dream can be realized in resource-limited countries, first, we need to produce digital-quality pathology material by using standard equipment and reagents. These are important for obtaining digital-quality images. Though these high-resolution WSIs provide diagnostic information similar to and in many instances beyond that obtained by direct microscopy of tissue sections and are proving useful in a variety of clinical activities, their role is still limited in many instances. Their novelty and utter volume have also led to a number of image and data management challenges. One of these challenges is that laboratory information systems (LISs), which drive workflow and data management in pathology, are not well equipped to manage image-level information.[2-7]

In summary, Gupta *et al*. have opened the door to the digitization of histopathology in India and the region and merit compliments. They have validated one aspect of the utility of WSI and image analysis in histopathology, that is, the accuracy of quantification of morphological parameters. WSI, DP, and CP have the potential to revolutionize the field of pathology, but to realize that goal, pathologists need to be in the driving seat. The use of these technologies can transform pathology from a largely manual, subjective, and qualitative field to one that is data-driven, objective, quantitative, and more accurate.

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