

Histopathology in present era

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Histopathology is the branch of pathology involved in the scientific study of disease at the tissue and cellular levels. It plays an essential part in the diagnosis, risk stratification and treatment monitoring of many diseases. It is a relatively young speciality with origins in clinical specialities such as surgery and medicine.¹ Histopathology, over the years has witnessed its evolution from a mainly autopsy based pathology to the current molecular histopathology.² With recent advances in science and technology and the incorporation of these to histopathological practice and acceptance of some philosophical concepts, in particular the functional correlation of morphological studies, the outlook of both histopathology and the Histopathologist has changed.² The molecular age Histopathologist of today is practicing pathology in a totally different scenario than the preceding pathologists. Upto the mid 20th century, the pathologists based all of their diagnosis and histogenetic considerations solely on the patterns of growth and cell shapes seen with Haematoxylin and Eosin (H&E) stained slides, with occasional modest help provided by one or more special stains with inherent subjectivity and limitations of these simple tinctorial stains. Objective measurement of microscopic features has been advocated for decades as a means to make the practice of histopathology more reproducible and "scientific". With advances in computing technology, it is now possible to make this procedure suitable for diagnostic and prognostic determinations in histopathology by computerized morphometry.³ Pathologists have also been trying for some time to combine their human skills in histopathological diagnosis with the advantages offered by computer systems. One such programme, artificial neural network (ANN) has been successfully used in selected areas of surgical pathology and cytopathology.⁴ Briefly, an artificial neural network (ANN) is a nonlinear, computational, mathematical model for information processing, with architectures inspired by neuronal organizational biology. The network is constructed of discrete artificial neurons or nodes, which are interconnected by routes or links that correspond to the axons in biological neurons. Like biological neurons, an artificial neuron summates the signals arriving from incoming connections. If this reaches a certain threshold, a signal is fired down the outgoing axons. The input data are presented to the layer of input neurons or evidence node

with one input neuron required for each item of input data. The prediction of the neural network is given by the layer of output neurons or decision node. A hidden layer is interposed between input and output layers for the network to be able to perform more complex classification tasks.⁴ The authors⁵ studied ANN in the early and accurate diagnosis of acute cellular rejection in renal allograft recipients. This systematic approach increased the sensitivity of detection of early acute rejection (19 out of 21 cases) more than any of the 37 pathologists achieved by conventional histopathological assessment (17 out of 21).

The first and most widespread application of modern techniques in histopathology perhaps came in the form of Immunohistochemistry (IHC), which has become an indispensable tool for the practice of histopathology. During the last three decades, it has truly transformed the practice of histopathology, particularly tumour pathology, in a manner that no other special technique has done before or after.⁶

Since the last decade or so, histopathologists are in the midst of another transformation, resulting from the application to tissue specimens of vast amount of new knowledge derived from molecular biology revolution.^{2,7,8} Gene array technology, which allows gene expression measurements of thousands of genes in parallel, provides a powerful tool for pathologists seeking new markers for diagnosis. With such kind of data accumulating rapidly, it won't be long when molecular signatures would be assigned to each and every pathological lesion and a molecular diagnosis would even come before the paraffin sections are ready, and the Histopathologist would already know what to look for in the sections.⁹ Tumour heterogeneity was a formidable challenge, but with the development of laser capture microdissection, it is now possible to obtain pure population of tumour cells to study for gene expression analysis.²

By DNA micro array analysis and proteomics it is possible to build a comprehensive gene expression database for each of the organ systems/tumour type and use it as a clinical diagnostic and prognostic tool. It is prudent, however, that the histopathologist uses this molecular information in conjunction with his background knowledge of morphology to have a better and optimum diagnostic and prognostic yield from tissue specimens.²

Last few years have also witnessed an increasing role of electronic information technology in practically all activities that take place in the histopathology laboratory. Advances in information communication technology have particularly been of enormous help in the fields of telepathology. The latter is the sub-discipline of telemedicine that deals with the capture, transmission, and viewing of pathological images via the telecommunication channels such as the internet, dedicated satellite or telephone. Telepathology over the years has undergone drastic evolution from static telepathology, to dynamic, real time telepathology, using fully motorized robotic systems. A concurrence rate of as high as 99-100% has been reported between telepathology and light microscopic diagnosis.¹⁰ A more recent innovation in this field is the concept of "virtual slide", which has to a great extent removed the most fundamental drawback of telepathology, that is the limitation of available image for diagnosis. Virtual slides are digitalized images where the entire slide is scanned at a very high resolution, acquiring the entire image of the histopathology section at all magnifications available on the microscope. The novel array microscope DX-40 is the world's first digital imaging device that combines 80 miniature microscope objectives in a single instrument. Scanning a glass slide with the array microscope produces seamless two-dimensional image data of the entire slide i.e. a virtual slide. Image acquisition can be as rapid as 58 seconds for a section on glass slide and upto 40 slides can be scanned in an hour. It is anticipated that, with the advent of virtual microscopy an expert referral pathologist in the near future will be interpreting virtual images on LCD screens rather than glass slides.^{2,10} Since Histopathologist's job was and still is to play with the images, be it live or captured, the photography has been an integral part of pathology practice since its inception. But chemical photography has been almost completely replaced by digital photography and it is highly desirable that a postgraduate student in pathology attends a short course on photography at the beginning of his training.²

Another important change that has taken place

during recent times concerns with increasing demands of standardization, obedience of regulatory controls, and legal accountability, which have prompted various professional organizations to produce sets of guidelines to help pathologists face this increasingly complicated system.^{7,8}

Today, Histopathologists stand on the cross roads of a traditional 'visible' morphological science and an 'invisible' molecular science. As molecular biology techniques find more and more applicability in histopathological diagnosis, it is time for the policy makers and teachers of Pathology to reframe the process of accreditation and re-accreditation of the modern histopathologist in context to the rapid changes taking place in this science. The assessment and re-assessment procedure hence needs to incorporate not only the traditional histopathological techniques but also the fields of biotechnology, telecommunication, information communication technology and professional photography to produce a modern Histopathologist.

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