Chapter 2

Digital Image Analysis in Clinical and Experimental Pathology:
An Ode to Microscopy

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ABSTRACT

Conventional pathology using a light microscope is rapidly shifting towards digital integration. Digital imaging plays an increasing role in clinical diagnosis, biomedical research, and continuing medical education. Currently, pathology platforms are composed of clinical and molecular pathologists and engineers with the sole intention of investigating cellular and molecular basis of human health through applied research in disease aetiology, pathogenesis, diagnosis, and treatment. Molecular diagnosis using technical advances and the application of specific biomarkers in clinical practice are the two main pillars of modern personalized medicine especially in oncology. Thus, it has become evident that accredited clinical and molecular pathology laboratories using digital imaging and advanced technologies can make the most of diagnostic and specific biomarker analyses as well as incorporating other key aspects of translational research and data analysis.

INTRODUCTION

Clinical pathologist is a physician who specializes in the diagnosis and management of human diseases using appropriate laboratory methods. Conventional analysis of surgical or core biopsy specimens (histopathology) and body fluids, needle aspiration and exfoliative materials (cytopathology) using a light microscope is rapidly shifting towards digital integration. Digital imaging plays an increasing role in clinical diagnosis, biomedical research, seminar and continuing medical education. Currently, pathology platforms are composed of clinical, molecular, and translational pathologists and engineers with the sole intention of investigating cellular and molecular basis of human health through applied research in disease aetiology, pathogenesis, diagnosis and treatment. Molecular diagnosis using technical advances and the application of specific biomarkers in clinical practice are the two main pillars of modern personalized medicine especially in oncology. There are two levels of biomarker analysis in clinical trials; specific biomarker analysis to determine the patient's stratification and general biomarker analysis to predict patient response to treatment (Salto-Tellez *et al.,* 2014).

Clinical and molecular pathology platforms and translational research laboratories use the same tissue and fluid samples, phenotypic analysis, digital imaging and advanced technologies, under strict standards, in both clinical diagnosis and biomedical research. They play a central role in identifying mechanisms of carcinogenesis, gene expression, signalling aberrations, tumour microenvironment, cancer stem cells, tumour invasion and metastasis, metabolism, extracellular matrix regulation, angiogenesis, autophagy, ribonucleic acid (RNA) and protein expression, deoxyribonucleic acid (DNA) damage, non-coding RNA (ncRNA) deregulation and apoptosis (Meseure *et al.,* 2014; Drak Alsibai & Meseure 2018).

The precision medicine and new scientific research approach of disease generate enormous amounts of information "big data", that require database construction, analysis, storing and managing their storage (i.e. biobanking and bioinformatics). As technique complexity and data increase, so too do the amount and the complexity of data analysis. The complexity of data highlights the importance of integrating an alternative multi-parametric data assays into the clinical practice and scientific research (Gondhalekar *et al.,* 2018).

It has become evident that accredited clinical and molecular pathology laboratories can make the most of specific biomarker analyses as well as incorporating other key aspects of translational research and data analysis. Currently, these laboratories are well equipped by tissue-based techniques {i.e. tissue microarray (TMA),

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