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Hepatology Snapshot:

Digital pathology: What is the future?

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Digital Pathology (DP)

is based on converting stained tissue sections on a glass slide into a digital image through a scanner.
It allows the pathologist to assess a histological sample using a computer workstation instead of a conventional microscope.

The pathologist can navigate across the virtual slide at any chosen magnification.

Digital Conversion

Applications in Liver Pathology

Multiplex quantum dot staining & image analysis — Evaluation of multiple cell population on same section

CPA — Shown to correlate with semi-quantitative fibrosis scores and to predict outcomes in patients with chronic hepatitis and cirrhosis.

SHG/TPEP — Excellent correlation with Metavir and Ishak scores for collagen quantification in fibrosis. May enable quantification of additional histological features.

Keywords: Digital pathology; Fibrosis; Steatosis; Quantification.
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Background

Digital pathology (DP) is based on converting stained tissue sections, laid onto a glass slide, into a digital image through a scanner. It allows the pathologist to assess a histological sample using a computer workstation instead of a conventional microscope. The pathologist can navigate across the virtual slide at any chosen magnification.

The future "Gold standard" for pathology

The quality of the DP images has improved considerably in the last few years and their resolution is now very close to that obtained by routine diagnostic microscopes at standard magnifications. Advantages of DP include full section low magnification "bird's-eye" view, comparison of different tissue sections on the same screen (particularly helpful in evaluating interval changes in samples taken at different time, or different stains from the same sample), on-screen measurement tools for tumour size and clearance measurements and direct connectivity to image analysis software.[1,2] The recent review by Williams and colleagues makes the case for implementing DP for clinical diagnostic use in response to the continuous increase in histopathology workload, both with respect to volume and complexity, allowing off-site diagnosis for primary interpretation, second opinion, and intra-operative frozen sections.[3]

Incorporating DP into clinical practice may be a way to standardize histological diagnosis by reducing interobserver subjectivity, and to provide population-based repositories including annotated histological images along with clinical, molecular and radiologic data, which will facilitate multidisciplinary team meetings. Accordingly, clinical applications have been implemented in various fields including breast, skin, and gastrointestinal histopathology.[2] Lastly, DP is a powerful teaching tool allowing simultaneous viewing and discussion of the same image by multiple students using conventional electronic devices and a standard internet access.[4]

Digital pathology and liver diseases: A wide range of applications

DP offers the opportunity to apply image analysis to whole tissue sections, a major advance from the rather cumbersome and limited single field image analysis of conventional microscopy. This is of particular value when using image analysis to assess liver fibrosis, a key element for staging chronic liver diseases. The measurement of the area occupied by collagen (stained with the Picrosirius red method) as a proportion of the liver biopsy core section surface area (Collagen Proportionate Area, CPA), has been shown to correlate with semi-quantitative fibrosis scores, and predict outcomes in patients with chronic hepatitis and cirrhosis.[5,6] However, CPA measurement does not take into account the lobular architectural changes related to vascular compromise and structural remodelling which accompany fibrosis and require the interpretation of a pathologist.[7]

Future developments in DP based liver fibrosis image analysis include the application of techniques such as second harmonic generation/two photon excitation fluorescence (SHG/TPEF). This method provides a qFibrosis value based on identification and quantification of main collagen patterns (portal, septal, and fibrillary collagen), and is based on a staining-free approach obviating the variability related to the staining process. Collagen quantification using SHG/TPEF in experimental models of liver fibrosis and human liver samples from patients with chronic hepatitis B infection showed excellent correlations with Metavir and Ishak scores, and demonstrated superior performance to CPA measurement.[8,9] Interestingly, further development of this technology may allow the quantification of additional histological features such as steatosis, apoptosis, and hepatocyte ballooning, which may be of potential significance in non-alcoholic fatty liver diseases. The combination of DP with techniques such as multiplex quantum dot staining and image analysis allows the evaluation of multiple cell populations on the same section, a major step forward from conventional single stain methods on sequential tissue sections.[10] This applies particularly well to the investigation of lymphocytic subpopulations in the context of liver transplantation.

Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2018.03.023.

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