This interview was made by Dr Ahmed Youssif the assistant lecturer of Pathology in Theodor Bilharz Research Institute , Dr Ahmed is now finishing a 3 month training in the pathology department of Beaujon Hospital under the direction of Prof Paradis and Prof Bedossa

First of all, allow us to express our deep gratitude for giving us this interview, we hope this will be the cornerstone for more future cooperation

1) **Liver biopsy; still the gold standard for evaluating livers of hepatitis B and C patients?**

In the era of non-invasive markers of liver fibrosis, indications of liver biopsy are currently decreasing. In HCV hepatitis, diagnosis of patients with no or little fibrosis (F≤ F1) and advanced fibrosis (F≥ F3) may be achieved without biopsy with confidence. Nevertheless, liver biopsy is recommended in patients showing discordances in fibrosis stages provided by non-invasive markers. Presence of co-morbid factors, such as metabolic syndrome, alcohol consumption, auto-immune markers, etc, may also motivate to perform liver biopsy in order to assess the contribution of each different risk factor in the severity of the tissue damages. In patients with HBV hepatitis, indications of liver biopsy appear to be wider, especially in the management of antiviral therapy, allowing the selection of patients who need to be treated and when to be treated (EASL guidelines 2012). Notably, HBV hepatitis may be associated with significant necro-inflammatory liver lesions, accurately assessed on biopsy, but may interfere with the performance of the non-invasive tools for the diagnosis of fibrosis.
Finally, and thanks to the increasing efficiency of antiviral drugs, cases with fibrosis reversal are more and more expected. In that context, accuracy of non-invasive tools for the diagnosis of fibrosis has not been extensively investigated. Therefore, biopsy may provide significant information, in terms of fibrosis extent, aspect of fibrosis, intensity of necro-inflammatory lesions, …. .

2) **Our main issue in interpreting a liver biopsy for viral hepatitis is the grading of inflammation and staging of fibrosis. What else can a liver biopsy tell us about the patient?**

Liver biopsy in patients with viral hepatitis is able to provide additional informations, especially regarding comorbidity factors. Among them, metabolic syndrome incidence, leading to NAFLD and NASH, is growing worldwide. Therefore, degree of steatosis, presence of steato-hepatitis (as tissue markers of metabolic syndrome), should be screened. In addition, presence of iron overload, a cofactor for fibrogenesis and HCC development, may also be systematically assessed.

3) **Diagnosis of hepatic nodules suspected to be HCC in liver biopsies can sometimes be problematic; can you give us some tips on how to avoid over- and under-diagnosis of HCC?**

In patients with chronic liver diagnosis, the main differential diagnosis of HCC is dysplastic nodules. An international pathological consensus of small nodules (<2 cm) in cirrhotic liver has been obtained, recognizing regenerative, low- and high-grade dysplastic nodules and small HCC, mainly based on architectural and cytological features. Significant input of additional immunohistochemistry has been shown for differential diagnosis between high-grade dysplastic nodules and early HCC, using a panel of 3 antibodies [Glypican 3, HSP 70 and Glutamine synthetase]. Importantly, accurate morphological diagnosis of such small nodules warrants analysis of both tumoral and non-tumoral liver.

4) **From your experience in liver pathology, what are the main elements of your final pathology report?**

In patients with chronic liver diseases, the pathological report should include the following elements: stage (fibrosis) and grade (activity) of the disease with its adequate scoring system (i.e Metavir for viral infection, SAF score for metabolic syndrome), steatosis (grade according to Brunt or SAF score), additional features if significant (iron overload, …). Lastly, final report must indicate the nature of the risk factor for chronic liver disease.

5) **How do you see the future of *digital pathology;* a research and educational tool or a potential everyday routine?**

Digital pathology is taking an increasing place in our practice for teaching, research but also diagnostic purposes. Indeed, it will be very useful for pathological expertise. Thanks to dedicated softwares, accurate quantification of elementary features (fibrosis areas, necrotic foci, …) and more sophisticated parameters using immunostainings (proliferation index, vascular density, …) can be achieved in a reproducible and automatized procedure.

6) **Could you advice the young pathologists who are interested in the study of liver?**

Liver pathology encompasses a wide range of disorders including acute / chronic diseases and tumors. Interestingly, liver pathology is based on a multidisciplinary approach involving radiology, clinics (hepatologists and surgeons), biology and molecular biology. Altogether striking advances have been performed in the refinement of tumor classification including benign hepatocellular adenomas or mixed hepatobiliary carcinomas for instance.

Finally, thank you again for this opportunity. We wish you the best of luck and we hope we can meet you again very soon.