

Investigating chronic liver diseases and cancer by SR-FTIR microspectroscopy

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Alcoholic or metabolic fatty liver diseases, viral chronic hepatitis progressively lead to cirrhosis and hepatocellular carcinoma. The physiopathology of these liver diseases is highly complex. Spectroscopic analyses were performed on tissue sections from human normal livers, steatotic livers, cirrhotic livers and hepatocellular carcinoma to image the distributions of the biochemical components in these different pathologies. Serial tissue sections of 5-6 μm thick were alternatively stained by H&E for histological evaluation and used for spectroscopy experiments. Synchrotron microspectroscopy was performed using the beamlines SMIS at SOLEIL.

Infrared (IR) spectroscopy on normal liver was able to reveal metabolic liver zonation. IR spectra were acquired in both periportal and centrilobular areas and then analyzed using statistical method based on principal component analysis (PCA). Interestingly, data analysis of IR spectra allowed distinguishing a class of spectra specific to centrilobular hepatocytes. Moreover, major differences observed by this approach on centrilobular and periportal hepatocytes were focused on lipid content. Imaging the distribution of lipids on a large map on lobular hepatic led to visualize a gradient of distribution of lipids.

Spectroscopic studies were further applied to pathological conditions such as non alcoholic steatosis, cirrhosis and hepatocellular carcinoma. IR microspectroscopy on steatotic livers detected the presence of unsaturated lipids into steatotic vesicles in a particular lipid environment. The concentration of unsaturated lipids into steatotic vesicles which has not been hitherto demonstrated constitutes a potential highly reactive trigger for lipid peroxidation which is known to produce important molecular and cellular damages through iteratively propagated radical reaction. The molecular mechanism underlying the formation of lipid droplets has never been described and will have to be addressed in further studies. In addition, IR microspectroscopy investigations performed on the non steatotic areas of the fatty liver using has revealed important changes when compared to the normal liver. These results demonstrated that multimodal spectroscopy is a powerful approach for characterizing subtle biochemical changes associated with various liver pathologies.