A new approach to the early diagnosis of liver diseases

In a multidisciplinary study jointly conducted by three French research groups, analyses were carried out on hepatic steatosis. These studies have provided evidence of the localized heterogeneity of the pathological tissue and shown that variations in its composition can be detected at very early stages by spectroscopic approach, in particular using infrared, with facilities such as at synchrotron SOLEIL. This work, supported by the Pôle de Recherche et d'Enseignement Supérieur (PRES) UniverSud, will be published on the 12th October in the journal PLoS ONE. It widens the scope for studying pathologies in liver or other tissues for improved diagnosis and prognosis.

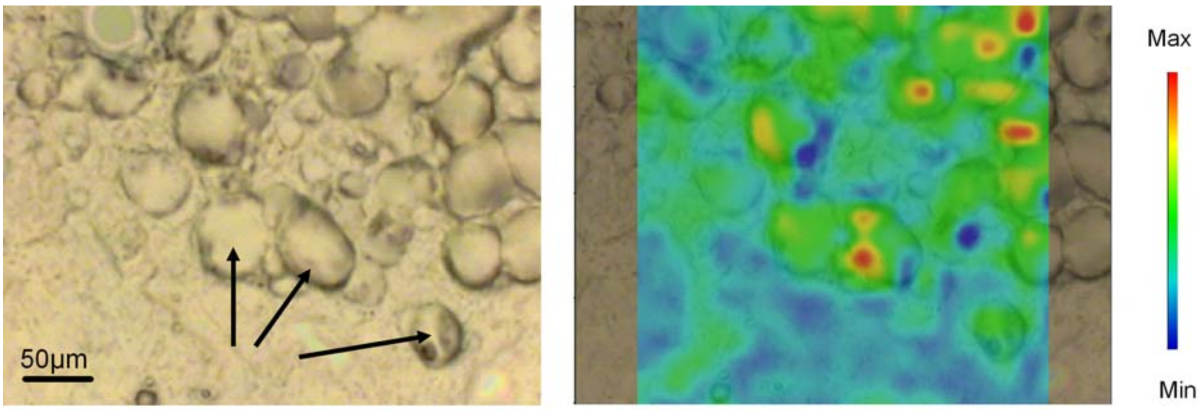
Steatosis results from an accumulation of lipids in the liver. Many factors can contribute to the onset of this disease, including obesity or metabolic problems such as diabetes. Although it is reversible and asymptomatic, steatosis can evolve into cirrhosis and in some cases, liver cancer. In Western societies, steatosis has become a major public health issue.

With the aim of studying the composition and distribution of lipids in a steatotic liver, Dr. Le Naour, a researcher at INSERM (Institut National Scientifique d'Etude et de Recherche Médicale), has worked in collaboration with the Paul Brousse Hospital Pathological Anatomy Department at Villejuif and the dedicated infrared microscopy beamline, SMIS, at SOLEIL synchrotron, headed by Dr. Dumas, to run microspectroscopy experiments on hepatic tissue slices.

Using infrared it is possible to detect very early changes in tissues

Infrared radiation at SOLEIL has been used to detect localized biochemical modifications in steatotic liver. This work has shown the selective accumulation of unsaturated lipids in droplets within cells. By combining spectroscopy with a particular mass spectrometry method (called ToF-SIMS) developed at the Institut de Chimie des Substances Naturelles (Gif-sur-Yvette) and adapted to the analysis of lipids *in situ*, it has become possible to decipher their molecular composition. This work has opened up new avenues of research into understanding how steatosis develops, as the molecular mechanisms that lead to the selective concentration of unsaturated lipids have not been understood until now. It also shows the potential danger of this pathological state, for a long time considered benign. Indeed, the concentration of unsaturated lipids inside the vesicles is potentially a highly reactive site for iterative chemical reactions that could result in cell and tissue damage, leading to more serious disease states. Infrared spectroscopic observations made using SOLEIL synchrotron radiation have made it possible to detect significant variations in composition in regions considered as identical to that of healthy liver when using standard methods. This work highlights the sensitivity of spectroscopic approaches in being able to detect early changes in biochemical composition during the pathological process.

This work has many potential applications. Such an approach could be used to identify early diagnostic markers or to be of prognostic value, leading to improved treatments for patients. It could also be used to check the quality of donor organs for transplants.



Steatosic liver tissue sections

On the left: optical microscope image. Steatosis is characterized by the formation of vesicles (arrows).
On the right, distribution of unsaturated lipids using infrared spectroscopy: The range of colors corresponds to an increasing quantity of lipids. Infrared spectroscopy allows the distribution of unsaturated lipids to be visualized in the tissue, and to show their presence inside the steatosic vesicles.

What can you see with infrared (micro)spectroscopy?

If a sample of biological tissue is irradiated with infrared wavelengths, each group of molecules that make up the tissue will resonate with one or several of them. The intensity changes of all of the infrared wavelengths is recorded, thus creating a spectrum, that is, a collection of peaks corresponding to all the vibration signatures of the different molecules present in the tissue being studied. Infrared spectroscopy therefore provides the global composition of a tissue's components: proteins, lipids, carbohydrates and nucleic acids (DNA and RNA).

When microscopy is combined with spectroscopy, it then becomes possible to determine these compositions down to the scale of a few microns, and to create a biochemical map of the tissue. Furthermore the spatial resolution of the technique having been greatly improved by the use of the synchrotron as the infrared source: by measuring a spectrum on each pixel of the sample (a "pixel" corresponding to the projected size of the infrared beam onto the sample) and by compiling the data obtained ,it is possible to reconstruct, on the sample probed, the distribution of the different constituents of the tissue, thus making it possible to understand their heterogeneous distribution, and superimpose each biochemical image with the visible image.

SOLEIL

Located on the Saclay Plateau in the Essonne department, SOLEIL is the third-generation French synchrotron. SOLEIL is a research centre directed by the CNRS (French National Centre for Scientific Research) and the CEA (French Atomic Energy Commission). The building of this type of facility involves major construction work as well as precision mechanical work. Its purpose is to accelerate bunches of electrons until they radiate extremely bright light covering a very wide range of wavelengths: from infrared to x-ray, with ultraviolet in between. The characteristics of this light (intensity, focus, stability, polarization, etc.) allow scientists to observe matter down to the atomic level and perform experiments that would previously not have been possible, in the interests of fundamental, applied, and industrial research. SOLEIL serves many areas currently of particular interest to the scientific and industrial communities: biology, chemistry, materials science, the environment, physics, Earth sciences, cultural ancient materials. SOLEIL's specifications (operating energy, number of undulators, broad spectrum from infrared to x-ray, brilliance, continuous injection for beam stability to within a micron, etc.) make it competitive at the top level on the international scene.

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