# When the physician may identify microscopic tissue architecture in real time

Diagnosis of disease is the fundamental goal of medicine as treatment and prognosis rely on it. The diagnostic process ends eventually with tissue sampling (biopsy) for microscopic evaluation. The paradigm "tissue is the issue" reflects the modern trend of disease investigation and therapy.

There are different methods of performing biopsies directed by imaging (ultrasound, computed tomography, magnetic resonance, positron emission tomography etc). The material collected is then sent to microscopic evaluation that may require hours to days for completion. The complexity of these laboratory analysis and the experienced personnel and sophisticated technologies involved requires a high degree of sample accuracy. This means that the sample is suitable for a diagnosis. Unfortunately this is not the case in all biopsies. Fibrotic (scar) and necrotic tissue may affect the ability of reaching a disease diagnosis by limiting the possibility of identifying blood vessels and cells ("viable tissue"). In the era of "personalized medicine" this may delay accurate therapy.

Various imaging technologies were developed in order to improve the yield of biopsies and a dedicated technician is sometimes present at the site of biopsy performance (radiology or surgical/endoscopy rooms). This method is called Rapid Onsite Evaluation (ROSE). It evaluates the adequacy of the sample by microscopic examination after the biopsy is performed. In case of non- adequacy the procedure is repeated until a satisfactory sample is microscopically validated. Biopsies may complicate with bleeding or air penetration of tissues. The complication rate depends on operator experience and the number of passes through the tissue. Optical biopsy may become real.

Confocal Laser Microscopy (CLM) is a novel technology based on the fluorescent properties of tissues irradiated with various wave light mainly LASER. Some human tissues have fluorescence when irradiated by LASER due to proteins or cell components (autofluorescence). In contrast fluorescence may be induced by exogenic molecules named "fluorophores". One of these fluorophores is fluorescein a dye used in ophthalmology for blood vessels "coloring" for many years. LASER may "light" blood vessels of various tissues if it contacts the tissue and fluorescein is intravenous injected. CLM was used in laboratory and recently clinical applications were made possible in different medical disciplines: dermatology, gastroenterology and pulmonology. CLM allows physician to receive a microscopic image of the tissue in real time by blood vessels and cellular identification. This allows a better targeting of the diseased area and theoretically improve the biopsy yield.

Cellvizio$^{R}$ is a novel technology that allows probe based CLM to reach human tissues and provide a microscopic image in real time. These probes are able to pass through the working channel of an endoscope and touch the examined tissue while a dedicated software "translates" into

electronically acquired images on a computer monitor. By using the microscopic differentiation between normal and diseased tissue the biopsy is better targeted.

In a proof of concept pilot study CLM was used for the first time in an attempt to improve the yield of CT guided biopsies of mediastinal and lung tumors. A dedicate probe was introduced through the biopsy needle before sampling. Injected fluorescein allowed blood vessel identification (viable tissue not necrotic or fibrotic) in both locations and malignancy was identified in mediastinal tumors. The complication rate was minimal. This feasibility pilot study may start a new way of performing biopsies in interventional radiology. Optical imaging at cellular level in real time may reduce the number of tissue passes and obviously the complication rate. With improved technology it may be possible to avoid tissue sampling all together if characteristic morphological images will be obtained at direct examination (for ex. using endoscopic techniques).

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## Publication

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