Fraunhofer IPMS

MEMS-based confocal laser scanning fluorescence microscope for tumor demarcation in oncological surgery

Every year, approx. 500,000 people in Germany are diagnosed with cancer. Diagnostics and treatment are continually evolving. However, it is still almost impossible for physicians to quickly determine the success of a tumor resection during surgery. Still today it is customary to take a tissue sample from the wound margin and have it pathologically examined in the laboratory in order to ensure that all tumor cells have been removed. The Fraunhofer Center MEOS has developed a novel system that can be used quickly, reliably, and directly on site in the operating room: a MEMS-based, confocal microscope for rapid detection of tumor boundaries during surgery.

The goal of tumor surgery is to create tumor-free resection margins while preserving the surrounding healthy tissue. This is currently hindered by the fact that 3D imaging of the tumor margin is not possible with current technical solutions. Histological analysis during surgery is generally feasible. However, it is time-consuming and not feasible for all tissue types (e.g., bone). There is thus a great need for an easy-to-use optical method that differentiates healthy tissue structures from tumor tissue intraoperatively and within a short period of time.

The Fraunhofer Center MEOS has therefore developed a MEMS-based laser scanning microscope and a fluorescence marker method of tumor cells. The goal is to localize tumor boundaries as best as possible in order to ensure complete preservation of brain cells and arteries during neurosurgical procedures.

In the first step, the tumor margin must be stained. Here, a special method for the specific staining of tumor cells is used, which entails using fluorescence-labeled antibodies at the cell culture level.

An image of the cut surface is then captured through the confocal microscope. At the heart of the microscope is a scanning mirror developed at Fraunhofer IPMS. This allows light to be deflected in the x- and y-directions, thereby generating an image virtually in real time. A lateral resolution of 1.0 µm can thus be achieved in the fluorescence image with an image field size of 400 × 400 µm² (960 × 960 pixels). For sectional images, the system is equipped with a z-shifter with a maximum path length of 2000 µm and 5 nm minimum step size.

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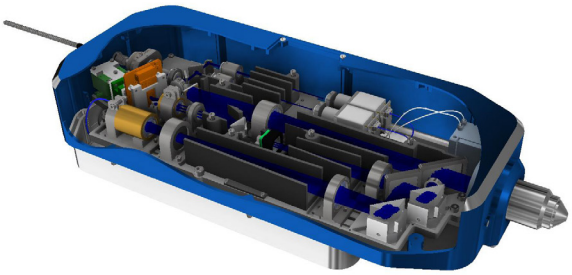


CAD design of the demonstrator.

Close-up of the demonstrator.

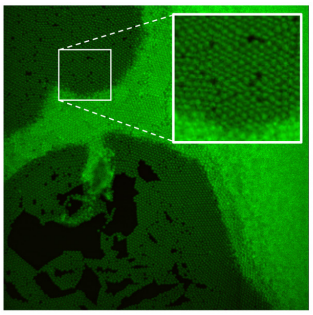
Functional demonstrator

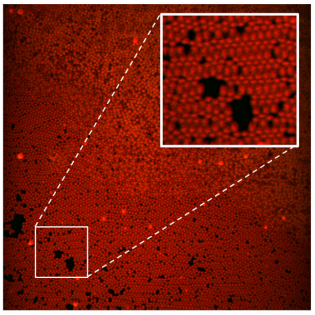
A demonstrator of the confocal microscope was developed and built, which can be operated via a specially programmed graphical user interface. It acquires fluorescence images at two laser wavelengths (488 nm, 638 nm) and is also equipped with a system camera including Koehler illumination.

The entire demonstrator consists of an optical scan head and a supply module (incl. laser and power supply). The mobile scan head with a total weight < 5 kg is mounted on an automated x/y/z stage and can be positioned via joystick with respect to the sample.

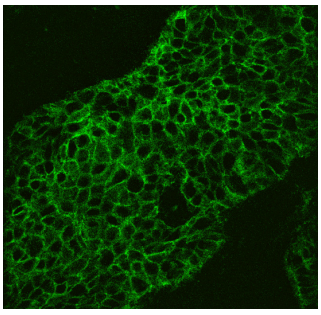
Extensive research was carried out by our project partner Fraunhofer IZI in Leipzig on fluorescent dyes suitable for use and on tumor-specific antibody staining. After the first successful tests on fixed cells from cell cultures, a cooperation was initiated with the Helios Klinikum Erfurt, which, after a positive ethical vote, provided tumor samples for testing the entire system.

The demonstrator is available for further evaluation of tumor tissues (and other indications) at the Fraunhofer Center MEOS.





Fluorescence image of microspheres of 1.0 µm diameter (left, 488 nm excitation) and 2.0 µm diameter (right, 638 nm) obtained with the confocal microscope.



Fluorescence-labeled tumor sample at 488 nm excitation (200 x 200 µm field of view).

Parameter	
Lens	Apochromat 10x (WD 4.0 mm)
Image field size	1100 µm x 820 µm / (camera) 400 µm x 400 µm (fluorescence)
Depth scan	up to 2000 µm (5 nm step size)
Laser	488 nm, 638 nm
Optical resolution	1 µm (lateral, fluorescence)
Software	µManager (open source)
Weight	< 5 kg (optical scan head)

Technical parameters of the system.