PRESS RELEASE

The Fraunhofer Center MEOS at MEDICA trade fair

1 Speed meets precision: A new laser scanning microscope improves cancer cell detection

Surgically removing a tumor is a delicate process. The cancerous tissue must be removed in its entirety, with great precision and as few incisions as possible. Afterwards, the surgeon must ask themselves a number of questions. For example, were all the cancerous cells completely removed? And did the removal damage the surrounding tissue? With brain tumors in particular, it is important to remove as few healthy nerve cells as possible.

Now, Fraunhofer researchers working in the LSC-Onco (Laser Scanning Oncology) project have found a quick, reliable solution to this problem by combining laser scanning microscopes and fluorescent tumor markers. Using the microscope, doctors can examine the tissue surrounding the area the tumor was removed from — without even leaving the operating theater. Michael Scholles, Head of the Fraunhofer Center for Microelectronic and Optical Systems for Biomedicine MEOS, explains: “A fluorescent marker applied beforehand allows doctors to see any cancer cells that may be left behind after the incision. Then these cells can be completely removed, with great precision.” The technology was developed at the Fraunhofer Center in Erfurt, where MEOS works on key technologies in the fields of life sciences, microelectronics, optics and photonics. The project involved researchers from the Fraunhofer Institute for Photonic Microsystems IPMS in Dresden and the Fraunhofer Institute for Cell Therapy and Immunology IZI in Leipzig.

In the LSC-Onco project, experts from Fraunhofer IPMS developed the tried and tested concept of a laser scanning microscope further, using a microscanner mirror manufactured with MEMS (micro-electro-mechanical systems) technology. Inside the microscope, the mirror oscillates at a rate of several thousand times per second, directing blue laser light with a wavelength of 488 nanometers over the entire image field point by point. The mirror simultaneously directs the fluorescent light emitted by the tissue towards a highly sensitive photodetector. The signals from the photodetector can then be used to construct a two-dimensional image. Images can also be recorded on different planes, so that tumor cells beneath the surface also become visible. “This means that, for the first time, a powerful, portable laser scanning microscope that can be positioned right next to the patient in the operating theater is a feasible reality,” says Scholles.

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Before the microscope can detect cancer cells, the cells themselves must first be marked. Researchers from Fraunhofer IZI used their biomedical expertise to develop a fluorescent tumor marker liquid that, simply put, makes cancer cells glow beneath the microscope. The team from Fraunhofer IZI developed the markers for use on brain and skin tumors and are currently investigating whether other types of tumors will react similarly. The Helios Hospital Erfurt provided the tissue samples necessary for developing the tumor markers, with the consent of patients.

After the tumor is removed, the tumor marker is applied to the surrounding tissue and the laser scanning microscope is positioned directly above the wound. When the microscope's blue laser beam encounters healthy cells, the reflected light is blocked by dichroic filters, which have the ability to pass only specific wavelengths. As a result, the image on the microscope display stays black for those cells. However, if the blue laser encounters cancerous cells, the tumor marker emits a fluorescent green. This light passes through the dichroic filters and appears on the display as a green dot or patch. The resolution of the system is so high that even individual cancer cells can be detected and shown on the display. "It only takes a few seconds to examine the operating field with the laser scanning microscope," says Scholles. By referring to the image on the display, doctors can cleanly remove any remaining cancer cells (normally found at the edge of the wound) in their entirety, all without damaging the healthy tissue.

When compared to current practices in oncological surgery, LSC-Onco represents a huge step forward. Prior to this development, surgeons have generally taken tissue samples from the edges of the wound following the removal of a tumor and sent these samples to a hospital laboratory. After a few minutes wait, a diagnosis would be delivered as to whether the sample cells were cancerous. If so, the surgeon would then have to cut away more tissue. This method is very time-consuming, which adds to the strain on the patient undergoing the operation. "With LSC-Onco, all these steps can be carried out in one go during the operation, and what's more, the precision is much greater. It also protects the surrounding tissue, because you can see exactly where the healthy tissue starts on the microscope display. And now, waiting for lab tests results is a thing of the past," says Scholles, Head of MEOS.

As a result, operations can be completed faster and patients can be taken off anesthetic. This technology also improves the patient´s chances of a complete and permanent recovery, as it ensures clean removal of all cancer cells." We have already received extremely positive feedback from doctors. The demand for this technology is very high," says Scholles.

Now, the project team wants to take the next step and bring LSC-Onco into medical practice. An LSC-Onco demonstrator will be presented in the Fraunhofer booth #F74 in Hall 3 at the MEDICA trade fair (November 14-17, 2022) in Dusseldorf.

2 Non-invasive diagnostics of diseases: detection of biomarker VOCs with ion mobility spectrometry

The COVID-19 pandemic and the detection of antibiotic-resistant bacteria show that there is an urgent need for portable or even wearable devices that enable point-of-care (POC) diagnostics to enable rapid diagnosis of diseases. A special focus for POC devices is the analysis of gaseous biomarkers. It is well known that diseases change the metabolism in the human body cells. This affects the composition of urine and exhaled air for example. Common marker substances belong to the group of volatile organic compounds (VOCs). The most important key to entering this attractive market of POC devices is (1) the reliable and high-precision detection of individual VOCs and (2) the linking of the measured data to diseases to enable a reliable diagnosis. A conceivable area of application would be compact and cost-effective systems in medical practices or care facilities that enable quick and easy diagnosis.

The Fraunhofer Center MEOS is working on a portable sensor concept for determining the VOC concentration as gaseous biomarkers based on a special type of ion mobility spectrometry (IMS): the field-asymmetric ion mobility spectrometry (FAIMS). This type of IMS lends itself very well to miniaturization and the use of microtechnical processes to manufacture the central filter element. Building on this concept, scientists have developed a microsystem whose core component is an IMS chip containing a FAIMS-based ion filter and detector fabricated using silicon-based microtechnology. In combination with the required electronics, a laboratory demonstrator was created that is able to detect typical VOCs. The disease-specific molecules are separated according to size, weight and charge by the chip installed in the demonstrator. A measurement curve can then be used to determine which and how many connections are included. Since a large number of different compounds are measured per sample, an AI helps with the analysis by learning to distinguish between sick and healthy breathing profiles. Together with customers, the Fraunhofer Center MEOS would now like to develop new medical solutions on this basis, which are possible thanks to the ongoing IMS chip development, coupled with the interdisciplinary methodological competence available at the site.

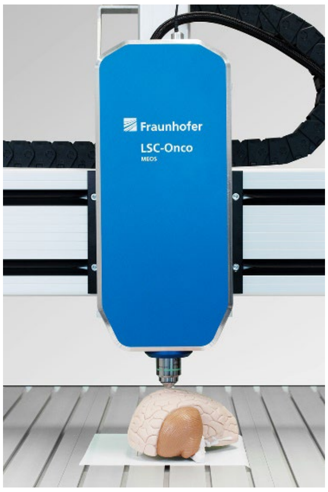
3 Photonic integrated in a silicon chip: photonic biosensors

The Fraunhofer Center MEOS is presenting its optical biosensor technology at the MEDICA trade fair. It enables the detection of biomarkers in liquids such as blood plasma with very high selectivity. The core elements are integrated waveguides manufactured using silicon nitride-on-silicon (SiN-on-Si) technology, the surface of which is functionalized, i.e. equipped with catcher molecules. If a liquid that is passed over the sensor surface contains biomarkers that match the capture molecules, the latter are bound to the surface and change the optical properties of the waveguide.

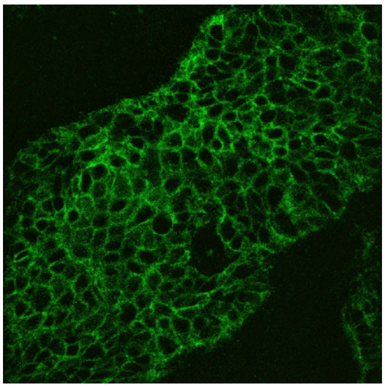
The photonic components can be manufactured in large quantities on 200 mm wafers using processes that are established in microelectronics and microsystems technology. In addition to these components, the Fraunhofer Center MEOS is also working on all other essential aspects of photonic biosensor systems – microfluidics, biofunctionalization of surfaces, development of biocomponents and system integration. At MEDICA 2022 a biosensor system based on a silicon nitride microring resonator chip with multiplex architecture operating at 1550 mm will be presented.

An important application of photonic sensors is the detection of so-called micro-RNAs (miRNAs). Due to their small size and detectability in the bloodstream, these molecules are ideal for minimally invasive diagnostics of various diseases. The multi-channel silicon nitride microring resonator biosensor system developed at the Fraunhofer Center MEOS demonstrates the fast and sensitive detection of several miRNA biomarkers specific for neurodegenerative diseases such as Alzheimer´s and Parkinson´s in one measurement.

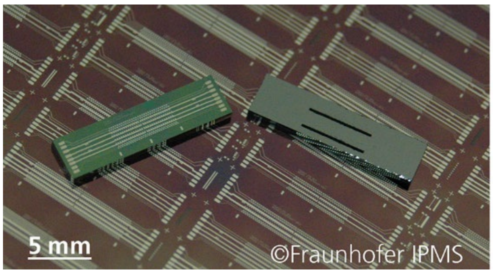
Fraunhofer Center for Microelectronic and Optical Systems for Biomedicine
https://www.meos.fraunhofer.de/en.html



Picture 1 **Thanks to the use of MEMS technology, the laser scanning microscope from the LSC-Onco project is so small and compact that it can be used to examine patients right on the operating table.**

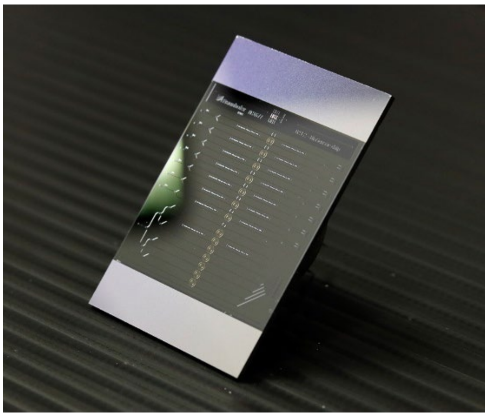


Picture 2 **This fluorescent image shows a tumor section recorded with the LSC-Onco microscope. The fluorescent green area indicates cancer cells.**



Picture 3 **The core of the miniaturized ion mobility spectrometer to be developd is the Novel FAIMS chip with a dimension of approx. 5 mm by 15 mm.**

Picture 4 **Photo of the developed IMS demonstrator with an attached mouthpiece for analysis of biomarkers in exhaled air.**



Picture 5 Integrated waveguides in silicon technology fabricated on 200-mm silicon wafers and used in combination with a functionalized surface as highly sensitive biosensors.