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## PROJECT EXAMPLE: "RAMANCTC" – IDENTIFICATION AND CHARACTERIZATION OF BLOOD-CIRCULATING TUMOUR CELLS

### Starting situation

For many cell-diagnostic investigations, an individual-cell diagnosis is necessary. These investigations are particularly challenging when they involve a large number of cells. An application example addressed within the framework of the project "RamanCTC" is the recognition and counting of circulating tumour cells in a defined quantity of blood. The quantitative change of tumour cells in the peripheral blood over time is an important indicator for the evaluation of the success of tumour therapy and for the estimation of a prognosis for the patient. Today there is a wide range of modern methods and high-throughput processes in molecular biology, microscopy and molecular imaging for the individual cell analysis.

However, before the cells can be investigated, it is necessary to isolate individual cells. The standard methods for qualitative and quantitative determination of the cells include cell sorters with and without fluorescence activation. These methods do not, however, deliver satisfactory results for tumour cells circulating in the blood.

### Solution

Within the framework of the project "RamanCTC" the identification of tumour cells is being carried out with the aid of Raman spectroscopy. For this purpose the Fraunhofer IBMT has provided new microchips that make a high cell throughput possible by allowing the precise positioning of a very high number of cells and thus their quasi-parallel investigation. Chips are currently being used with which around 200,000 cells can be arranged in less than two minutes in a regular, two-dimensional grid. The exactly positioned individual cells

are on a transparent membrane of silicon nitride which is about 1  $\mu\text{m}$  thick. Studies have shown that these membranes are ideal for Raman spectroscopy. In the Raman spectrum they generate only a very weak and barely structured background which can be easily filtered out of the Raman spectrum.

### Potential

With the microchips described, tumour cells can be isolated and arranged directly after the erythrocyte removal from blood with unprecedented speed and precision. This leads to a reduction in the costs for diagnosis and therapy as the quantification and characterization of the circulating cells allows prompt adjustment of the therapy. As the cell positioning does not cause any damage, the technique can also be used to take individual cells from the chip after characterization for further use or investigation.

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1 *Microscope image of positioned cells.*

2 *Microchip in injection moulding case with fluidic connections.*