Medical Technology | Imaging Techniques | Technology Offer

Marker-free, high-content screening for digital pathology

Field of application

Scientists, physicians and patients benefit from the digitization of medicine and the newer diagnostic techniques that are becoming available. Nowadays, the classification of a tumor no longer involves the elaborate analysis of data obtained through imaging techniques. The methods of classic histopathological diagnostics have been extended. We can now compute immediate results for predefined questions. Direct digital data processing uses specialized algorithms that allow us to compare data with reference data of interactive databases.
The method presented here takes diagnostics even a step further. Previously, tissue samples had to be stained in a lengthy procedure. Now it is possible to perform a marker-free analysis of tissue sections or cells. In addition to saving time, the risk of treatment is minimized, since the pathologist only needs to apply the objective (physically based) method of optical spectroscopy to classify the tissues by malignancy. By implementing an additional function into high-content screening systems it is now possible to make a demarcation between the tumor and the physiological tissue. Another application of the new method is the automated creation of karyograms based on chromosome metaphase preparations. These allow for the detection of certain hereditary diseases.

State of the art

High-content screening (HCS) is applied to human / animal cell cultures, model organisms, tissues and yeast cultures to answer biological/medical questions. It is also used for pharmaceutical drug developments. The samples on the microplates or microscope slides are automatically photographed, if necessary, under fluorescent lighting. The digital images then undergo classic image analysis. Digital pathology (DP) integrates HCS into comprehensive digital processing, analysis and archiving for tumor characterization or karyotyping. The data of tissue section preparations is available in high resolution and can be further processed in other databases and compared to reference data. Until today, conventional HCS and DP have not made use of the significant added value that lies in the collection of spectral data. Currently, chemical information is only accessible via the use of dyes that specifically bind to certain areas of the sample. Morphological information is only evaluated to the extent that it is available via standard brightfield illumination.

Innovation

Researchers at Reutlingen University have succeeded in developing a marker-free method that allows for the characterization of chromosomes, cells and tissue sections in terms of their chemical properties (absorbance) and their morphological properties (scattered light). Measurements were carried out in ultraviolet and visible light, with a compact spectrometer module that can easily and inexpensively be built into a standard microscope or an automated screening tool. During the measurements brightfield and darkfield lighting is used. Darkfield lighting is used to separate the elastically scattered light and obtain information on the morphology and texture of the sample. The appropriate multivariate analysis algorithm for spectral imaging enables the recognition of spectral key factors (interference patterns) that are substantiated through local differences in the calculation index, variations in layer thickness or the geometrical alignment of scatter centers. These interference patterns are very specific, like a fingerprint, for chromosomes as well as for cells of certain tissues and particularly for tumor cells.
A major advantage of this method is the flexible combination of optical hardware and different software, depending on the field of application. Applications for karyotyping metaphase chromosomes and for a marker-free characterization of glioma cross-sections by tumor grade have already been tested. Another application is currently being tested to examine head and neck tumors, both in human specimens and mouse model. In the long term, the industry might also become interested in this new type of screening, e.g. businesses working in the field of process monitoring.

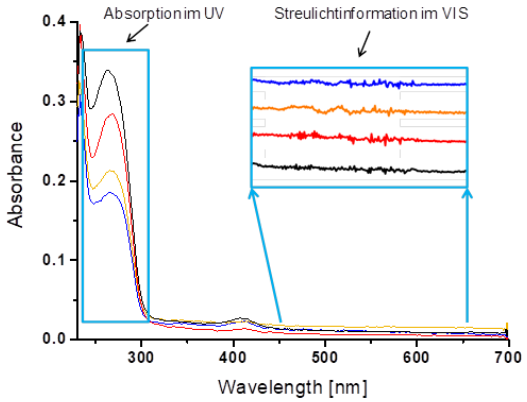

Figure 1: UV/VIS spectra with absorbance in the ultraviolet range (chemical information) and overlaid fine structures in the visible range due to scattered light interferences (morphological information).

Patent portfolio

An EP application for the marker-free characterization of glioma cross-sections is pending. Patents for the karyotyping of metaphase chromosomes have already been granted for the USA, FR, GB and DE (see 044/07TLB).

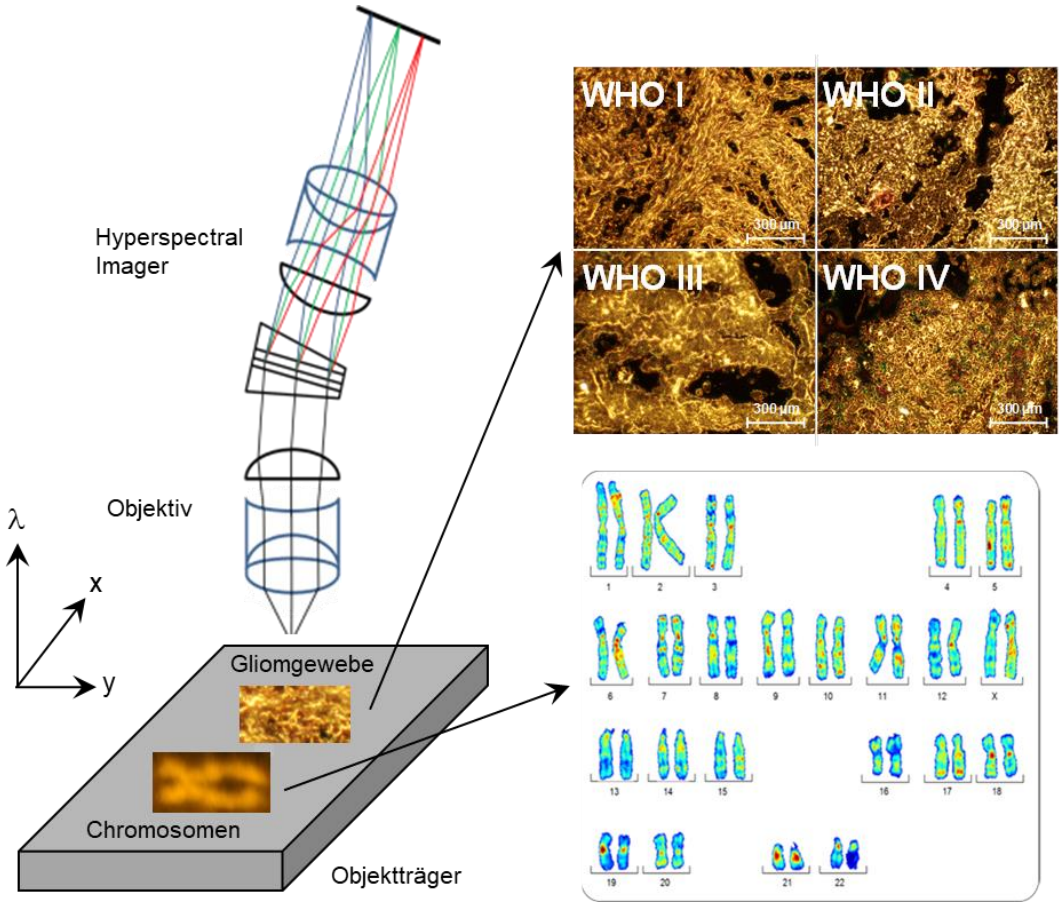

Figure 2: Using the compact spectrometry module with different software packages allows you to perform various marker-free analyses. The characterization of glioma tissue (top right) and the creation of a karyogram (bottom right) are just two examples of applications which have been successfully tested at the Institute.

Technology transfer

Technologie-Lizenz-Büro GmbH is responsible for the exploitation of this technology and assists companies in obtaining licenses.

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Your benefits at a glance

- ✓ Marker-free technology
- ✓ Additional contrasts in chemistry and morphology for HCS of biological materials
- ✓ For cells, tissues, metaphase chromosomes
- ✓ Method for karyotyping available
- ✓ Method for glioma characterization available
- ✓ Ideal complement to the digital pathology
- ✓ Can be integrated into all imaging methods (e.g. microscopy, endoscopy, HCS systems)
- ✓ May be combined with high-resolution methods
- ✓ Measurement hardware for multiple software modules (e.g. karyotyping, glioma characterization, etc.)

Reference number: 12/088TLB

