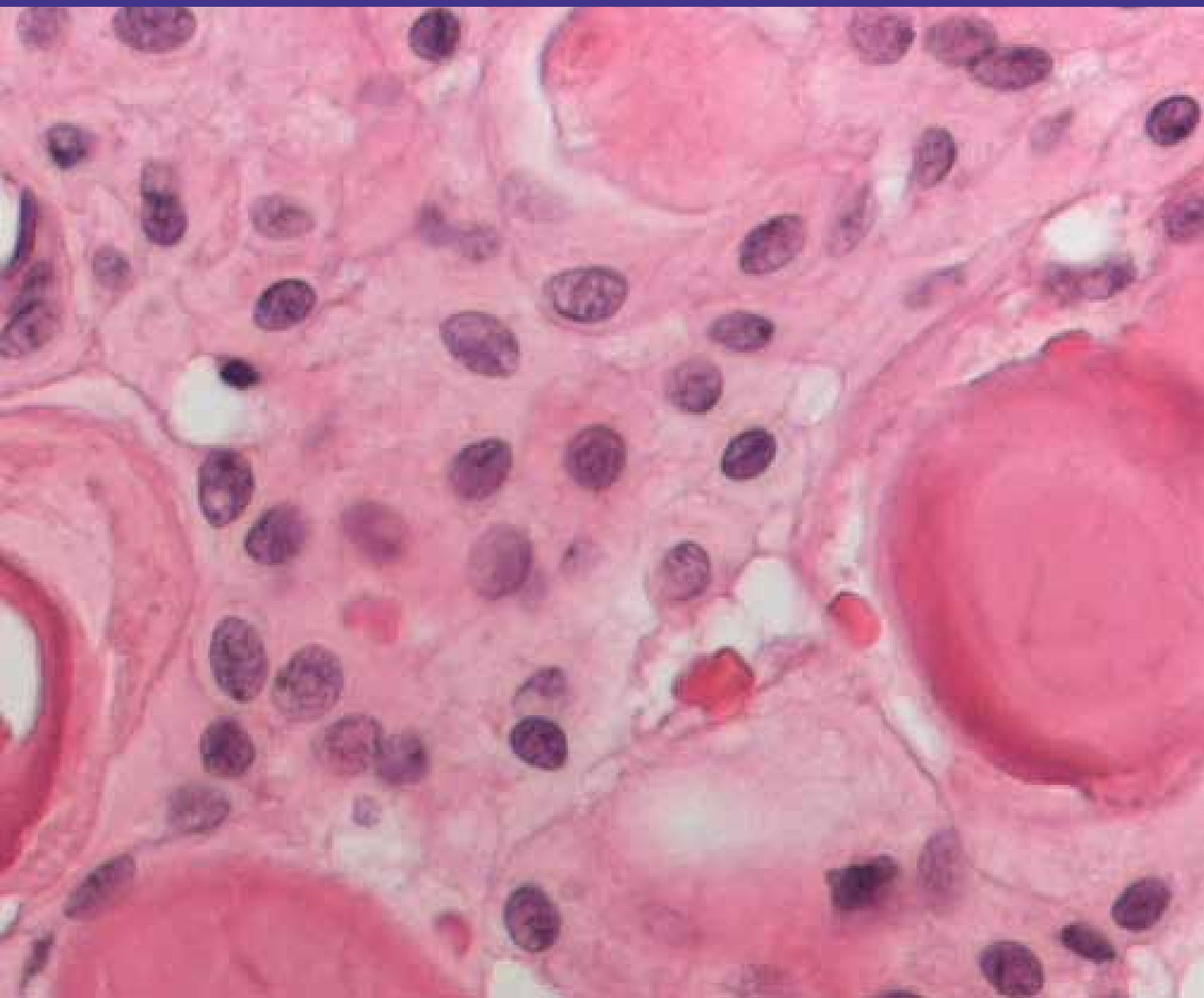
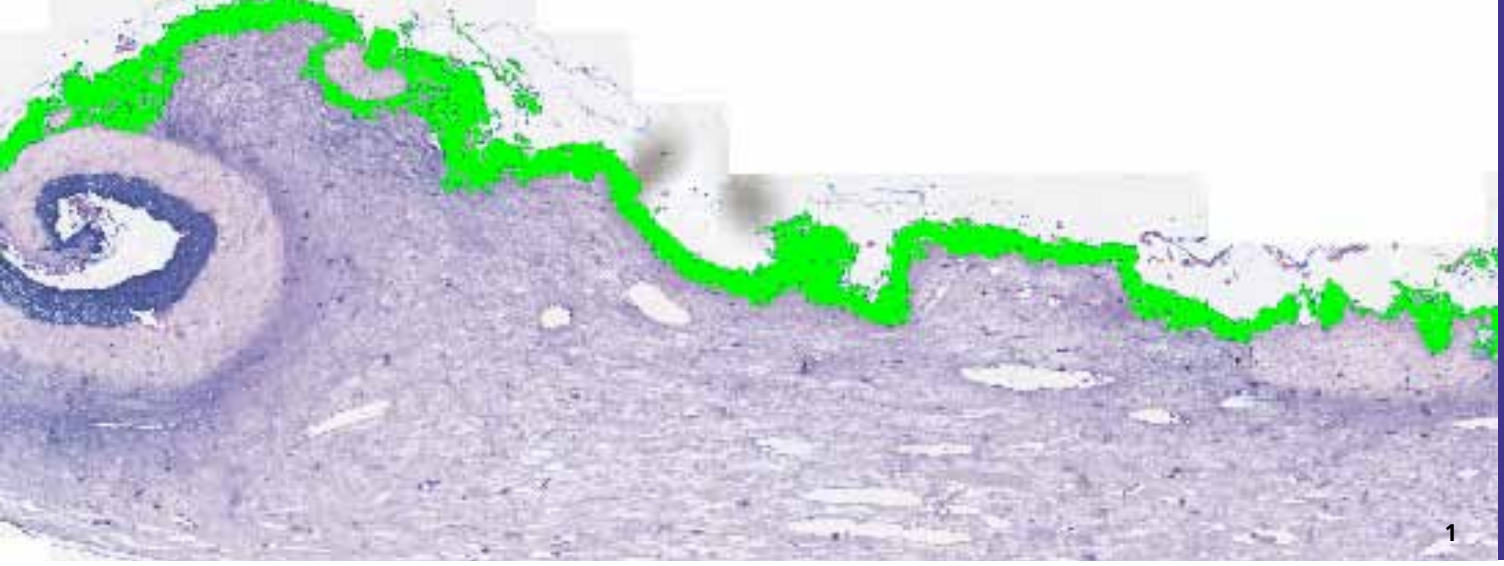
Fraunhofer
IIS

FRAUNHOFER INSTITUTE FOR INTEGRATED CIRCUITS IIS

MICROSCOPY

SOFTWARE AND SYSTEMS FOR HISTOLOGY





1

BACKGROUND

Examination and assessment of tissue samples by the pathologist represent an essential element of medical diagnostics and with therapy control of pathological changes of the organs. Microscopy based examinations of stained tissue sections are used to detect and diagnose type and scope of pathological changes, particularly with regard to malignancy of tumors, which would not be possible by only using clinical or radiological examinations. However, the diagnoses based on pathology require particular and long-term expertise; correspondingly, they are generally connected to time-consuming visual inspection of the tissue samples by using a microscope. Furthermore, recent technologies such as confocal laser endomicroscopy enable in-vivo visualization of cellular structures and require comprehensive pathological expert knowledge.

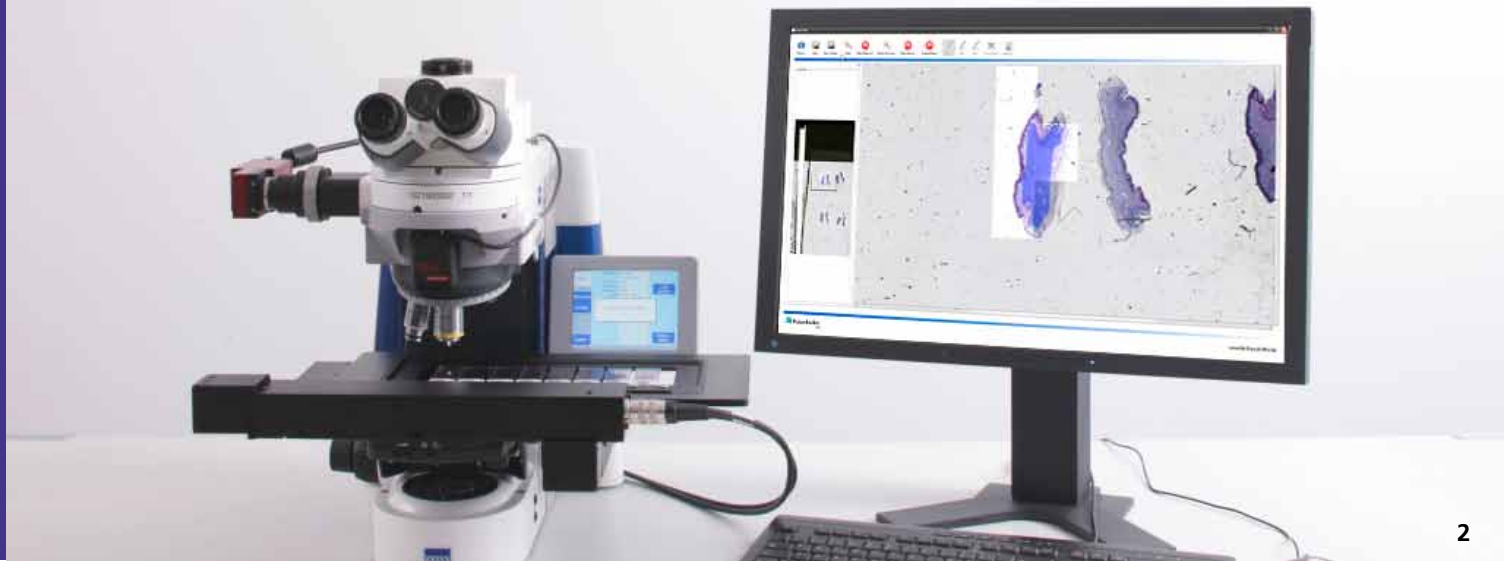
With the focus on computer-assisted microscopy (CAM) the Department of Image Processing and Medical Engineering of the Fraunhofer IIS offers software and system technologies for objective and automatic examination of microscopically captured tissues as well as support and assistance with various types of analysis tasks.

DIGITALIZATION

Automated microscopes can be used to efficiently and rapidly digitize and age-resistantly conserve and archive histological prepared specimens. Such so-called ‚virtual slides' can be flexibly displayed and intuitively navigated on the screen of computers or tablet PCs. Thus, complete image datasets are available via Intranet or Internet virtually anywhere and anytime.

Fraunhofer IIS develops software platforms and basis technologies for various applications that are required for efficient and safe digitalization of slides. A semi-automatic universal scanning platform enables digitalization, visualization and annotation of various prepared specimens. Histological sections, but also cytological samples such as blood, bone marrow, cerebrospinal fluid and cell samples can be correspondingly digitized. Individually configurable profiles allow for adjustment of recording parameters to various tasks. An overview image of the slide is obtained with a low magnification and displayed in an initial step. Based on this overview regions manually selected by the user are then digitized in a second step with any possible higher magnifications (e.g. 5x, 10x, 20x, 40x, 100x). The result of such process is a so-called ‚virtual slide' that consists of the overview image and the high-resolution views included into the same coordinate system.
Application-specific analysis modules can be integrated into the modular platform at any time.

Possible fields of application include image documentation of prepared specimens at pathological departments and institutes, digitalization of slides for scientific purposes, presentations and conferences as well as creation of digital prepared specimens for training and education. Adjustment and extension for specific purposes is possible at any time.



COMPUTER-ASSISTED HISTOLOGY

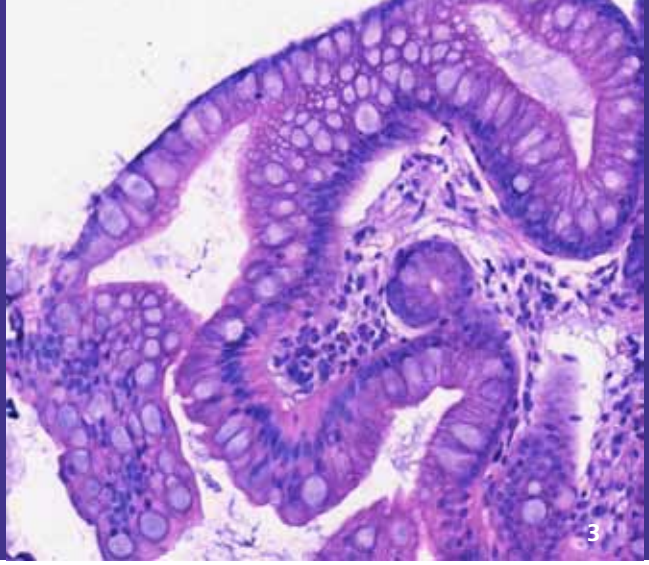
Today, histo-pathological examination and assessment of tissue samples by using the microscope represent indispensable elements of routine diagnostics and follow-up control of therapy, and they correspondingly represent the ‚gold standard' of clinical diagnostics. However, such medical diagnostics are always based on subjective observations and analyses of the pathologist so that they are highly dependent on the individual's qualification, experience and day's form. Systems for computer-assisted histology may contribute to objectivity of analysis and medical diagnostics of stained tissue sections.

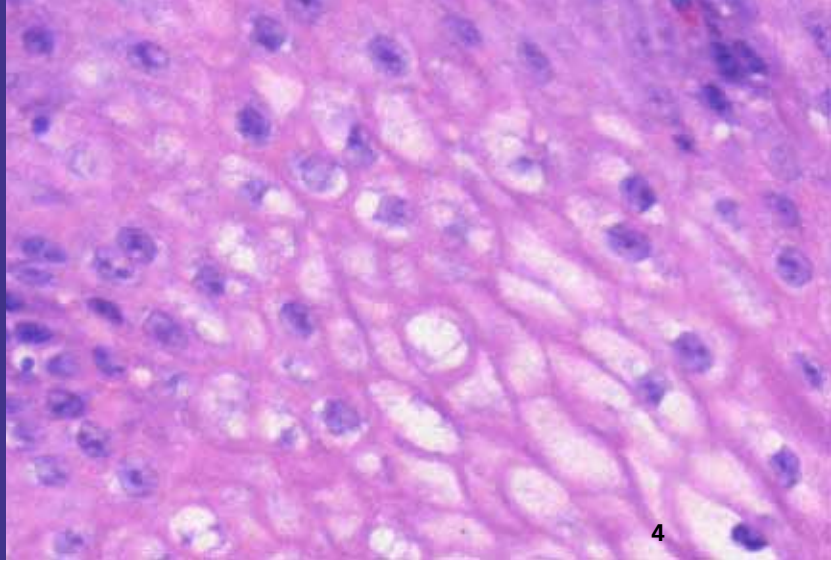
Fraunhofer IIS develops systems that are able to provide support with medical diagnostics on the basis of digital prepared specimens and image-based characterization. The use of such systems can be seen with fully digitized and correspondingly documented work flows, simplification of routine work, increased objectivity and a higher personal safety with diagnostics. Examinations of Fraunhofer IIS with stained tissue sections of cerebral tumors and esophagus showed that automatic differentiation of different diagnostic tissue classes is possible by means of digital image analysis. Based on the two stated examples, classification rates of more than 90% could be achieved during first examinations. Adaption of such methods to other tissue types is possible at any time and can also be made within the scope of studies.

ANALYSIS FOR IN-VITRO TEST SYSTEMS

Complex three-dimensional cell and tissue systems are increasingly developed; such systems can e.g. be used for formation of human tissue and organs. Such so-called ‚tissue models' cannot only be used as transplants, but also as in-vitro test systems for the pharmacological, cosmetic and chemical industry. For example, safety-toxicological examinations can be performed and irritating effects of substances to the skin can be examined and analyzed by using suitable skin models. However, today the respective evaluations are mainly performed by means of histological diagnostics.

Using artificial skin as an example, the Fraunhofer IIS develops automatic methods and systems for image-based analysis of such prepared tissue models. Such prepared tissue specimens are digitized with an automated microscope and then analyzed on a high-performance computer. Damage to epidermis (uppermost layer of the skin) due to exposure to toxic substances becomes apparent by erosion of the epidermal layer. Here, the continuous contour is interrupted and the layers become thinner. Such toxicological effects can be quantified by various parameters that are based on automatic image analysis of the skin layers. The degrees of damage to the skin surface are directly reflected in the extracted parameters and can be correspondingly measured in an objective and systematic manner.





QUALIFICATION

Learning of the difficult morphologic differentiation of different types of cells and cell structures by means of microscopy requires years of experience. Such ability must be continuously perfected by viewing and studying of numerous microscopic images in atlases as well as selected prepared specimens. In training of health professionals and pathologists it is absolutely necessary that - besides the normal lectures - there is also the possibility to regularly solidify the learned knowledge independently and freely by means of microscopy of various suitable prepared specimens. However, temporal limitations, limited availability of prepared specimens as well as personnel-consuming care of microscopy laboratories represent limiting factors of education and training.

Nevertheless, innovative technologies make it possible to offer Internet-based microscopical examination in addition to regular lectures by using digitized, so-called ‚virtual slides'. The technologies developed at Fraunhofer IIS such as stitching of large-area micrograph panoramas enable rapid and ergonomic access to correspondingly processed digital prepared specimens. Such digital prepared specimens can also be easily enhanced by textual and graphical annotations. Furthermore, digital specimens can be sorted as per certain anatomical and pathological characteristics, and cross references (hyperlinks) to alternative prepared specimens and additional sources of information can be defined and used.

Approx. 200 pathological prepared specimens have been digitized and processed so far in cooperation with the University Clinics of Erlangen. Further prepared specimens are continuously added. Since the summer term 2011, free microscopical examination is offered as regular supplement to the lectures in pathology and anatomy by using a software of Fraunhofer IIS. Adaption to further fields of application is easily possible.

1 Automatic segmentation of epidermal layer of an artificial skin model.

2 Universal scanning platform for digitalization of microscopy slides.

3+4 Histological prepared specimens of esophagus (Barrett's mucosa and squamous epithelium).

Title: Histological section of meningioma.

OUR OFFER

The Department of Image Processing and Medical Engineering develops concretely realizable technical solutions for medical technology, laboratory diagnostics and biomedicine. Industry and service providers of any size benefit from contract research. We offer know-how to small and medium-sized companies without own R&D department and may serve as an ‚extended workbench'.
We are pleased to offer our services - from feasibility studies for your specific problem and customized evaluation of large amounts of image data to research and development projects. Besides adaption and licensing of available algorithms and methods into existing systems, we also implement the whole control software and user interface upon request. We provide support with technical documentation, performance of risk management as well as planning and performance of clinical studies and performance assessment studies in accordance with the applicable directives (DIN EN14971, 93/42/EEC, 98/79/EC) and the legal requirements as per Medical Devices Act, particularly via the Fraunhofer IIS Medical Engineering Test and Demonstration Center (METEAN), which is located in and connected to the University Clinic of Erlangen.

- **TECHNOLOGY AND MARKET STUDIES**
- **FEASIBILITY STUDIES AND DEVELOPMENT OF CONCEPTS**
- **DEVELOPMENT OF ALGORITHMS AND SYSTEMS**
- **RESEARCH AND DEVELOPMENT SERVICES**
- **CUSTOMER-SPECIFIC EVALUATION OF IMAGE DATA**
- **TECHNICAL DOCUMENTATION AND RISK MANAGEMENT**
- **PLANNING AND PERFORMANCE OF CLINICAL STUDIES**

WWW.IIS.FRAUNHOFER.DE/MED

Fraunhofer Institute for
Integrated Circuits
Executive Director
Prof. Dr. Albert Heuberger

Am Wolfsmantel 33
91058 Erlangen, Germany

Department of Image Processing
and Medical Engineering
Dipl.-Inf. Christian Weigand

Contact
Dr. Christian Münzenmayer
Telephone +49 9131 776-7310
Fax +49 9131 776-7309
christian.muenzenmayer@iis.fraunhofer.de

11/2011 Ritter