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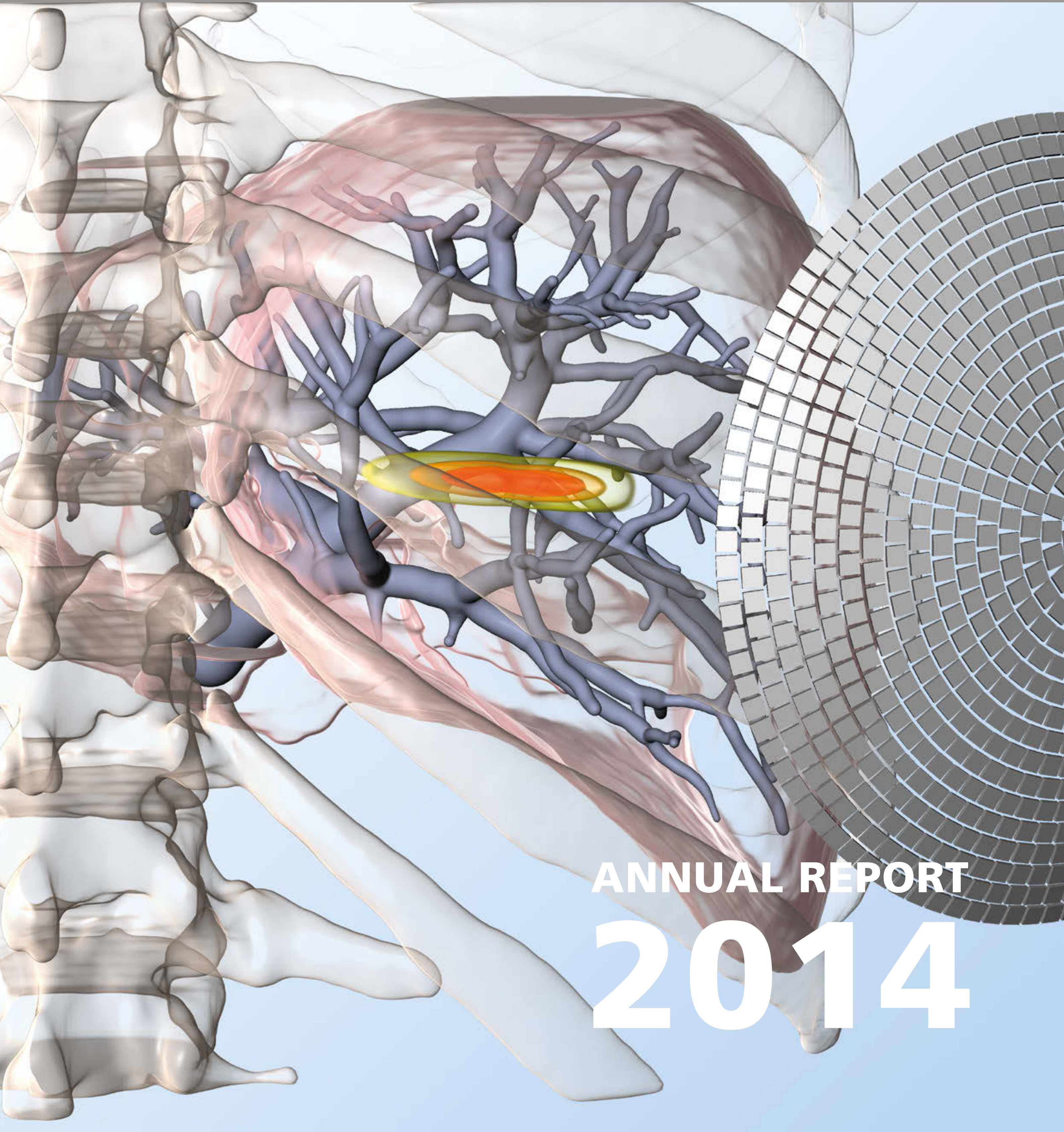
MEVIS

INSTITUTE FOR MEDICAL IMAGE COMPUTING



ANNUAL REPORT 2014

FRAUNHOFER MEVIS

ANNUAL REPORT 2014

Illustration of numerically simulated high-intensity focused ultrasound therapy: A multi-element transducer focuses ultrasound waves in a target in the patient's liver, where the temperature increases locally. Temperatures above 60°C are shown in red, above 55°C in orange, and above 45°C in yellow. The greatest challenges during HIFU liver treatment are the shielding of the ultrasound waves by the rib cage, the cooling effects of the surrounding vascular system, and the movement of the target due to patient breathing.

European Union:
Investing in your future
European Regional Development Fund

TABLE OF CONTENTS

The directors of the Fraunhofer Institute for Medical Image Computing MEVIS, Prof. Dr. Horst K. Hahn and Prof. Dr. Ron Kikinis.

PREFACE

It is with great pleasure that we present the Fraunhofer MEVIS 2014 annual report in a new format. Articles highlight some of the dimensions of our institute: from technological research and professional software engineering to clinical validation and translation into industry-supported medical products.

Our mission at Fraunhofer MEVIS is to improve both the quality and availability of personalized, image-based health care procedures. Since our founding in 1995, we have brought together an outstanding team of scientists, doctors, and engineers, supported by technicians, students, and administrative staff. This team is the biggest asset of Fraunhofer MEVIS, which now consists of over 120 members. The team is organized as a dynamic network of experts and defies the traditional, department-like organization.

The contributions of our team members towards reaching our mission goal are two-fold: First, we target the accuracy, safety, and efficiency of diagnostic and therapeutic procedures. We achieve this through novel imaging methods, dedicated computer support, and partial automation, often tailored to a specific clinical use case. Second, we provide a platform for translating image computing technology from academia to research and from research to marketable solutions. The platform, which includes our quality assurance services, is available to both clinical and academic partners and lowers barriers for their intellectual property to enter commercialization and widespread routine use.

In our core research area, medical image computing, successfully translating technological capability into clinical practice is significantly more complicated than in many other technological fields. Prototypes resulting from academic research in the engineering sciences require conversion into functioning tools to conduct biomedical research and clinical validation. Tools that exhibit clinical impact need translation into medical products marketed by companies and used in clinical practice.

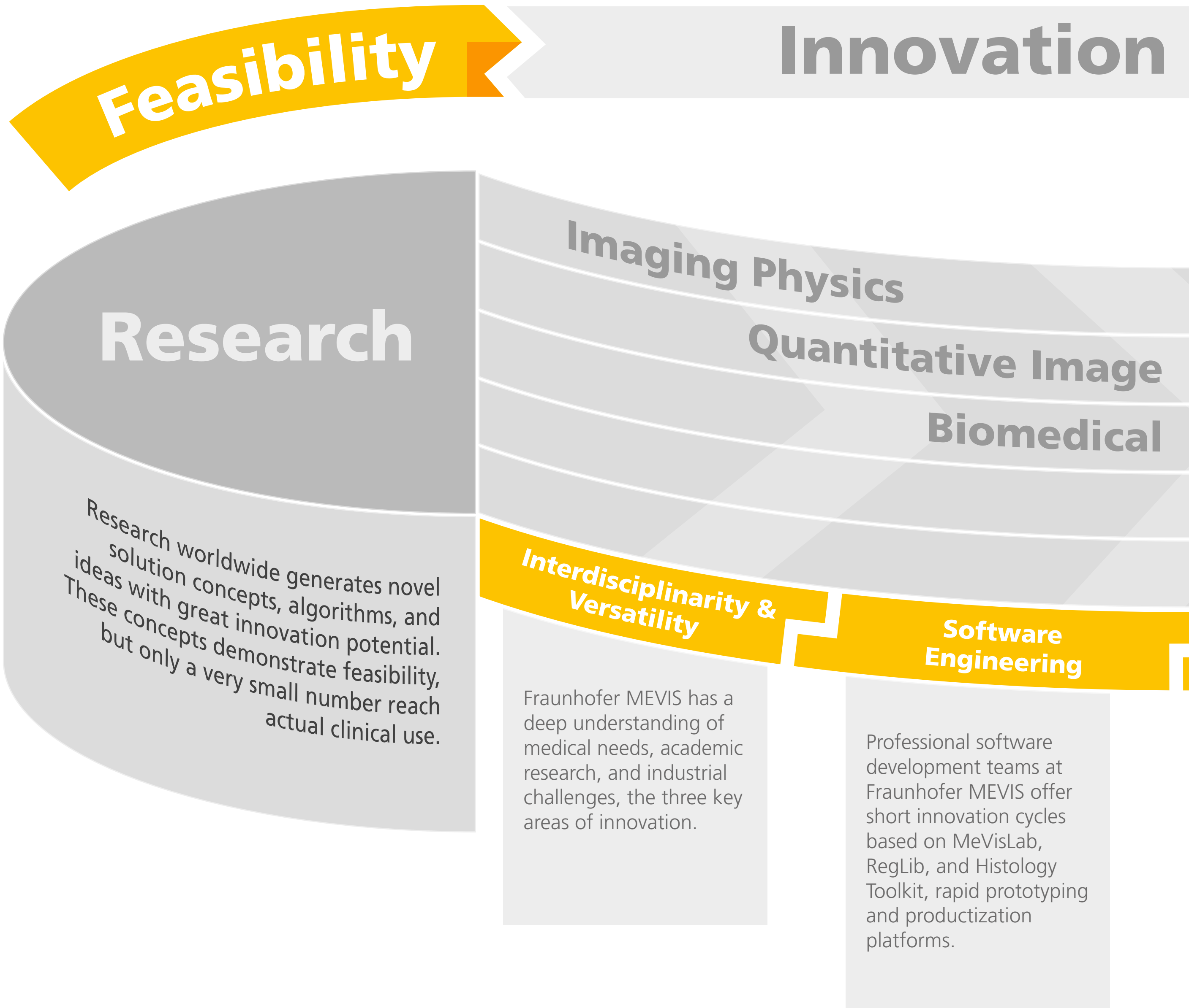
This two-step translation does not fit current research funding models, resulting in the well-known innovation gap, also known as the valley of death, between research and application. This occurs when outstanding, innovative ideas and concepts are demonstrated as academic prototypes (proofs of concept) but not carried to the next stage. Unfortunately, necessary funding for medical evaluation of these academic prototypes is scarce. Many funding agencies are interested in either novelty (as opposed to enabling innovation) or require industrial participation. Unfortunately, industrial organizations are often hesitant to invest in concepts that are not clinically validated.

Fraunhofer MEVIS, as a non-profit independent research center, helps bridge this gap with numerous approaches, each dependent on topic and context. One example covered by this report is our contribution to the German National Cohort. In this ongoing project, a fully web-based collaborative reading and quality assessment system was designed and implemented by Fraunhofer MEVIS. MRI data from 30,000 subjects acquired at five German study centers are transferred to the central data storage and web server located in Bremen. The software delivers analysis and annotation services to participating physicians across the country.

The previous year has witnessed the completion of both the transition in leadership to the next generation and the full transition of the Lübeck Project Group Image Registration into the Fraunhofer model. Together with our partners, we consider ourselves in an excellent position to face the challenges of research and translation and turn them into opportunities for both the institute and society.

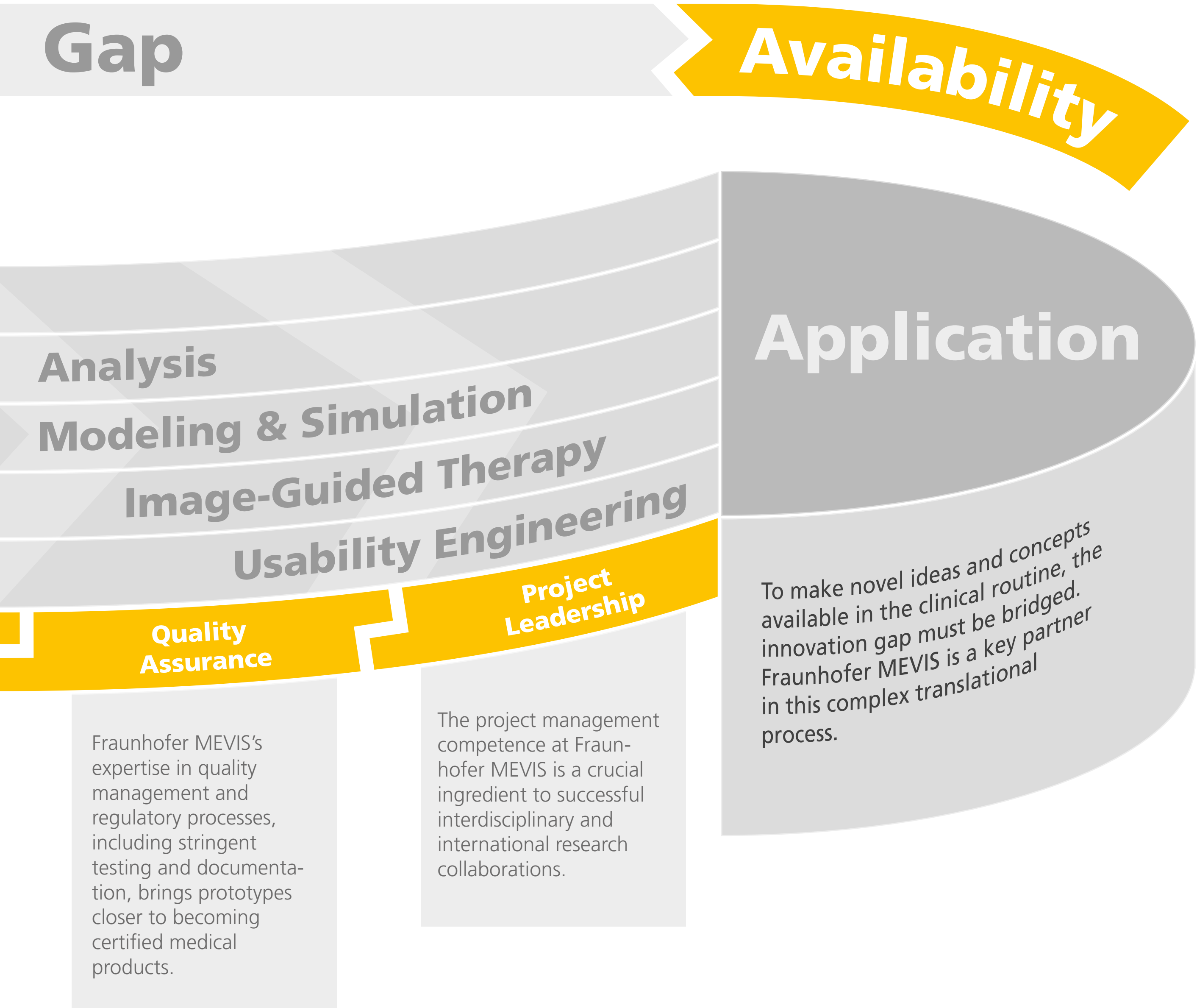
Horst Hahn

Ron Kikinis


Feasibility
Innovation
Research
Imaging Physics
Quantitative Image
Biomedical
Research worldwide generates novel solution concepts, algorithms, and ideas with great innovation potential. These concepts demonstrate feasibility, but only a very small number reach actual clinical use.
Interdisciplinarity & Versatility
Fraunhofer MEVIS has a deep understanding of medical needs, academic research, and industrial challenges, the three key areas of innovation.
Software Engineering
Professional software development teams at Fraunhofer MEVIS offer short innovation cycles based on MeVisLab, RegLib, and Histology Toolkit, rapid prototyping and productization platforms.

FRAUNHOFER MEVIS – PARTNER IN TRANSLATION

From Feasibility to Availability




Positronen-Emissions-Tomographie (PET)
Magnetresonanztomographie (MR)
Einzelphotonen-Emissionscomputer-tomographie (SPECT)
Magnetresonanztomographie (MR)
Magnetresonanztomographie (MR)
Computertomographische Angiographie (CTA)

RECOGNIZING DISEASES EARLIER, TREATING PATIENTS MORE SAFELY

How Patients and Doctors Benefit from Image-Guided and Computer-Assisted Medicine

The flood of digital medical images cannot be stopped. In the time it takes to read this article, over 100 medical images will flood into computers at clinics around Germany. Two-thirds of these are high-resolution 3D images. The annual production of images in medicine has doubled between 2005 and 2013, when the sum totaled around 10 million. On one hand, this is excellent: new imaging methods give detailed insight into the structure and function of the human body. On the other hand, doctors cannot use the full extent of information contained in these images. Unassisted, humans cannot meaningfully process these vast amounts of complex data. In the future, intelligent systems will give doctors treatment suggestions based on the collected patient data.

Steering this flood of information into the right direction and filtering and processing decision-relevant knowledge for doctors provide great challenges. This requires efficient patient data management, intelligent workflows, and new assistance systems.

How can the available patient information be used properly? How can diagnoses and therapies become more reliable, flexible, and tailored to each patient? How can assistance systems be designed and integrated into daily routines in such a way that they help make more accurate and cost-effective diagnoses and therapy decisions?

"Image Man" is a life-size figure that comprises ten segments. The body parts depicted on the segments were produced with different imaging methods. At the center of the installation is a touchscreen showing the beating heart. By touching the screen, visitors can interactively navigate through the results of different imaging methods. A 3D-CT image serves as a spatial illustration of the heart. A sequence of blood-flow MRI reveals the blood streaming through the vessels and swirling turbulently. The exhibit was developed for the Science Center Universum® Bremen.

Fraunhofer MEVIS investigates and develops solutions to the issues underlying these questions. Close cooperation with physicians from different specialties is at the core of these efforts. Topics include computer-aided and image-guided methods for early recognition, diagnosis, and therapy for cancer and cardiovascular, brain, breast, liver, and lung diseases.

Merging medical images for better breast cancer diagnosis

Early recognition and precise classification of tumors is crucial to the diagnosis and treatment of breast cancer. When examining suspicious tissue, doctors take several images of the breast, using different methods, such as ultrasound, mammography, tomosynthesis, or magnetic resonance. Each method provides different insight. On mammograms, for example, doctors can more easily detect microcalcification, an indicator for certain types of tumors. Ultrasound helps distinguish between benign cysts and malignant tumors. Piecing together an overall picture from the gathered information challenges diagnosticians. One particular challenge when fusing information: during each scan, the breast is shaped differently depending on patient positioning and the imaging method employed. During mammography, the woman stands with her breast clamped between two panels. For ultrasound images, the woman lies on her back and the breast is slightly pressed towards the ribcage. Fraunhofer MEVIS developed a mathematical breast model to fuse the acquired information concerning suspicious tissue. Every point of a breast image is mapped onto a corresponding position on the model, thereby accounting for breast deformation. The diagnostician is automatically shown the integrated complementary information for faster and more accurate diagnoses.

Simulating and improving therapy planning for complete tumor destruction

Radiofrequency ablation (RFA) is an established clinical treatment method for small liver tumors. During this minimally invasive procedure, doctors insert needle-shaped applicators into tumors. Electrodes attached to the applicator send high-frequency electrical current into the diseased tissue, heating it up to 100 degrees Celsius and thereby destroying it. After a successful therapy, the tumor is eliminated, leaving no cancer cells in the body. Here, traditional RFA methods show weaknesses – clinical studies have shown that many tumors are not completely destroyed. To ensure tumor eradication, Fraunhofer MEVIS developed SAFIR (Software Assistant for Interventional Radiology). SAFIR provides multiple benefits to the attending radiologist. When planning a procedure, the physician can see, in 3D, important anatomical and risk structures, including tumors and blood vessels. The assistance system simulates, in advance, the amount of the tumor destroyed by the heat. The doctor can determine whether the planned treatment will destroy the entire tumor. The software calculates and adjusts for the liver deformation caused by breathing, helping radiologists evaluate therapeutic success and plan optimal courses of treatment. During procedures, the system assists doctors during needle insertion by giving auditory feedback similar to the tones produced by common auto parking assistance systems.

Biophysical simulations for safe, scalpel-free ultrasound therapy

Using ultrasound, doctors can achieve more than taking medical images from inside the body: they can also treat tumors. A high-intensity ultrasound beam is directed into the patient's body, heating the diseased tissue to above 60 degrees Celsius. In many cases, this non-invasive therapy is an alternative to surgical procedures. Until recently, however, it has only been approved to treat the prostate, bone metastases, and benign tumors of the uterus. Two problems prevent applying ultrasound treatment in other organs, such as the liver. First, the patient's breathing changes the position of the liver. Second, while treating a liver tumor, the ribs might enter the path of the beam. Fraunhofer MEVIS is developing software that will enable individual biophysical simulations for more precise ultrasound therapy planning. The simulation will incorporate patients' breathing movements and current rib position, allowing ultrasound beam adjustment and repositioning. In cooperation with doctors, Fraunhofer MEVIS scientists are testing the assistance system in clinical studies to permit ultrasound liver therapy.

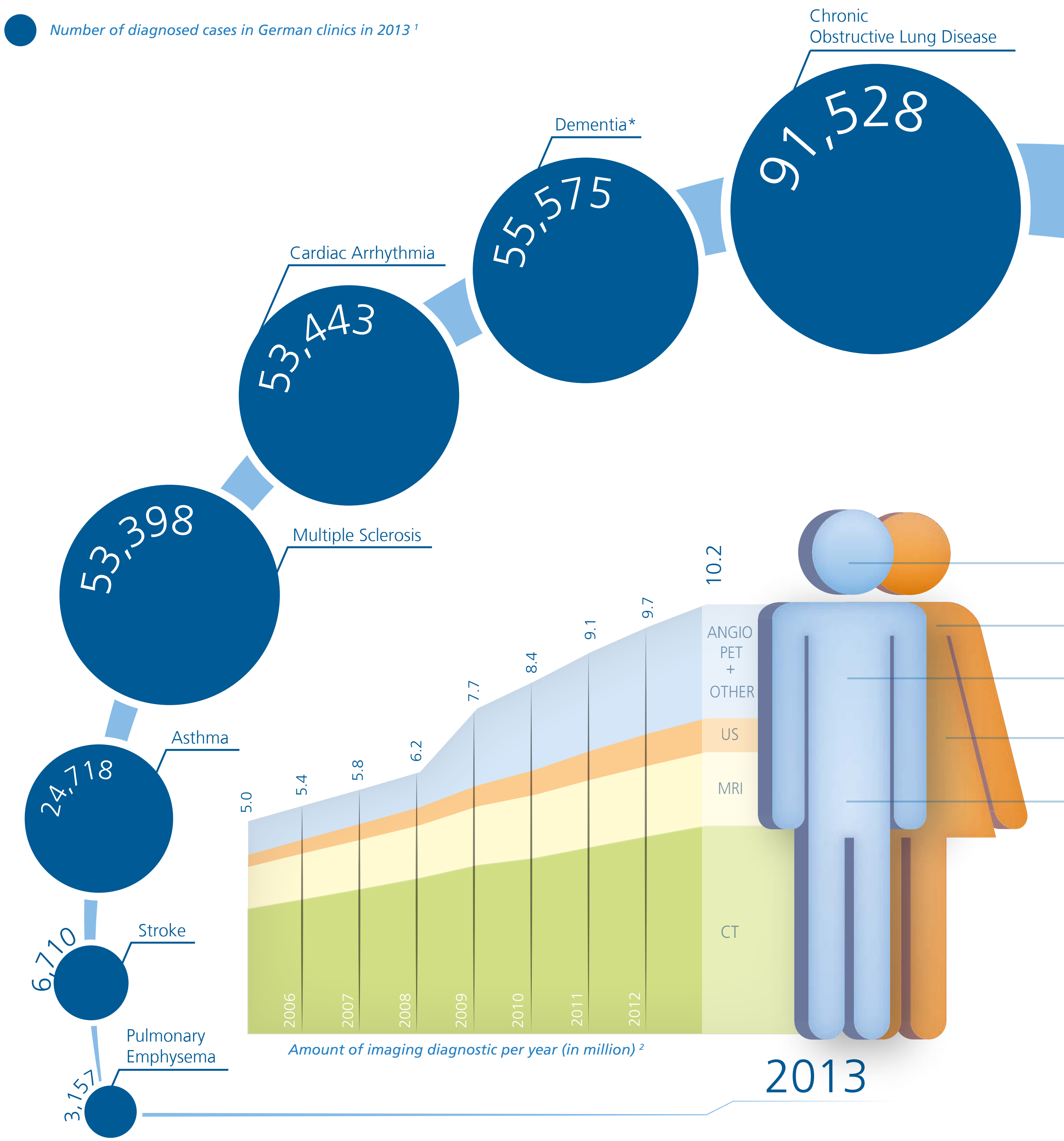
New training tool helps physicians choose the safest therapy option for stroke patients

After suffering a stroke, thrombolysis medication can dissolve a patient's blood clots. If the stroke occurs during sleep, administering the medication becomes problematic. According to current treatment guidelines, doctors can only administer the medicine in the first four and a half hours after the stroke. Thereafter, the risk of intracranial bleedings increases. It is important to establish a time frame in which the seizure occurred. In the WAKE-UP project, funded by the European Union, scientists are exploring ways of precisely determining the time of the seizure. Special MRI scans, including diffusion weighted imaging (DWI) and fluid attenuated inversion recovery (FLAIR), are used for this purpose. DWI images show how water molecules move in nerve cells and their immediate environment. FLAIR images depict organs' anatomical structures. If the blood supply to the brain is insufficient after a stroke (including oxygen and glucose levels), doctors can view these changes on the DWI images within a few minutes. Prolonged insufficient blood supply to the brain can cause permanent damage. These changes appear hours later on the FLAIR images. If a disruption is visible on DWI images and not on FLAIR images, doctors assume the stroke most likely occurred in the previous three to four hours. In these cases, thrombolysis therapy could still help the patient. If changes can be seen in both types of images, the stroke most likely occurred more than four hours prior to image acquisition. Administering medication in these cases would constitute an unacceptable risk of bleeding. In the scope of the WAKE-UP project, Fraunhofer MEVIS is developing a training tool that helps physicians more accurately interpret and evaluate DWI and FLAIR images. In the future, doctors will have automatic tools for measuring images at their disposal.

Better medication through research – imaging can help discover new medication for Alzheimer's disease

The pharmaceutical industry is researching new medications for the currently incurable Alzheimer-type dementia. Imaging methods such as positron emission tomography (PET) and magnetic resonance tomography help determine whether a new drug is effective and how well patients can tolerate new active agents. Fraunhofer MEVIS is working on methods that display and measure amyloid plaque in the brains of dementia patients. The existence of these deposits could previously only be determined by examining deceased patients. Now, this plaque can be seen using nuclear medicine imaging in PET scans. With the help of these new methods, physicians can view amyloid plaque distribution in a patient's brain and measure the amyloid levels individually. In clinical studies, these methods can help physicians more quickly and easily determine whether new medicine is helpful.

Bianka Hofmann



Number of diagnosed cases in German clinics in 2013 [1]
Chronic Obstructive Lung Disease
91,528
Dementia*
55,575
Cardiac Arrhythmia
53,443
Multiple Sclerosis
53,398
Asthma
24,718
Stroke
6,710
Pulmonary Emphysema
3,157
5.0
5.4
5.8
6.2
7.7
8.4
9.1
9.7
10.2
ANGIO
PET
+
OTHER
US
MRI
CT
2006
2007
2008
2009
2010
2011
2012
Amount of imaging diagnostic per year (in million) [2]
2013

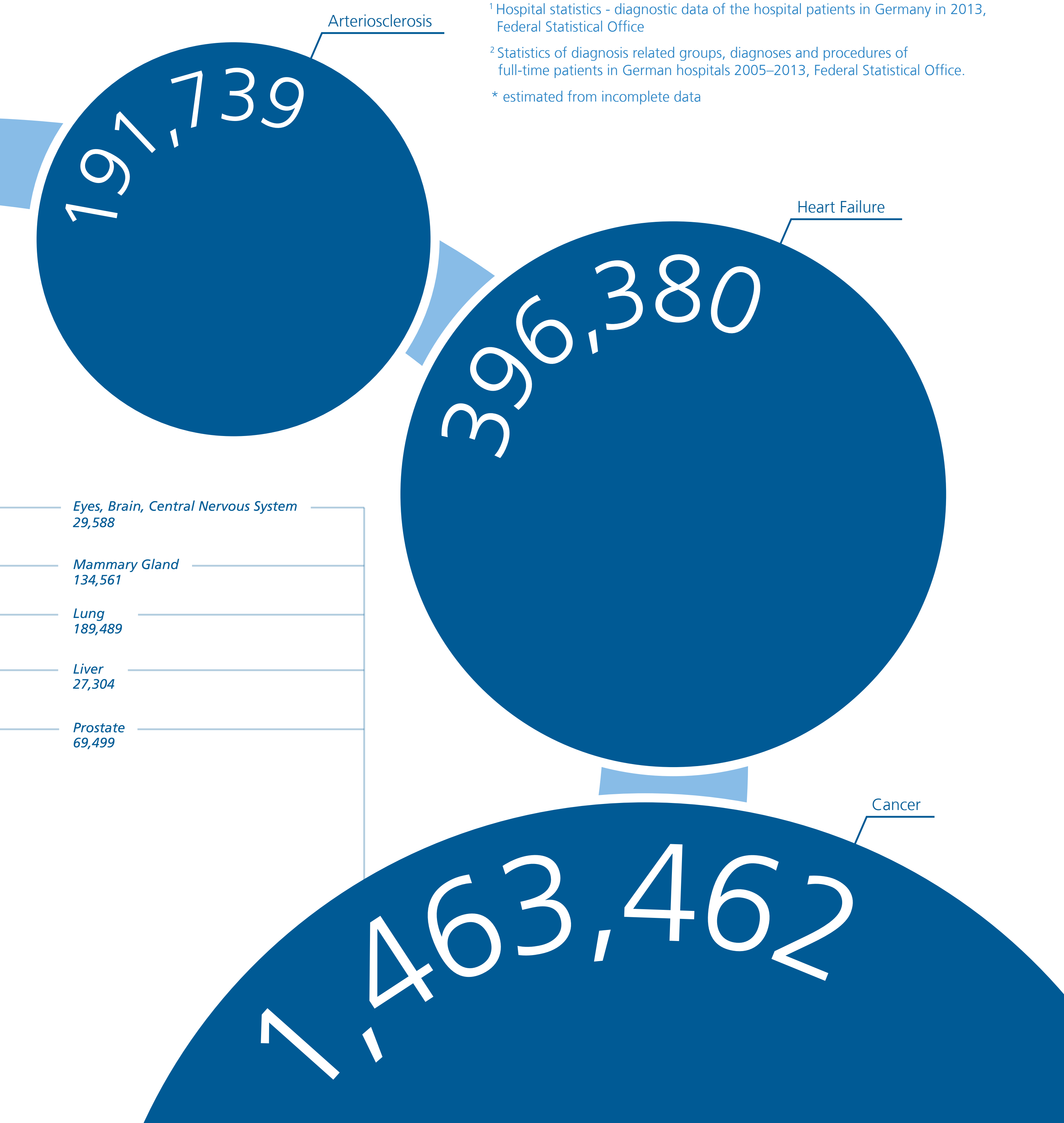
ASSISTED BY FRAUNHOFER MEVIS – DIAGNOSING AND TREATING SIGNIFICANT DISEASES

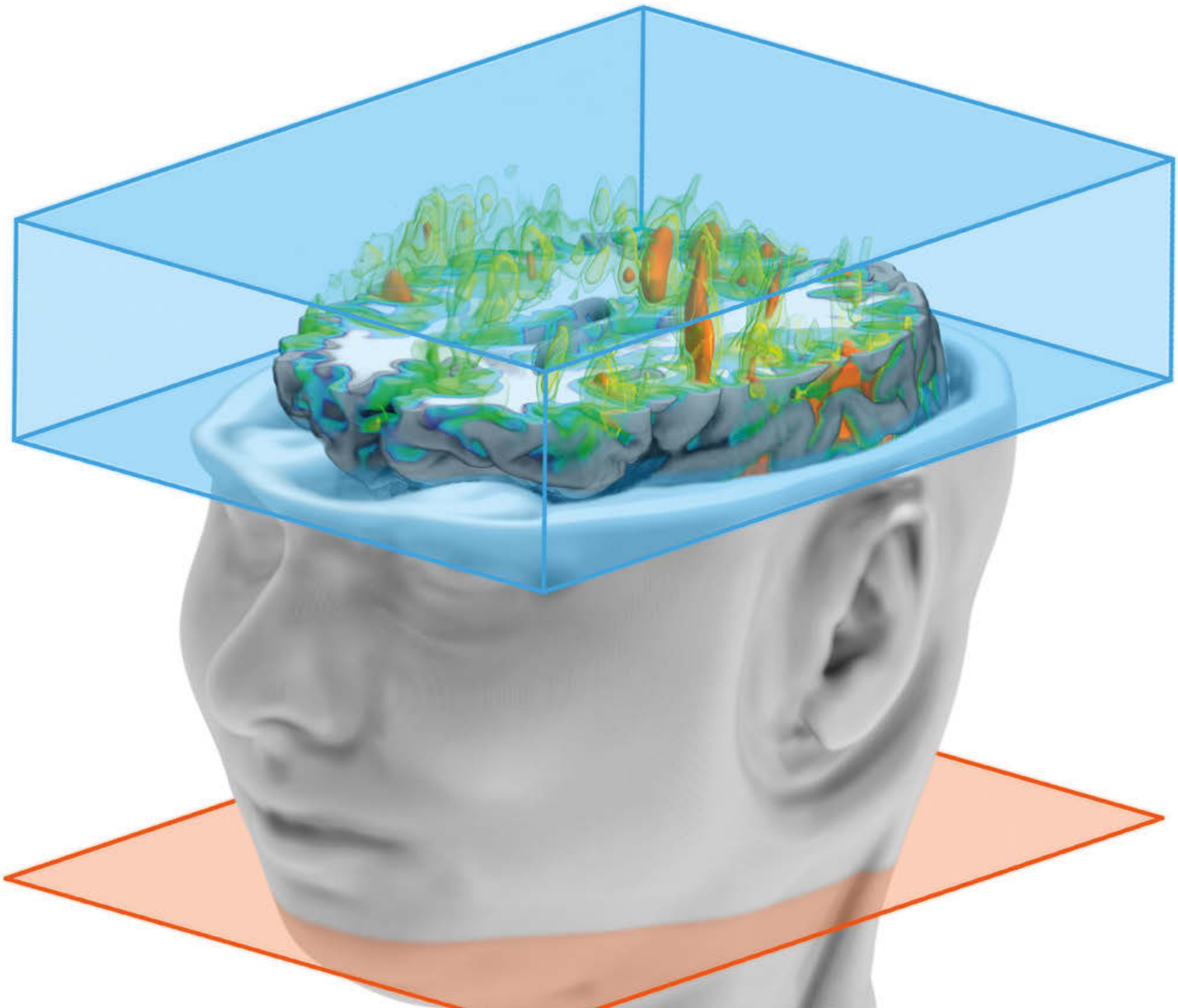
Steering, Filtering, and Processing the Flood of Data

[1] Hospital statistics - diagnostic data of the hospital patients in Germany in 2013, Federal Statistical Office

[2] Statistics of diagnosis related groups, diagnoses and procedures of full-time patients in German hospitals 2005–2013, Federal Statistical Office.

* estimated from incomplete data





ARTERIAL SPIN LABELING

Towards Clinical Reality of Truly Non-Invasive Blood Flow Measurement

For more than two decades, research in medical imaging has been moving towards gaining functional information in addition to images of structures. Clinicians want to know how viable a tissue is rather than only knowing its type. An important measure for this is perfusion, the transport of blood to tissues to supply nutrients and oxygen and drain waste. Currently, clinical routines commonly employ contrast agents or markers to measure perfusion. These substances are injected into blood vessels, and their paths through the tissue can be traced using modern imaging devices. However, contrast agents sometimes cause patients to experience severe side effects such as kidney dysfunction. Recent research has also shown that the most common contrast agent in magnetic resonance imaging (MRI) becomes permanently deposited in the brain. These reasons have motivated the search for an alternative to contrast agents, for which arterial spin labeling (ASL) is a promising candidate. Perfusion can be measured using ASL without injection, special preparation, or additional devices. To achieve this, inward-flowing blood is magnetically tagged upstream of the tissue or organ of interest. This tagged blood can then be measured within the tissue to determine perfusion.

The first application of ASL was documented in a publication more than 20 years ago. ASL did not, however, find its way into clinical routines. Instead, the technique has grown into over 30 different variants currently used in research. This multitude of ASL flavors prohibits clinicians from easily choosing the appropriate variant for a certain application. Fraunhofer MEVIS is dedicated to easing clinicians' decision-making. After almost ten years of research, the team succeeded in convincing leading MRI device manufacturers to market ASL. More importantly, Fraunhofer MEVIS has helped define a standard and publish a recommendation based on ASL community consensus. Because a single institution cannot undertake this effort alone, Fraunhofer MEVIS started to amalgamate the interests of the entire community. This initiative has grown to include a number of international partnerships and led to the foundation of the ASL Network, the predecessor of ASL in Dementia (AID), a COST Action program funded by the European Commission. AID unites scientists and clinicians across Europe and coordinates the development of an alternative, cost-effective, ASL-based tool for reproducible brain perfusion measurement.

Fraunhofer MEVIS and its international partners strive to further improve, validate, and establish ASL technology as a reliable clinical tool for the diagnosis and follow-up examination of a number of diseases, most notably dementia, ischemic stroke, and cancer. The application of ASL has also expanded to cover body regions other than the brain, including kidney, lung, breast, and liver. Scientists at Fraunhofer MEVIS are developing cutting-edge methods for time-encoded ASL and prospective motion correction to tackle the challenges of daily clinical work, fill clinicians' needs, and advance the field of clinical imaging. The multidisciplinary focus places Fraunhofer MEVIS at all stages of ASL research and application. The team provides tailored software tools that harmonize the planning, acquisition, post-processing, and interpretative processes of clinical trials, such as the German National Cohort.

Matthias Günther, Cristoffer Cordes

ASL perfusion of the brain: After inverting the blood protons in the labeling slice (red plane), the tagged blood travels to the tissue of which a 3D volume image is acquired (blue box). The colored data depicts the measured cerebral blood flow - a perfusion parameter.


TN - Cut1, Extended Right Hemihepatectomy, HV
100%

ASSISTING LIVER SURGERY

From Research to Clinical Application and Products

Many image analysis algorithms have been developed in the scientific community, but relatively few methods and applications have found their way into the clinical routine. Reasons are manifold, including algorithm quality, time requirements, and usability and workflow issues. Special demands on the software arise when developing for different clinical user groups with diverging technical and medical backgrounds. In addition, complex algorithms and sophisticated visualizations on mobile devices and inside sterile environments such as an operating room present further challenges when applying image-computing research to clinical application. As an example, image analysis methods for liver surgery planning and their clinical implementation will be discussed. Fraunhofer MEVIS has 20 years of expertise in this field, and the developed algorithms have been used in research projects and applied in different software tools for both clinical routine and studies.

The liver is a complex organ with four interwoven vascular systems, and liver interventions challenge physicians greatly. Surgery is currently the best option to cure liver cancer and metastases, but is unfortunately not possible for many patients. Deciding whether an intervention is feasible and how it should be performed is difficult. The number and location of lesions in the organ influences and limits the surgical strategy, and the volume of the remaining liver and its functional capacity may be insufficient for patient survival, prohibiting surgery. Analysis of patients' radiological image data and dedicated risk assessment of different surgical strategies can solve these problems, enable surgery, and support surgeons in planning and performing optimal individual therapies.

The mobile tablet application during a liver operation at Yokohama City University Hospital. The hepatic vasculature as well as the resection strategy resulting from the preoperative planning are visualized on the tablet computer and provide guidance during the surgical incision.

Fraunhofer MEVIS has been developing image processing algorithms and applications for liver data analysis since 1995, closely collaborating with several clinical partners. These methods have been integrated in clinical analysis software and used to plan more than 5,000 tumor resections and living-donor liver transplantations (LDLT). The results of two clinical studies showed a change in the surgical strategy of non-trivial liver resections in one third of cases when normal planning was enriched by the results of the Fraunhofer MEVIS planning. In some patients, the software results even enabled surgery that was assumed to be infeasible.

The developed risk analysis for planning LDLT, including the estimation of outflow obstruction of the middle hepatic vein after surgery, was a ground-breaking innovation. It was not only the basis for novel surgical decision criteria, but effectuated that no current adult LDLT is performed without volume computations and risk analyses for recipient and donor. Retrospective clinical studies of cases with liver remnant failure in recipients after LDLT have shown that the Fraunhofer MEVIS planning would have uncovered risks and prevented organ loss.

The challenge of different user groups

With respect to clinicians' expertise and time limits, different user groups include young physicians and technically less experienced users, surgeons with highly limited time resources in countries with specific reimbursement, and clinical experts with radiological and technical backgrounds. The latter group prefers to perform their own analysis, whereas others may prefer a distant expert service. Users of the first group may also be interested in anatomical, surgical, and technical teaching.

To fulfill the demands of the different user groups, Fraunhofer MEVIS has developed customized applications. The first was the certified MeVis LiverAnalyzer software, employed by MeVis Medical Solutions AG, a commercial company. Here, experienced technicians analyze the data, radiological experts check the results, and data and results are transferred over a secure internet connection. In hospitals, these results can be explored in a 3D PDF or imported into viewing software. The second application is syngo.via CT Liver Analysis, a medical software product, offered by Siemens directly to the clinicians and used in hospitals. The third application, the Mobile Liver Explorer, is an iPad app which uses data analysis results and works as a viewer with dedicated features aiming to support surgery in the operating room.

Remote module technology

All three software tools and related distribution paths were developed using the MeVisLab research and development platform. MeVis Medical Solutions and Fraunhofer MEVIS created this software system together to develop image computing algorithms and specialized clinical prototypes. It supports integrating image processing and visualization methods into a variety of medical software products. The Remote Module (RM) is important software that delivers MeVisLab-based applications to clients on any platform. For a stand-alone workstation, client and server processes run in parallel on one physical computer hidden from the user. This model was used to create the syngo.via CT Liver Analysis software. To transfer planning results into the operating room, the client was implemented in a tablet app. For other systems, the client software can also be integrated into a web browser for system-independent use. The RM concept of MeVisLab simplifies integrating existing image analysis algorithms developed, for example, in research projects into complex workflows and medical products.

Application in the operating room

Whereas planning software helps analyze risks and determine the optimal resection strategy, the mobile device in the operating room aligns the planned resection to the surgical incision into the patient's liver. In addition to providing the surgical plan as a 3D model, virtual and real organ can be overlaid: The tablet films the liver and, using augmented reality, superimposes virtual planning data onto the organ in real-time. A surgeon can immediately compare the liver anatomy shown on the computer model with the actual organ during an intervention. This affords fast quality checks with relatively little effort. Further software functions include vessel length measurement and interactive identification of partial liver volumes, which is necessary following intraoperative detection of additional tumors that must be removed. Another tool can 'erase' virtual vessels with finger gestures after their resection to expose underlying structures. With these tools, doctors can easily transfer surgical resections that were planned in advance or adapt them during the intervention. The app is currently being evaluated in a clinical study in Yokohama and was used by Prof. Oldhafer for the first time in Germany at the Asklepios Klinik in Hamburg-Barmbek.

"In an ongoing clinical study, 13 patients have been operated with iPad support so far. A comparison of these cases with 15 previous similar resections – presented at the IHPB 2014 in Seoul - showed a tendency to reduced blood loss and decreased operation time. Currently, the results are not statistically significant due to the small number of patients but highly promising. Furthermore, iPad navigation surgery may be very useful from educational aspect as well. During surgical procedures, our young colleagues also look at the iPad monitor and learn how vascular structures exist in the liver parenchyma. Repeated experience of such kind of navigation must be valuable and may shorten to be a good surgeon."
Professor Itaru Endo, Yokohama University Hospital, Japan

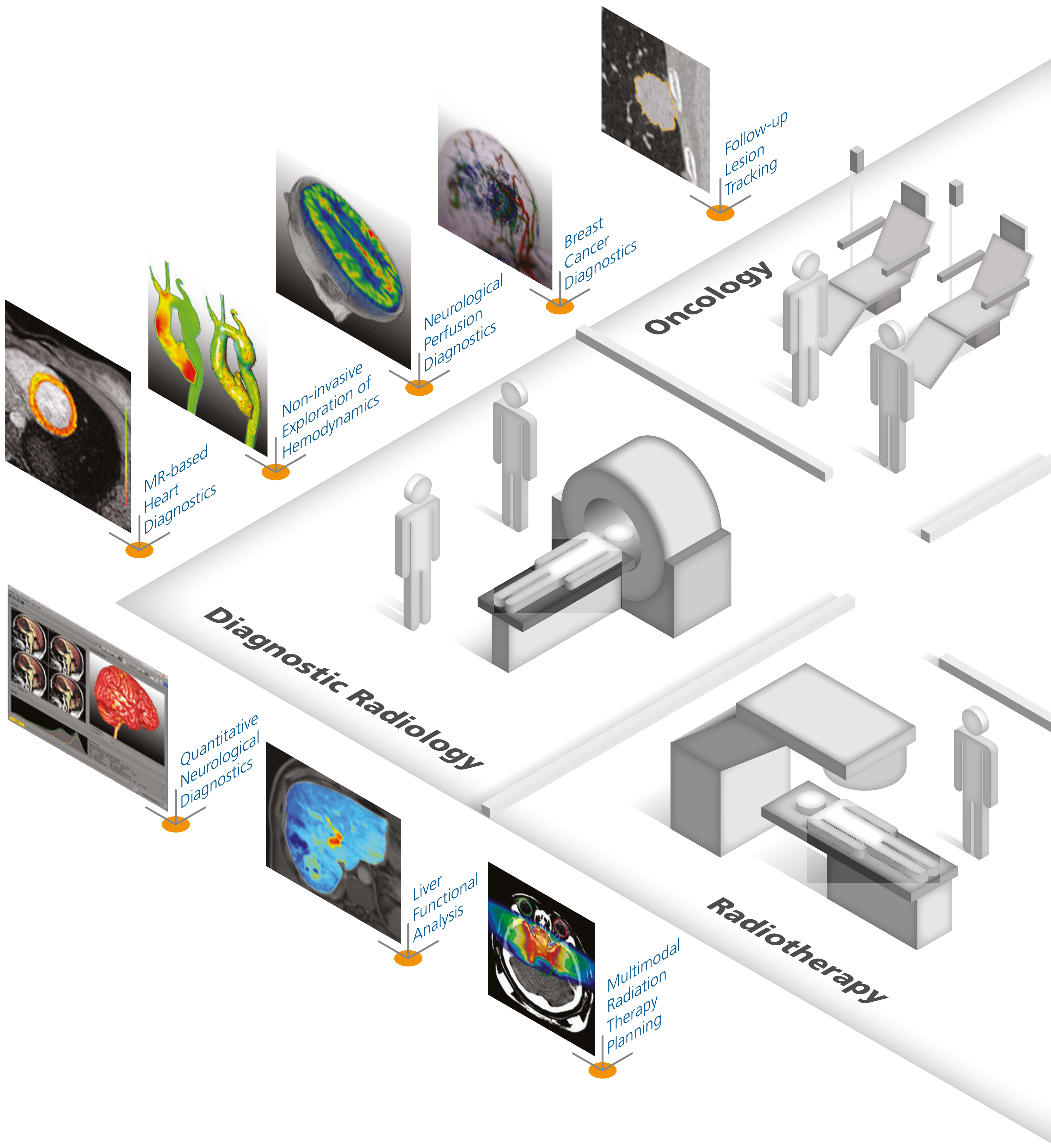
Further application areas and outlook

Fraunhofer MEVIS also applies image analysis algorithms from liver surgery planning to other projects and products. In the VIRTUAL LIVER system biology project, funded by the German Federal Ministry for Education and Research (BMBF), these algorithms were used to gain new insight into liver anatomy and regeneration. The new knowledge and derived parameters were used to develop and implement numerical models of organ growth and blood perfusion that can estimate, for example, the local distribution of drugs in the liver. Some of the developed image processing algorithms support planning minimally invasive and non-invasive liver therapies, such as radiofrequency ablation and high-intensity focused ultrasound.

The planning data can either be transferred into the operating room onto an app on a mobile device or imported into the CAS-ONE navigation system from CAScination AG (Bern, Switzerland). This system allows visualizing the 3D liver model and planning results simultaneously with intraoperative ultrasound and tracks the surgical instruments for visualization inside the virtual organ model.

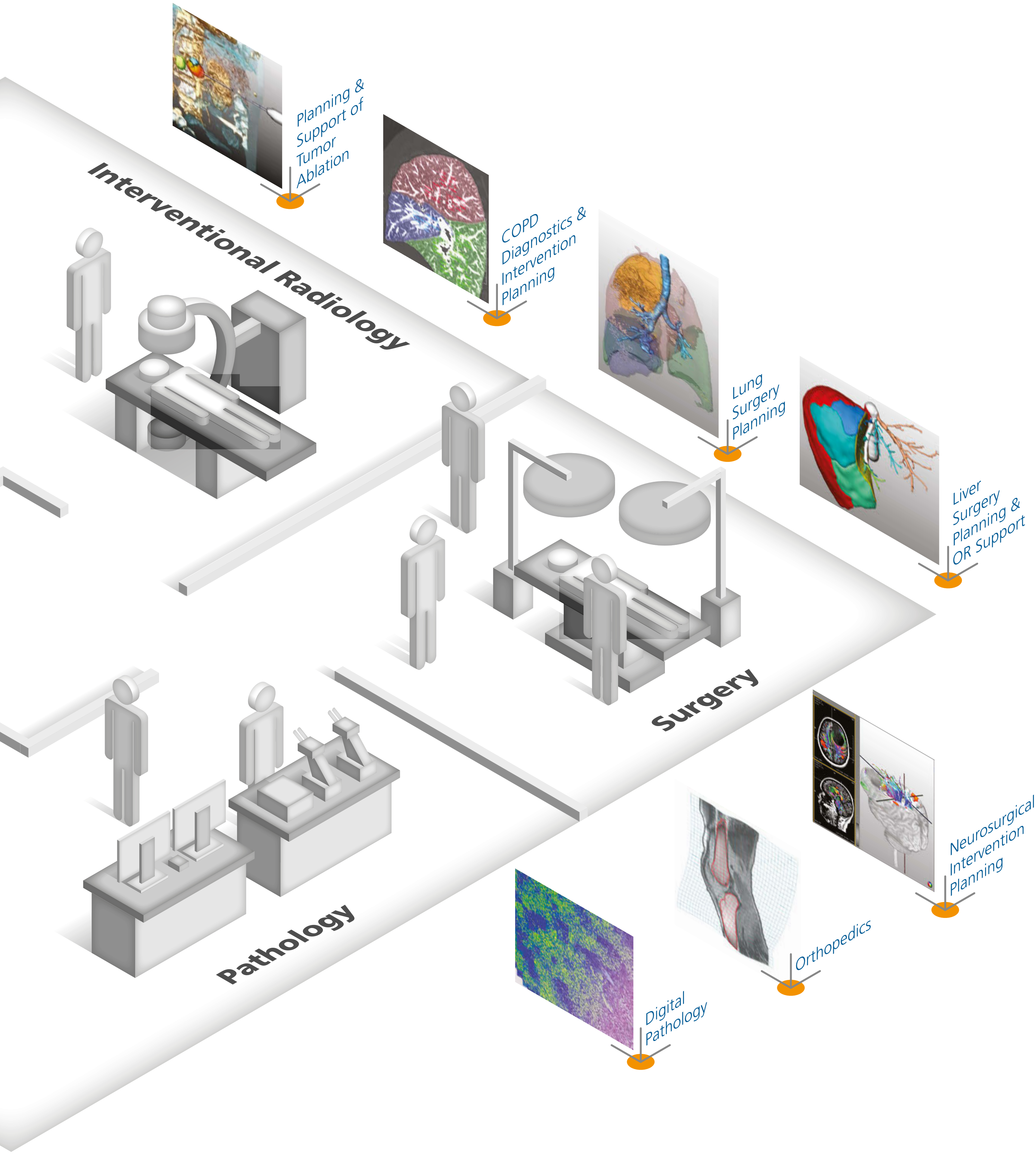
Current research focuses on extending the planning and risk analysis for liver surgery to magnetic resonance imaging (MRI) data with the benefit of including further functional information derived from dynamic contrast-enhanced image series and different MRI sequences. Future studies, especially those testing the mobile liver app currently undergoing certification, and expansion into other surgical fields and medical applications are planned.

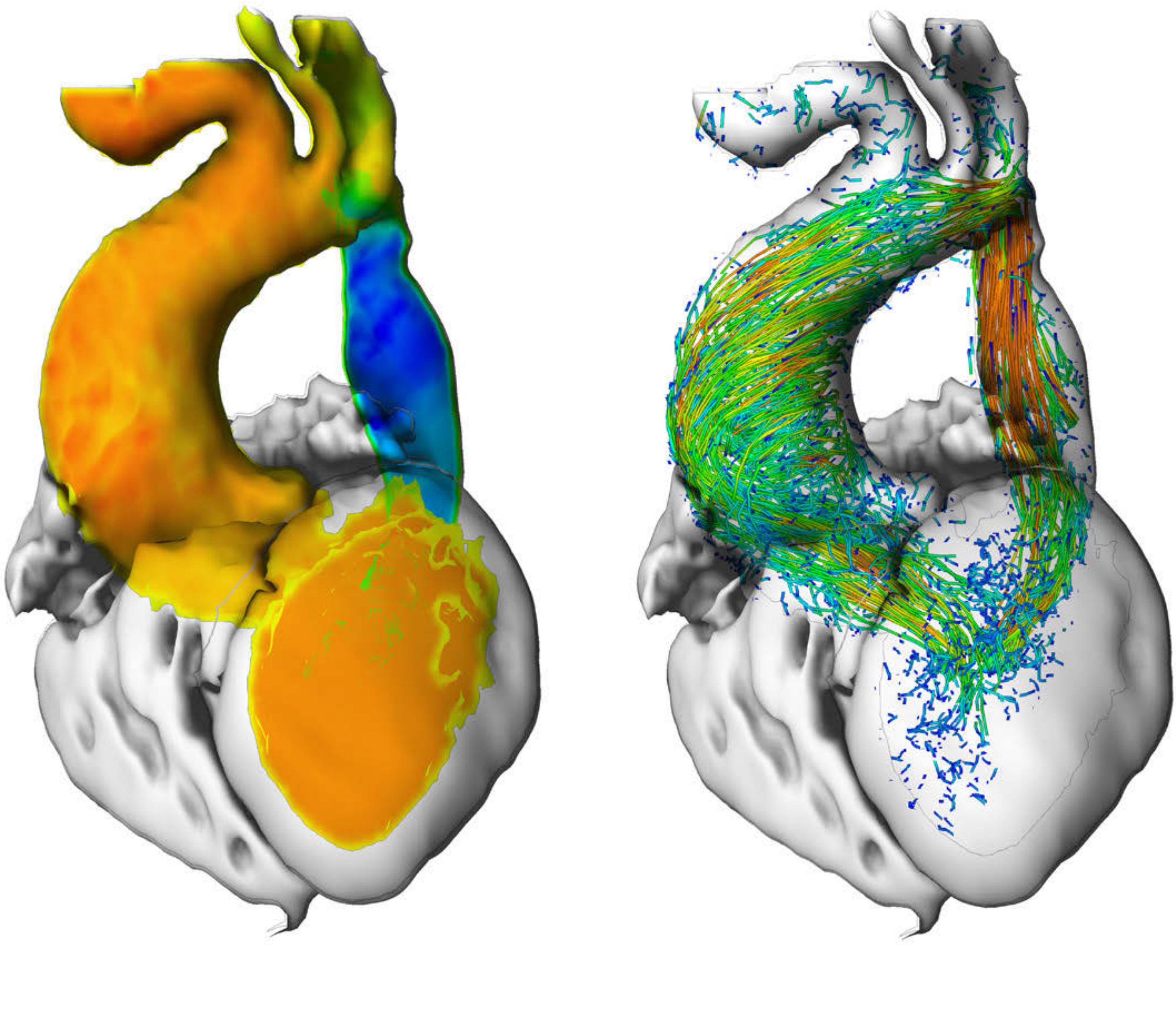
Andrea Schenk


Follow-up Lesion Tracking
Breast Cancer Diagnostics
Neurological Perfusion Diagnostics
Non-invasive Exploration of Hemodynamics
MR-based Heart Diagnostics
Oncology
Diagnostic Radiology
Quantitative Neurological Diagnostics
Liver Functional Analysis
Multimodal Radiation Therapy Planning
Radiotherapy

ENHANCED BY FRAUNHOFER MEVIS – INNOVATIVE CLINICAL SOLUTIONS

Integrating Robust and Effective Applications into the Workflow





INSIGHT FROM OUTSIDE

Pressure Maps for Assessing Congenital Heart Defects

Deciding the necessity and the best time point for treating congenital constrictions of the aorta requires regularly assessing a child's blood pressure ratio. Clinicians perform this by inserting a wire through an incision. When the wire tip is positioned at the constricted vessel segment, the attached sensor measures local blood pressure. Researchers from the German Heart Institute in Berlin and Fraunhofer MEVIS have developed an alternative, non-invasive examination strategy. This approach calculates 3D maps, which show blood flow and pressure distribution based on magnetic resonance imaging (MRI). First studies have shown that the results achieved in a clinical setting are comparable to those with the conventional catheter-based technique.

"We appreciate the great collaboration and the software tools provided by the Fraunhofer MEVIS team."
Prof. Dr. Titus Kühne and Dr. Leonid Goubergrits, German Heart Institute in Berlin

Coarctation of the aorta is a common congenital cardiovascular defect. Children suffer from the consequences that the constriction of the aorta imposes on blood circulation. Because the blood has to be pumped through this bottleneck to enter the lower body, the blood pressure in the upper body increases. The high pressure on the vessel wall can cause complications, such as dilation of the aorta and intracranial hemorrhage. Congestive heart failure may develop through high resistance during systole (afterload). The vessel section following the constriction is affected by the jet of blood. The forces of this jet on the vessel wall can cause aneurysms and wall dissection.

Coarctation of the aorta is a lifelong disease which requires monitoring and often repeated treatments to relieve constriction, control hypertension, and treat associated complications.

The image displays the pressure map and the blood flow trajectories of a young patient with coarctation of the aorta (left to right). The drop of pressure and the increase of flow velocity at the vessel narrowing are clearly visible.

Measuring flow – relevant information for therapy management

The blood pressure difference before and after stenosis is the key parameter for determining when to treat the constriction by either surgery or minimally invasive stent placement. Blood flow patterns are predictors of undesired pathological alterations of the vessel. Currently, echocardiography or flow sensors are applied to assess patient blood flow. With the first method, clinicians can roughly estimate the pressure difference between two measurement locations. Sensors provide a much more accurate assessment of local pressure values, but must be placed inside the blood vessel. In a diagnostic intervention, the clinician inserts the catheter with the sensor tip into the patient's aorta.

If therapeutic intervention is required, computed tomography (CT) or MRI provide anatomic information to plan the corresponding vessel geometry alteration.

Form and function – assessing aortic coarctation with MRI

MRI allows data acquisition to show anatomy and cardiac function without contrast agents or radiation. Current guidelines recommend MRI when assessing congenital heart disease. State-of-the-art phase-contrast MRI now permits measuring blood flow velocities. Using this information, visualizing blood flow trajectories and calculating flow-related biomarkers has become possible.

Applying this technique in children with coarctation of the aorta poses several problems, such as limited acquisition time, fast heartbeat, and variation of the blood flow velocities caused by vessel narrowing. It is therefore challenging to define an imaging and post-processing solution that can be applied in clinical practice.

Fast and comprehensive – a new approach for assessing anatomy and blood flow

To enable the combined assessment of the aorta geometry and corresponding blood flow properties, the team of Prof. Kühne at the German Heart Institute in Berlin introduced an acquisition protocol that combines anatomical and phase-contrast MRI. A high-resolution 3D angiographic image displays the anatomy of the heart and aorta. Phase-contrast MRI shows the blood flow velocities at a lower resolution and a relatively high noise level. This information can be acquired in under 30 minutes.

Fraunhofer MEVIS has developed a post-processing solution that enables fused analysis of this information. The user interactively extracts the aorta geometry from the 3D image, which is then applied to visualize flow and calculate the pressure difference maps from the 4D phase-contrast MRI measurements. Analyzing the 4D phase-contrast MRI data requires several processing steps to correct measurement artifacts. Calculating the pressure differences from the vector field measured by phase-contrast MRI constitutes a mathematical optimization problem to be solved numerically.

Integrating the algorithmic solution into a software assistant has enabled clinical validation. In a first study, Dr. Riesenkampff, pediatric cardiologist at the German Heart Institute, showed that pressure values calculated using the new method are consistent with invasive pressure sensor measurements. The suggested approach could become an alternative to the conventional, invasive technique.

Transfer into clinical practice – software support for multidisciplinary patient care

To apply the new approach clinically, user experience specialists analyzed the processes and stakeholders involved in the care of patients with aortic coarctation. Diagnosis and therapy decisions involve pediatricians, radiologists, cardiologists, and surgeons. The suggested 3D visualization provides a comprehensive overview of the patient's blood flow and pressure distribution, which can benefit interdisciplinary discussions. A web-based interface will provide access from different locations and from mobile devices.

Future projects will support therapy planning by combining this solution with virtual treatment simulation.

Anja Hennemuth

SOFTWARE MADE TO MEASURE

Support for Image-Based Clinical Trials

Clinical trials are necessary when approving new drugs. Two trends make trial management more and more challenging: Trials are often distributed to multiple clinical sites and increasingly involve imaging. Fraunhofer MEVIS has developed a software framework that helps to more quickly conduct trials and achieve more robust results. It offers image analysis and data management in the same application, allows remote reading on any device, and is adapted to the requirements of specific studies. Based on this framework, a tailor-made solution for oncological trials has been developed for a major pharmaceutical company.

The journey from first laboratory experiments to an approved drug is long: ten or more years may be needed for a clinical development program to prove the benefits of a new substance. The pharmaceutical industry bears the biggest share of these costs, which commonly reach one billion euros per drug.

Two trends complicate managing clinical trials. Medical imaging has gained an increasingly important role, enabling a paradigm shift from evaluating overall survival to earlier indicators of drug efficacy. When testing a new cancer drug, radiologists monitor tumor response using computed tomography or magnetic resonance imaging. This requires dedicated software and suitable hardware to view the images and measure tumor progress. Radiologists usually transfer the results to separate data management software manually. This approach is prone to errors and hinders verifying measurements at later stages of the trial, because the relationship between the stored results and the image measurements is broken.

A second trend is distribution of trials across several clinical sites to raise the objectivity of the results and increase the number of cases. For statistical assessment, it is crucial to collect consistent results from all sites. All participants must follow protocols concerning imaging and image assessment. These protocols differ from study to study and require the participating investigators (readers) to complete extensive training. Even after training, readers might not know how to apply the rules or might fail to comply. In these cases, examinations need to be repeated, otherwise sections of data become unusable.

To tackle these problems, Fraunhofer MEVIS, in cooperation with a major pharmaceutical company, has developed a software framework that supports clinical trials with three core concepts:

- Remote reading on arbitrary devices
- Image analysis and data management in a single application
- Incorporation of the specific rule set of a clinical trial

Reading in the cloud

In multicenter trials, all participants must use the same reading environment. To facilitate this, Fraunhofer MEVIS has developed technology to run complex applications in the web browser. All readers can use the same software, which does not need to be installed and maintained locally. Instead, a central server hosts the software. Participants can log in from any computer or mobile device and access all functions.

The central server is also responsible for managing data, storing all images, and allowing central image quality assessment (see box on p.29 for details). A sophisticated data transfer concept lets users interact with the images as fluently as if they were stored locally on their computers. Because the user interface is optimized for the browser and adapts to screen size, readers can use a device of their choice. All assessment results are directly stored in a database on the server. This simplifies data transfer and prevents transmission errors and data loss.

Image analysis and data management reconciled

An image-based clinical trial typically records two kinds of data in an electronic questionnaire. Some clinical information is entered directly, whereas other values are derived from image measurements. For example, the RECIST (Response Evaluation Criteria in Solid Tumors) guidelines for oncological studies require readers to report the diameters of up to five lesions. Fraunhofer MEVIS's concept connects measurements and the corresponding entries in the questionnaire. When the reader selects a caliper tool and draws a line on the image, its length is automatically entered in the questionnaire. Altering such an annotation updates the questionnaire. The database also stores coordinates of the annotation, facilitating measurement review and correction.

Values derived from multiple measurements, such as change in size over time, are computed automatically. It is important to consider the individual rules of the trial, because size change may refer to the first, previous, or largest measurement. Disregarding these rules frequently causes errors which can be avoided by software support.

This image-reading functionality benefits from Fraunhofer MEVIS's experience. Dedicated tools allow readers to perform robust 2D and 3D measurements more quickly and easily.

Software made to measure

Many clinical trials use special adaptations of standard rule sets such as RECIST. Thanks to the modular architecture of the Fraunhofer MEVIS software, new or adapted rules are easy to incorporate. The software automatically checks whether all required data and measurements are present, plausible, and consistent according to the rule set. For example, RECIST defines a minimum size for lesion eligibility. If a lesion is too small, the reader is informed immediately after measurement. Otherwise, such an error would be detected at a later stage and require tedious correction.

The user interface is tailored to each trial and streamlined to only include necessary features. It displays only the relevant images and a customized questionnaire that guides the reader through the workflow. This helps prevent distraction and errors.

MEREC – a customized solution

MEREC is a tailor-made application based on the Fraunhofer MEVIS framework that supports oncological trials at a major pharmaceutical company. By implementing concrete rule sets, it checks consistency for each specific trial. If a measurement violates the rules, MEREC displays a warning and prevents file saving. The application workflow is easy to use. For example, readers can undo and redo all interactions, which is immediately reflected in the questionnaire. Other special features include dedicated support for images from a large number of time points, a fast and intuitive 3D contouring tool for volume measurement, and a projection view that shows all annotations from different slices at a glance.

MEREC is integrated into an existing clinical trial management system. Readers tested MEREC in the training phase of a trial and reacted positively. Its flexible design also facilitates adding additional features for the actual trial.

Solutions for further trials are under development. Any image-based clinical trial can benefit from this technology, and Fraunhofer MEVIS tailors applications to the specific requirements of each study protocol. In addition to image viewing and interactive measurements, automated image analysis solutions are available at the institute to make reading faster and more robust. Image registration facilitates working with images from multiple time points and, for example, ensures that the same tumor is being measured. Segmentation algorithms can ease volume measurements and contribute to their establishment in clinical trials.

With its web technologies, Fraunhofer MEVIS can deploy newly developed image processing algorithms in multicenter trials. This increases the objectivity and robustness of future studies and supports researchers in evaluating new imaging biomarkers.

Jan Hendrik Moltz, Stefan Braunewell

NAKO – Fraunhofer MEVIS delivers digital infrastructure for centralized MRI data management

200,000 volunteers are participating in the German National Cohort (Nationale Kohorte – NAKO), the broadest long-term population study of its kind in Germany. An examination of the whole body using magnetic resonance imaging (MRI) is an essential part of this study, which focuses on health and the causes of widespread illnesses. By 2018, five dedicated MRI study centers will perform up to 30,000 exams.

As a partner in this major research project, Fraunhofer MEVIS has built a centralized infrastructure for digital data management, responsible for smoothly handling all image data and linked information during the entire study. All MRI scans are transferred to the central data storage at Fraunhofer MEVIS. Fully automated quality checks ensure consistent, reliable, and highly standardized image characteristics across MRI sites during the study. Two tailored web applications facilitate procedures for radiological review.

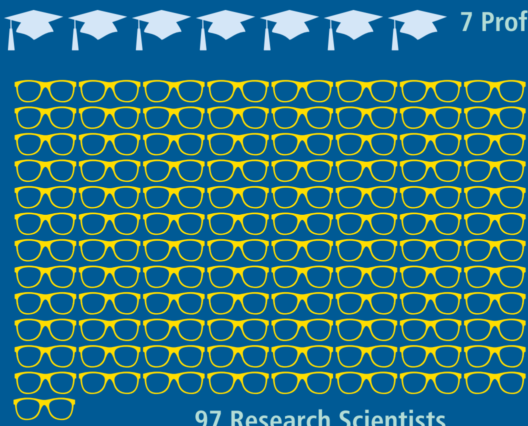
This groundwork enables data post-processing and evaluation for scientific research. Together with leading clinical researchers across Germany, Fraunhofer MEVIS will provide expertise in medical image processing and aid in gathering valuable insight into widespread diseases.

100+ Clinical Partners

Product Idea

For requirement engineering and product definition, Fraunhofer MEVIS provides services in technological consulting. User research and workflow analysis studies are conducted with a large network of clinical partners.

7 Professors



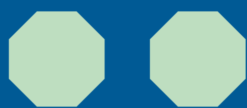
97 Research Scientists

Research & Development

For its commercial customers, Fraunhofer MEVIS researches customized solutions in medical image acquisition, post-processing, and modeling and simulation. User experience design and rapid prototyping ensure that novel solutions are effective for the end users. For evaluation and validation, Fraunhofer MEVIS serves as a gateway to clinical sites and offers image processing as a service.

Product Development

With its ISO-certified software development, Fraunhofer MEVIS acts as a translation partner to turn research results into products. From software design to algorithmic components and complete applications, Fraunhofer MEVIS develops software according to medical device standards.



ISO 9001 ISO 13485

MADE WITH FRAUNHOFER MEVIS – FROM IDEA TO MARKET

Contributing to Every Step of Product Innovation

Market Adoption

Fraunhofer MEVIS provides mobile and cloud access to medical computing including central management infrastructures. This lowers the barrier to market access and allows for new solutions to be brought to clinical trials or clinical routine.

Integration

For system integration, regulatory affairs, and market entry, customers are supported by established quality assurance and product delivery services. For technological solutions that extend beyond medical image computing, Fraunhofer MEVIS provides access to the Fraunhofer network of institutes.

66 Fraunhofer Institutes

Application Area	Contribution of Fraunhofer MEVIS	Impact for the Client
CT-based lung diagnosis and screening	Algorithms and application prototypes for segmentation, registration, quantification, visualization, and reporting	Integration into products for CT-based lung diagnosis
Lung cancer screening	Fast and accurate image registration of follow-up lung CT	Integration into a dedicated lung cancer screening software for a faster, enhanced workflow
Pelvis radiation	Image registration of planning and pre-radiation images	More precise radiation of pelvis with less side effects to organs at risk in a radiation planning system
CT-based oncological follow-up	Concept and development of algorithms and application prototypes for segmentation, quantification, visualization, and reporting; quality-assured software delivery; coordination of clinical evaluation	Integration into products of a major medical device manufacturer
Interventional oncology	Concept and development of algorithms and application prototypes for planning, intra-interventional support, and assessment of thermal ablations and biopsies; coordination of clinical evaluation	'Living' specification for product definition and support for discussion with clinical partners
MRI-based breast cancer diagnosis	Algorithms and quality-assured delivery of software components for motion correction in DCE-MRI data, segmentation of the pectoral muscle, and position correlation in multimodal image data	Integration into several medical devices for MRI-based diagnosis
MRI-based neuro diagnosis and surgery planning	Algorithms and quality-assured delivery of software components for DTI fiber tracking, visualization, fMRI, and perfusion analysis	Integration into a medical device for MRI-based neurological diagnosis and surgery planning

SELECTED INDUSTRY PROJECTS

Commercial, Technological, and Clinical Value

Application Area	Contribution of Fraunhofer MEVIS	Impact for the Client
MRI-based liver function analysis	Algorithm and application of a prototype for motion correction, segmentation, quantification of DCE-MRI liver data, and result reporting; data analysis for two clinical studies	Clinical trial support with a comprehensive quantitative evaluation tool
C-arm based orthopedic navigation	Algorithms for automated segmentation of femur head in fluoroscopic data	Partial automation and increased precision of an orthopedic navigation system
Planning and assessment for focused ultrasound ablation in prostate	Software for data import, visualization, and image registration	Cost efficient acquisition of specific know-how
Detection of swine pregnancy based on US images	Automated image analysis of US images and automated analysis of video streams to ensure correct positioning of the animal for US imaging	Integration into a system for pregnancy detection
Automated measurements in obstetric images of US devices	Algorithms for automated measurements of head circumference, abdominal circumference, and femur length	Substantial potential in automated analysis of obstetric US images
Development of MR sequences for faster abdominal DW imaging with a continuously moving table	Software development, optimization, and evaluation on models and volunteers	Outsourcing applied research on product level
Measurement of cerebral blood flow (CBF) without contrast agent	MRI sequence for Arterial Spin Labeling (ASL)	Advanced ASL methods
Measurement of renal perfusion without contrast agent	MRI sequence for Arterial Spin Labeling (ASL)	Transfer of ASL to a new field of application

Application Area	Contribution of Fraunhofer MEVIS	Impact for the Client
Automated image quality assessment (AQUA)	Consultancy service on design and implementation details	More efficient implementation of customer's automated quality assessment approach
MRI-guided, remote-controlled prostate biopsy	Algorithms and software for planning of positioning and inverse kinematics; quality assured delivery of software	Hardware-oriented company can market the complete system (software and hardware) as a medical device without establishing their own software know-how
Cardiovascular catheter ablation	Algorithms and planning software	Integration into a system for cardiovascular catheter ablation
Deep brain stimulation	Image registration of pre- and post-operational multimodal images	Integration into the customer's software for treatment assessment and tuning of steering parameters
Quantification of Alzheimer plaques with dedicated PET tracer (Florbetaben)	Automated classification (grading of severity) and software for regional quantification and comparison to normal values	Tool to perform comprehensive quantitative evaluation of studies and to optimize patient selection
Clinical trials: MR contrast agent	Dedicated software application for quantification of image-based parameters in trials for MRA and MR-based breast cancer diagnosis	Support of clinical trials by an integrated system for image analysis, quantification, and visualization
Clinical trials: generic solution	Generic cloud based web viewer for supporting image based clinical trials	Commercial web viewer use
Clinical trials: oncological	Web viewer and semi-automated quantification algorithms for workflow-optimized studies that allows flexible integration of various assessment criteria, such as RECIST or Cheson	Cloud-based tool for multicenter clinical trials
Clinical trials: lung diseases	Image registration for inhale and exhale scans; interactive lung lobe segmentation; airway segmentation	Integration into the customer software

CONTROLLING ROBOTS FOR PROSTATE BIOPSIES

From Sketch to Product

Reliably diagnosing prostate cancer requires precise retrieval of tissue samples. Magnetic resonance imaging (MRI) can be used to visualize and detect suspicious regions within the prostate gland. Fraunhofer MEVIS has developed software for a new robot for the Dutch startup company Soteria Medical for fast and precise targeting of these regions based on MRI. Soteria Medical benefitted from Fraunhofer MEVIS's expertise in fast development and certification of image-based software solutions. Within one year, the development was completed and the software was ready for certification.

Prostate cancer is the most common cancer in men. Prostate biopsy is vital for early cancer diagnosis and grading, and a proper biopsy position is important. Six to twelve biopsy samples are normally taken from different areas of the prostate to determine to which degree the prostate is affected by cancer. The most common verification of existing prostate cancer is transrectal ultrasound (TRUS) guided biopsy, although the image resolution and diagnostic accuracy of TRUS is limited. Due to a higher anatomical resolution than TRUS, MRI-guided prostate biopsy is a promising alternative. In particular, MRI permits more accurate visualization of suspicious regions within the prostate gland, increasing biopsy specificity and effectiveness. In addition, the localization of suspicious tissue within the prostate is a prerequisite when minimally invasive, localized therapies are applied.

Currently, manual procedures for MRI-guided prostate biopsy are lengthy due to several iterations of both manual position corrections and subsequent MRI scans. Soteria Medical invented an MRI-compatible robotic manipulator to improve accuracy and accelerate sampling, and thereby reach the target in a shorter time. Fraunhofer MEVIS developed the corresponding visualization and robot control software. The software guides the user through the interventional planning process. After selecting a target point, the application calculates the necessary adjustments, and an automatic execution can be performed. In case of further adjustments, the software also allows manual robot control to position the needle guide according to the acquired MRI scans.

The robot is composed of five linear motors. These motors are specifically designed for MRI use and are compatible with MRI. The motors move linearly to allow both fast movement and slower, more accurate movement, operating simultaneously to reach the desired position. Two motors control rotation and angulation of the needle guide, and three motors form a tripod and drive translational movement.

A faster workflow

With the software, the clinician can perform a prostate biopsy with the following workflow:

Diagnostic imaging: Multi-parametric MRI scans of the prostate are acquired to determine the precise size and dimensions of the prostate gland and the presence of suspicious areas. The imaging protocol includes T2-weighted, diffusion-weighted, and contrast-enhanced sequences and helps identify the location and size of potential cancerous areas. The user can examine the data with diagnostic viewers in which the image positions are synchronized and visualized with a crosshair.

Patient preparation and positioning: Once the radiologist has identified a suspicious area, the patient undergoes an MRI-guided prostate biopsy. The patient is positioned on the scan table and an MRI-visible, disposable needle guide is inserted transrectally and attached to the robot.

Calibration: After positioning patient and robot, the first MRI scan is acquired to calibrate the exact position of the robot with the 3D coordinate system of the MRI, providing the starting point for the intervention. The software automatically detects the needle guide after a single mouse click and an aligned overlay is displayed.

Intervention planning and biopsy: The radiologist can now select a target point within the interventional planning section of the application. After selecting the target and locking the position, the user can execute the motion of the robot according to the planned path indicated by graphic overlays. A newly acquired confirmation scan will show the new position of the needle guide, which lets the radiologist perform the biopsy using an MRI-compatible, disposable biopsy needle. Second or third samples can be taken from the same position or by slightly adjusting the needle guide using manual robot control.

"Fraunhofer MEVIS continues to be an outstanding partner in our product development. The project management and the team have been excellent throughout the projects, and the results have always been delivered on time, meeting specifications and expectations at the same time."
Jan Sabisch, CEO Soteria Medical, Arnhem, The Netherlands

From a technical perspective, the intervention consists of target selection and target adjustment. During target selection, the user chooses one point on the MRI scan, and the visualization of the needle guide automatically rotates around a pivot point so that it aligns with the target point. After the user confirms the target, the application converts the planned position and direction of the needle guide from the MRI coordinate system into the robot coordinate system and performs inverse kinematics: The lengths of the five motors are calculated and converted into motor steps, which are sent to the robot via a programmable logic controller (PLC). Low-level PLC programming was performed in cooperation with the Fraunhofer Institute for Manufacturing Engineering and Automation IPA (Mannheim project group). During target adjustment, the user can manually rotate the planned position left, right, up, and down around the pivot point.

Validation and quality assurance

After developing the hardware and software, preliminary lab tests were performed. The robot exhibited MRI compatibility and the planned position could be manually rotated around the pivot point in four directions. The clinical validation tests were performed at Radboud University Nijmegen Medical Center. Fraunhofer MEVIS developed a standalone application with quality assurance for a Class B product, including workflow support, connection to clinical image networks (PACS), visualization, and measurements. The core algorithms include calibration, inverse kinematics, path planning, and needle guide segmentation. The software was ready for certification in 2014, one year after the project started. The system was introduced on the market in early 2015.

In the future, such robotic manipulators could also be applied to other clinical applications, such as therapeutic procedures including drug delivery, robot-assisted surgery, and other image-guided interventions that take place in an MRI environment.

Stefan Kraß

NOT A CAR, NOT A PLANE

Highly Complex Models of the Human Breast

Breast surgeons use simulations to match preoperative imaging information to the situation in the operating room. Surgeons desire increased certainty about achieving cosmetically optimal results when performing a complete excision of a breast tumor. Researchers at Fraunhofer MEVIS address this need by using intelligent extensions to a fast simulation method delivered on a tablet computer in the operating room.

Female breasts are mostly composed of glandular tissue and fat. They deform following gravity. On the operating table, the patient lies in a supine position, while diagnostic magnetic resonance images (MRI) are acquired in a prone position. MRI can provide particularly helpful soft tissue contrast but the surgeons have to predict the shifting location of the tumor when the patient lies supine. Breast tissue undergoes a large degree of deformation between lying face down and face up. According to Dr. Joseph Colletta, breast surgeon in Boca Raton, Florida, USA, "It is complicated to predict how deep to the skin a lesion is in supine."

Many engineering applications involve simulating material deformation. Simulation is an important technology when aerospace engineers optimize the profile of an airfoil or when auto manufacturers predict the stiffness of a car's protective elements, simulation comes into play. Results must be highly accurate and therefore require long computiation times. Surgeons in the operating room, however, expect instantaneous updates when repositioning a virtual patient model. Existing fast methods are too inaccurate, and the accurate methods available to date are too slow.

Improving mathematical deformation models

Researchers at Fraunhofer MEVIS have combined established fast finite element methods (FEM) with custom made extensions of those methods enabling the simulation of larger and more natural deformations. Researchers reduce the simulation object to its basic elements, simplifying the model for faster computation (discretization of space) in order to fit with the discretization of time. Next, formulas derived from physical laws allow computing the forces and changes in shape for each element, but only for brief periods of time (discretization of time). Assembling the piecewise results gives an overview of the changes and force for the whole object, which is impossible to calculate without discretization.

The deformation magnitude of each basic finite element depends on its elasticity, which connects two physical quantities: stress and strain. External forces, such as airflow around the airfoil, forces of a car impact, or the breast weight, exert stress. Strain is the visible or invisible reaction of elements to these forces.

Scientists have established the relationship between stress and strain for many materials. The laws for metal, for example, are comparatively simple, and the objects are often homogeneous. The deformations of airfoils and car bodies follow complicated but computable laws. Soft tissues, however, behave differently, prohibiting direct application of the laws of engineering. Breast tissue, for example, exceeds these laws' limits of deformation. Nonetheless, clinicians demand interactive surgery applications that provide fast and plausible results.

Step-by-step optimization

The research team at Fraunhofer MEVIS uses a particularly fast implementation of a simple physical model. Its elements are large, making it even faster to compute, because each of these large pieces may contain a mixture of fatty tissue, glandular tissue, or connective tissue. In addition, the model assumes a linear relationship between stress and strain, and the elements are indifferent to the directionality of forces: they behave the same in every pose (isotropy). Linearity and isotropy do not exist in natural tissues. Skin is anisotropic and can, for example, be sheared with little force, but not easily extended. It also behaves nonlinearly: too much force can tear it apart. Simulating near-realistic physics is theoretically possible but computationally demanding and slow.

In contrast, the simplified model of Fraunhofer MEVIS is fast, but scientists extended it to generate realistic results with more complex deformations. Importantly, the team no longer treated all elements equally. Instead, local stress was checked after each short time step. The elasticity of those parts of the model that undergo more stress was decreased. This emulates the natural behavior of many soft materials that stiffen under compression.

Linking breast composition and deformation

The researchers at Fraunhofer MEVIS wanted to learn how breast composition explains the observed breast tissue deformation when a patient lies on her back. Volunteers entered an MRI scanner once face up, and once face down. By comparing the images, the team discovered that breast tissue behaves similarly to viscous fluid and that it can almost 'slide' around the rib cage. The simulation accounted for the first observation, but the sliding was not yet part of the model.

The team produced a refined solution that simulates the supine, face-up patient position from face-down MRI. Surgeons can now view a simulated chest and visualize the movement of the tumor even when the breast shape changes. "Particularly with non-palpable and ultrasound obscure lesions, a 3D supine visualization can help before surgery," says Colletta. The visual result is convincing and closely matches reality. Comparing volunteer MRIs showed how well the simulated and actual supine positions match.

During ongoing evaluation and optimization, Fraunhofer MEVIS has already taken further strides. The team created tablet software that shows a live camera image of the patient and superimposes the simulated breast to create a virtual-reality view of the patient. The breast appears translucent. The surgeon can see the location of the cancer and determine how to access it. Although only a prototype, clinical partners are eager to test the software in practice.

Within the VPH-PRISM project, surgeons have this opportunity. Currently, the Fraunhofer MEVIS team is refining the software for clinical use. Dr. Colletta in Florida and the surgical team in Nijmegen, the Netherlands, who have collaborated in the design and definition of this support technology, will be the first to test this software.

Markus Harz

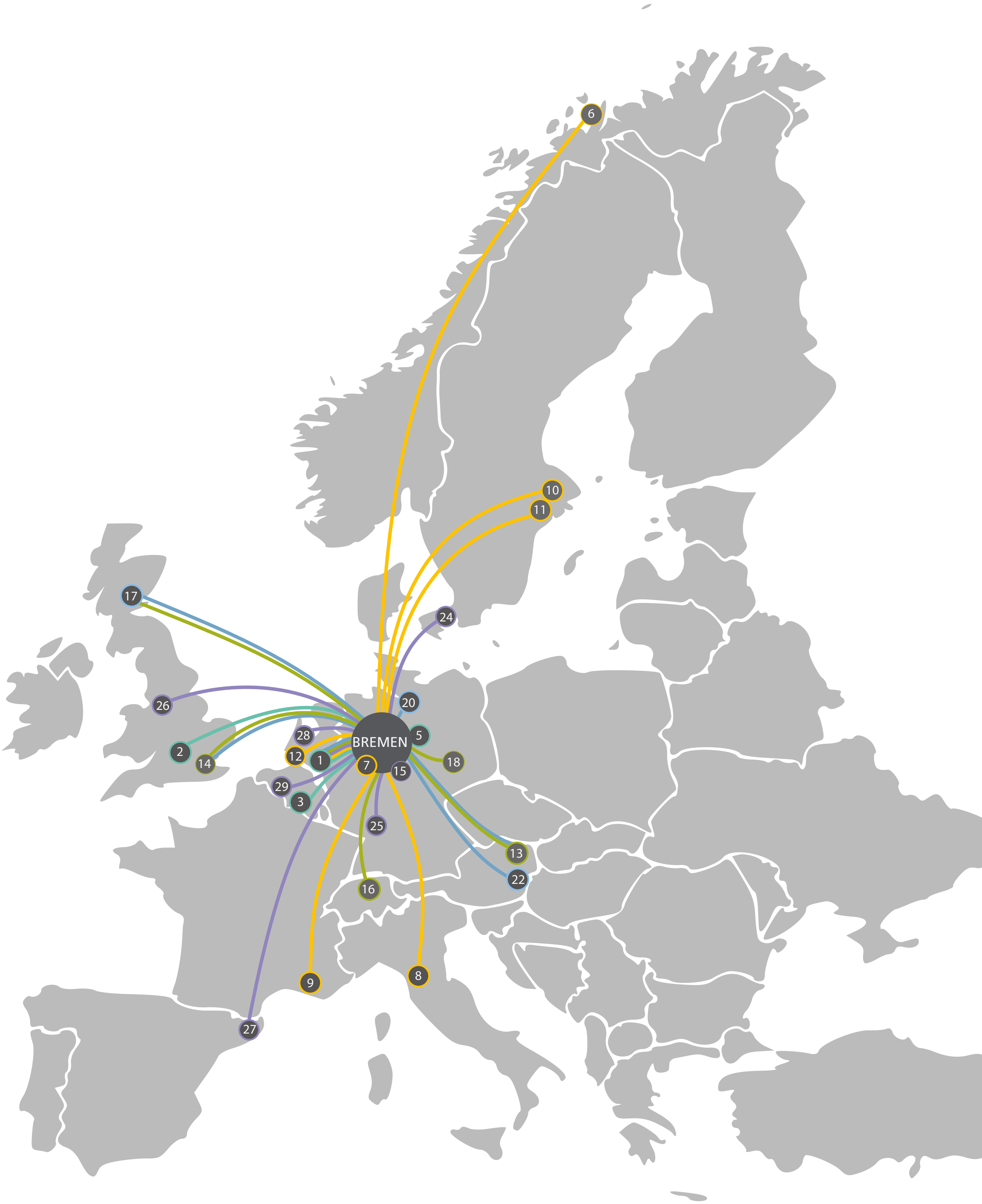
The VPH-PRISM Project

Breast cancer is life threatening, but curable if detected early. Characterizing early findings with optimized image understanding prevents overdiagnosis. Personalized breast cancer treatment prevents unnecessary, unsuccessful treatments. VPH-PRISM addresses these key topics with multidisciplinary, multiscale modeling of breast cancer with regard to environmental, genetic, and clinical factors. Biomarkers from digital pathology and advanced breast imaging are combined for the cancer and tissues in its vicinity. Breast cancer phenotypes are extracted from prospectively collected multidisciplinary data. A standard breast model enables efficient statistical modeling of the data, extending across disciplines, scales, structures, time, and patients. The project aims to:

- *Aid surgery and assess chemotherapeutic and radiotherapeutic response*
- *Optimize multimodal imaging methods*
- *Predict personal risks for cancer progression and select optimal treatment strategies.*

In VPH-PRISM, Fraunhofer MEVIS has partnered with researchers and clinicians from Nijmegen, London, Dundee, Hamburg, Vienna, Boca Raton, and Chicago. Four clinical centers collect unique sets of multimodal breast imaging and digital histopathology. The research centers collaborate in the three-year project to achieve computer-aided treatment decision-making. Philips (Hamburg) provides market access as an industrial partner.

VPHPRISM



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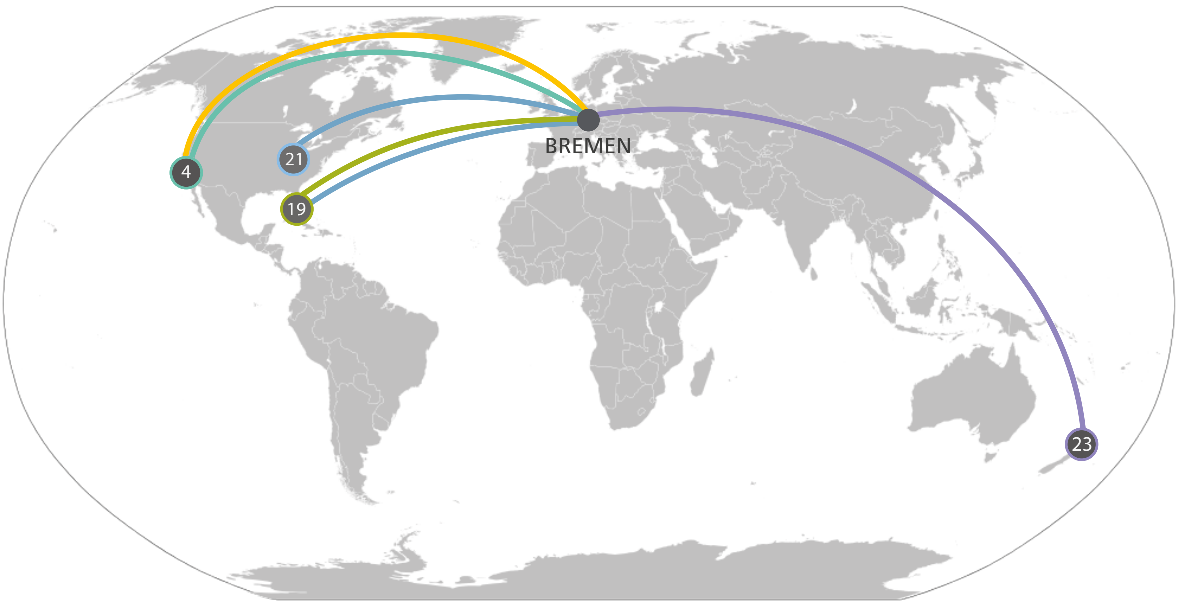
DRIVEN BY FRAUNHOFER MEVIS – EU-FUNDED BREAST CANCER NETWORKS

Improving and Personalizing Early Detection, Diagnosis, and Treatment



EU Project	Scientific Coordinator	Duration	Topic
SCREEN	Fraunhofer MEVIS	2000-2002	Digital Screening
SCREEN-TRIAL	Fraunhofer MEVIS	2002-2004	Digital Screening
HAMAM	Fraunhofer MEVIS	2008-2011	Multimodal Diagnosis
ASSURE	Radboud UMC Nijmegen	2012-2015	Personalized Screening
VPH-PRISM	Fraunhofer MEVIS	2013-2016	Personalized Therapy

1 Radboud University Medical Center Nijmegen, NL
2 University of Oxford, UK
3 BARCO NV, BE
4 R2 Technology Inc., US
5 MeVis Technology GmbH, DE
6 Tromsø University Hospital, NO
7 MeVis BreastCare, DE
8 Istituto Per Lo Studio E La Prevenzione Oncologica Ispo, IT
9 Arcades, FR
10 Hospital of Danderyd, SE
11 Siemens-Elema, SE
12 Preventicon, NL
13 European Institute for Biomedical Imaging Research, AT
14 University College London, UK
15 MeVis Medical Solutions, DE
16 ETH Zurich, CH
17 The University of Dundee, UK
18 Charité-Universitätsmedizin Berlin, DE
19 Boca Raton Community Hospital, Inc, US
20 Philips Technology GmbH, DE
21 University of Chicago, US
22 Medical University Vienna, AT
23 Matakina Ltd, NZ
24 Biomediq A/S, DK
25 Mediri, DE
26 University of Manchester, UK
27 University of Girona, ES
28 University Medical Center Utrecht, NL
29 Institute Jules Bordet, BE


Dose B: Accumulated F31 Dose for NNH+LA (boost)
Statistics
Projection
DVH Curves
DVH
Min Dose per Slice
Dose point
Annotations

THE RADIATION THERAPY OF THE FUTURE ADJUSTS ITSELF TO THE PATIENT

The SPARTA and DOT-MOBI Projects

Alongside surgery and chemotherapy, radiation therapy is one of the pillars of treatment of malignant tumors. Precisely targeting the tumor and sparing the surrounding healthy tissue are important prerequisites for therapeutic success. Together with physicians, other research groups and industrial partners, Fraunhofer MEVIS is developing software to improve therapy planning and optimize patient-specific treatment. The work has been supported by the German Federal Ministry for Education and Research (BMBF) in two successive research projects co-initiated and/or coordinated by Fraunhofer MEVIS.

Radiation can provide more than imaging for diagnosing bone fractures or internal diseases. Exposing tumors to a strong dose of high-energy radiation is a way of treating cancer. This type of radiation therapy is currently one of the most important treatment methods for cancer; about half of all tumor patients are now treated with photon or particle beams.

When clinicians treat tumors located near nerves or sensitive organs, they turn to special 'intensity-modulated' radiation therapy. Instead of exposing the tumor to a few relatively wide, strong photon beams, physicians apply many individually dosed partial beams from different directions. The beams coincide in the tumor and attain their maximum effect at this location. Ideally, this procedure only marginally affects the surrounding healthy tissue.

In practice, however, this method is limited because typically not only a single application of such radiation is administered. Patients undergo about 30 treatments spread over several weeks. During this time, the tumor size changes and the patient might gain or lose weight. These changes affect the tumor position and radiation target, increasing the risk that beams partially miss the tumor and instead damage healthy tissue.

Treating lung, breast, and abdominal tumors is complicated by the patient's breathing, which shifts the tumor position. To hit the tumor despite this motion, clinicians often select a relatively large target area, damaging more healthy tissue.

The BMBF-funded SPARTA project

Solving these problems is where SPARTA comes into play. In this BMBF-funded research project coordinated by Fraunhofer MEVIS, scientists from ten different fields develop innovative, adaptive, and expandable software systems to help clinicians plan and perform radiation therapy. SPARTA's overarching aim is to increase the safety and efficiency of radiation and support tumor radiation in a more patient-friendly manner using innovative systems.

"In the current version, the quick contour transfer generates very good re-contouring suggestions. The software will surely find its application in adaptive head and neck radiation therapy."
Reinoud Nijhuis, Medical Center of Ludwig Maximilian University of Munich

Accurately measuring variations: Computer-supported imaging and sensor systems should precisely measure when and how the patient's anatomy changes both over the course of treatment and during radiation sessions. The systems should determine the patient's precise position and monitor movements such as breathing. Exact measurement of individual variations is a prerequisite for optimally adapting the radiation therapy to each patient.

Precisely estimating dosage: The software should compare the original radiation plan to variations that occur between or during treatment sessions by reliably estimating the cumulative dose that the tumor has received after a certain number of treatments. This allows clinicians to determine whether radiation has reached the target as planned.

Intelligently adapting the radiation plan: The SPARTA project is developing a program to adapt radiation plans to measured

In clinical workshops, scientists from Fraunhofer MEVIS work with physicians to evaluate methods to compare two dose images.

changes or even to expected variations between and during treatments. How pronounced and regular are the breathing movements, and do they cause movement of the target region? This information should be incorporated into each radiation plan before treatment to increase accuracy. In addition, planning should become 'adaptive' by allowing simple and flexible adjustment during the course of therapy in case the tumor shifts due to weight loss or small changes in body position. The program should ensure that the planned radiation dose reaches the tumor and damages as little surrounding tissue as possible.

Autarkic extendibility: The SPARTA software allows for certification of the basic platform, which can be extended with plugins for additional functionality while maintaining the certification of the overall system. The software can thus be adapted to the specific needs of radiotherapy for individual patients or clinical studies.

The SPARTA consortium builds upon a software platform developed from 2009 to 2012 as part of the DOT-MOBI project funded by the BMBF. This software platform covers the complete spectrum from processing, quantification, and visualization of oncological image data to diagnosis and therapy planning and monitoring. The software allows for optimization of radiation therapy by combining the established morphological imaging with modern functional and molecular imaging. As a result, a growing variety of image information is employed to ensure differentiated analyses of specific disease courses.

Individually adjusting radiation over the course of treatment

At the beginning of radiation therapy, doctors develop a detailed treatment plan based on computed tomography (CT) imagery. This plan indicates how often and with which dosage certain areas of the body must be irradiated. To ensure that the tumor is targeted as planned and nearby healthy tissue is spared, doctors take routine control images of the patient. This helps determine whether the patient is lying in the device as planned. Likewise, these control images help determine whether the tumor has shifted in the body due to a patient's weight loss over the course of therapy. In such cases, healthy body areas can shift into the radiation path and become damaged.

To avoid this and to adjust the radiation optimally, doctors must compare the original planning images with the most recent control images. Often, the doctor must view old and new images and compare them mentally. However, the software developed in the SPARTA project can align both images in a single view and transfer the contours that define the radiation area. As a result, doctors can quickly recognize whether the original contours still apply to the current situation. If not, physicians can easily adjust contours with the software tools. With other solutions, replanning radiation therapy could take several hours – SPARTA can accelerate this process considerably.

Collaborative application development with doctors

To make the software user-friendly, Fraunhofer MEVIS experts exchange ideas with radiation oncologists several times a year and discuss progress during joint workshops. Is the program easy to operate? Do the algorithms deliver proper results? Are the software tools as practical as the clinicians desire? This ensures that the software will satisfy the demands of the clinical routine.

One of SPARTA's clinical project partners, the Ludwig Maximilian University (LMU) in Munich, has already started using the program for research purposes to evaluate its benefits. The software maturity achieved through close clinical collaboration will motivate the industry to bring these results to market and into clinical routine, benefiting both patients and doctors.

Guido Prause, Stefan Kraß

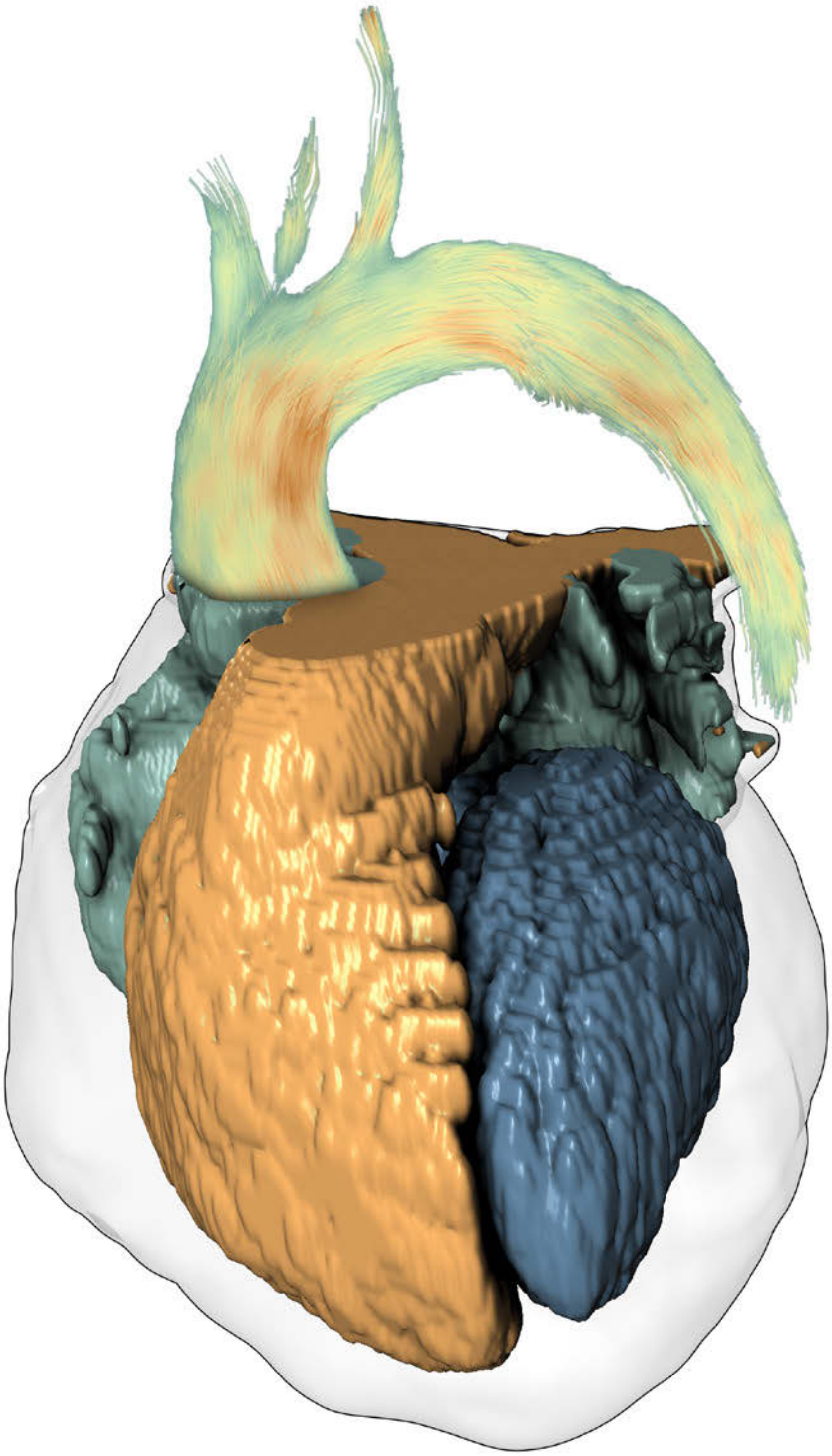
The SPARTA Project

The SPARTA project (Software Platform for Adaptive Multimodal Radio and Particle Therapy with Autarkic Extendibility) is funded by the German Federal Ministry of Education and Research (BMBF). It started on April 1, 2013 and runs for three years. The consortium encompasses ten partners, including research institutes, medical technology companies, and university clinics:

- *Fraunhofer Institute for Medical Image Computing MEVIS, Bremen/Lübeck (Coordination)*
- *Fraunhofer Institute for Industrial Mathematics ITWM, Kaiserslautern*
- *German Cancer Research Center DKFZ, Heidelberg*
- *Heidelberg University Hospital*
- *Medical Center of Ludwig Maximilian University of Munich*
- *Technische Universität Dresden, Faculty of Medicine*
- *Heidelberg Ion-Beam Therapy Center HIT, Heidelberg*
- *MeVis Medical Solutions AG, Bremen*
- *Precisis AG, Heidelberg*
- *Siemens AG, Forchheim*

www.projekt-sparta.de

SPARTA



OPENING DOORS FOR CLINICIANS AND SCIENTISTS

A Modular System for Clinical Research

Better understanding the causes of heart defects demands interdisciplinary research. Scientists are developing new techniques for image acquisition and processing. Clinical research explores the potential biomarkers provided by these techniques. Most researchers provide solutions for only one of these aspects. To interpret their data or compare it with existing approaches, researchers often need to access methods from other research groups. Fraunhofer MEVIS scientists have designed an extensible computer platform to interface between different research groups, granting clinicians access to innovative methods.

Clinicians investigate a variety of congenital and acquired heart diseases. Congenital heart defects are present at birth, whereas acquired heart defects are developed later in life. The complex structure of the heart and its interplay with blood circulation complicate diagnosing heart disease and planning therapy.

For a better understanding of heart defects, researchers explore complex heart functions on different levels: from the cellular processes, causing the alteration of heart muscle tissue, to blood flow patterns resulting from pathological changes. Imaging plays an important role in this research. Thanks to rapid technological advances, modalities such as computed tomography (CT) and magnetic resonance imaging (MRI) now provide a variety of imaging protocols to examine cardiac function, physiology, anatomy, and blood flow. An integrated exploration of these different images requires spatial and temporal alignment.

Fused visualization of the patient anatomy and blood flow from different imaging techniques. Geometrical models were generated with CAIPI.

"In a single cardiac MRI examination there are often 20 image series of different types and in various orientations. CAIPI is the first software that enables the fused inspection and analysis of all these image data resolved in the spatial and temporal dimensions."
PD Dr. med. Daniel Messroghli, Advanced Heart Failure Program, German Heart Institute Berlin

Specialized biomedical research – The need for interfaces

Researchers from various disciplines are involved in cardiac research. Image acquisition specialists, such as MRI physicists, focus on generating new images with better contrast or resolution and use image analysis tools to validate their work. Image processing teams focus on developing sophisticated segmentation algorithms. Other groups develop complex, customizable mathematical models to simulate cardiac biomechanics. Clinicians want to use these new images and methods, but are primarily interested in the additional value of these approaches for diagnostics and decision-making. Researchers, clinicians, and vendors can benefit from working together, but there are considerable barriers to collaboration.

Commercial vendors cannot provide solutions for all new images in early research stages, so scientists develop their own data analysis tools. In many cases, small computer programs or scripts are written to validate algorithms for a scientific article. Clinicians often cannot examine their patient data with these tools, because the data management provided by their software vendor is different from that used for the publication.

Cardiac imaging data varies in orientation, temporal alignment, and additional parameterization such as velocity encoding. Implementing support for all imaging formats is a laborious task. When a computer system is developed for a specific purpose, it is often impossible to compare the results of one examination directly with another type of data. Instead, users transfer results between different tools, which is tedious and prone to errors. Scientists require functional, easily extendable tools for managing cardiac images to deliver clinicians new techniques.

A multidisciplinary approach – Cardiology meets engineering

In 2009, Dr. Messroghli and Prof. Kühne of the German Heart Institute in Berlin approached Fraunhofer MEVIS with the idea of creating a platform for such tools to be integrated with OsiriX, a well-known viewer for picture archiving and communication systems (PACS). OsiriX is open-source and can be easily extended with plugins.

Using the MeVisLab development platform, researchers at Fraunhofer MEVIS designed CAIPI, an application that can also serve as an OsiriX plugin. The CAIPI framework can import, manage, and analyze cardiac MRI data. The software aligns the image data in a patient-specific model according to spatial position and heart contraction phase, which facilitates comparing different images. Researchers can extend its functionality by creating image processing algorithms or modules for clinical quantification.

"Fraunhofer MEVIS continues to be an essential partner in our development of real-time MRI as a clinical tool. The excellent project management and the outstanding quality of the team are of utmost importance in bringing this technology from the lab into the hospital."

Professor Jens Frahm, Director of the Biomedizinische NMR Forschungs GmbH at the Max Planck Institute for Biophysical Chemistry in Göttingen

CAIPI's modular design allows different combinations of image acquisition techniques, image processing algorithms, and quantification methods as well as easy integration of newly developed components. The standardized quantification in relation to an integrated heart model enables clinical researchers to compare biomarkers for corresponding heart regions provided by various image sequences. Image processing specialists can integrate new segmentation algorithms and rely on existing data management and clinical parameter extraction functionality. This simplifies comparing different algorithms.

CAIPI provides functionality for integrated visual exploration of cardiac CT and MRI data. A variety of plugins offers solutions for typical clinical concerns such as local and global cardiac function and blood flow measurements from 2D phase-contrast MRI.

Catalyzing research – CAIPI in biomedical engineering projects

A group of scientists, led by Prof. Frahm of the Max Planck Society, is developing innovative real-time MRI sequences. These rapid imaging techniques enable creating movies which show the variation of cardiac motion and flow over several heart cycles. Fraunhofer MEVIS has developed advanced image processing algorithms for quickly processing large datasets automatically. CAIPI combines these techniques so that clinicians can extract new quantitative biomarkers from heart movies. The clinical research, made possible by CAIPI, can provide insight into the local influence of diseases such as arrhythmia.

Generating personalized heart models requires extracting a patient's anatomy from image data. The difficulty of this task impedes applying biomedical modeling and simulation methods to real-world scenarios. To support researchers from the University of Graz and the Charité - Universitätsmedizin Berlin in their work on biomechanical modeling and computational fluid dynamics, Fraunhofer MEVIS supplemented CAIPI with new tools which generate geometrical models from image data. These models are used in research projects on model-based therapy support for minimally invasive interventions such as heart valve replacement.

Markus Hüllebrand

SMALLER, BETTER, FASTER, STRONGER

The Key to Efficient Image Registration

Inefficiency is a major obstacle for new image processing methods when bridging the gap between research and clinical routine. Scientists from the Fraunhofer MEVIS Project Group Image Registration employ high-performance computing to apply their algorithms in clinics and industry.

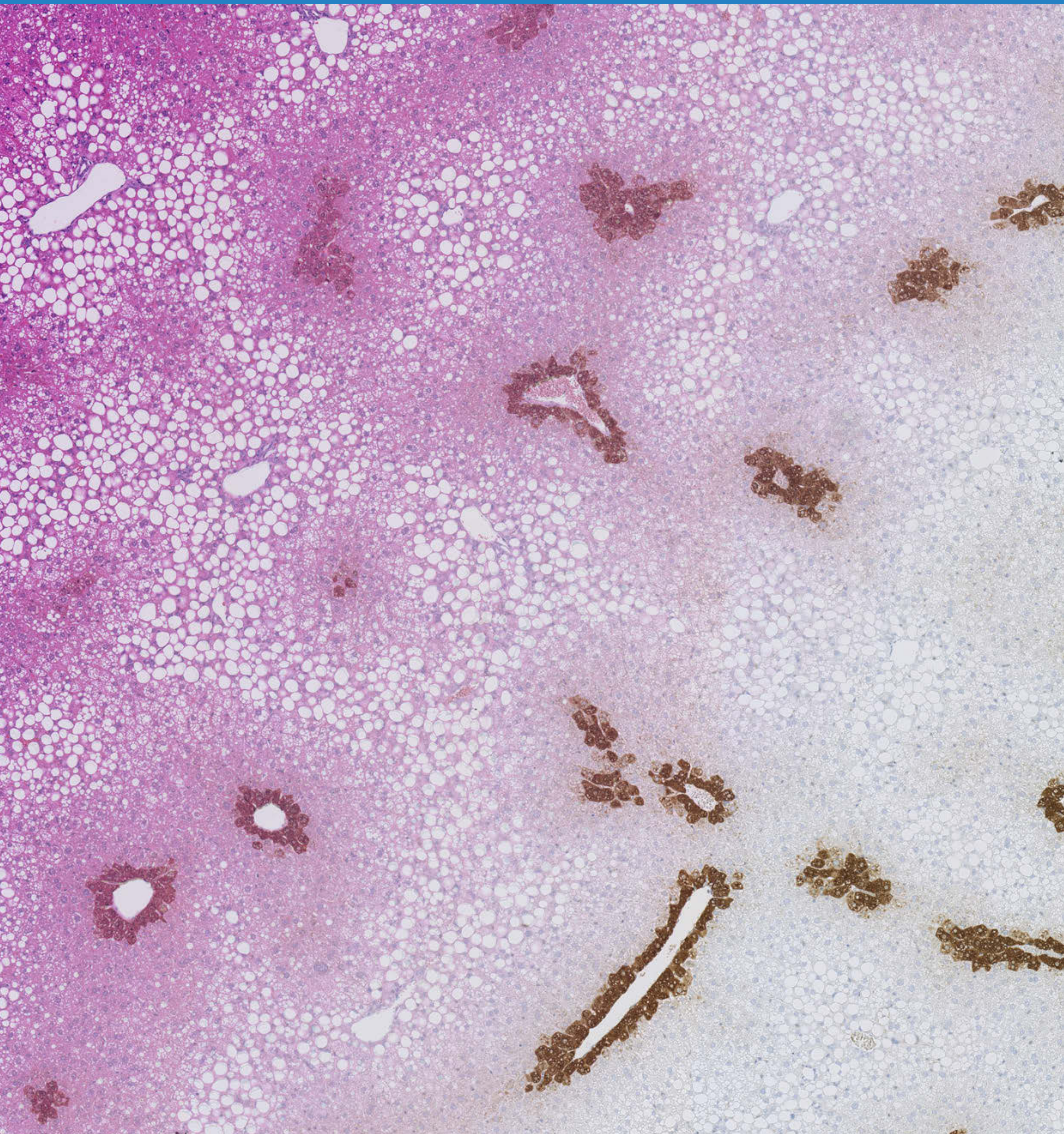
Nonlinear, elastic image registration computes motion and deformation between two or more images very accurately and on a fine scale. Clinicians use these techniques when comparing or fusing two image results to gain useful and important information. Doctors often attempt to determine whether a conspicuous anatomical structure found in a magnetic resonance imaging (MRI) scan is a tumor. They use image registration to automatically fuse a functional positron emission tomography (PET) image and combine the information from both modalities. Image registration enables physicians to evaluate lung deformations and motion caused by breathing to reveal diseases such as chronic obstructive pulmonary disease (COPD), which stiffens the bronchi in some areas and inhibits proper lung inflation. Radiation treatment planning, thoroughly prepared by experts, can automatically adjust to a patient's position before treatment. This allows continuous adjustment of the radiation focus. Despite the benefits that image registration provides, common software tools for nonlinear image registration require extensive computer memory and long computation times.

Scientists at the Fraunhofer MEVIS Project Group Image Registration in Lübeck developed a solution to these problems. They created algorithms that calculate more data on the fly, thereby minimizing memory use and eliminating the need for millions of variables. This allows optimally using multi-core processors and graphics processing units (GPUs) to dramatically reduce computation time, essential for industrial and clinical routines and day-to-day use. Originally developed for high-resolution registration of medical images in a research project, the new software convinced a company from the field of medical technology to fund a joint project to automatically fuse CT and PET images. In the project, the software underwent further optimization and adaptation to the customer's requirements. Previously, the images were only coarsely aligned. Now, the software produces image overlays with sub-millimeter accuracy in seconds for more accurate diagnoses.

This new tool is not only beneficial for customers and doctors; it was also an achievement for the scientists themselves. With minor modifications and embedded in a smart infrastructure, the code is the centerpiece of a new vessel-tracking method for ultrasound sequences of the liver. This method is the first to register images in real-time and achieved the highest accuracy of all contestants at an international challenge for liver ultrasound tracking (CLUST 2014).

Fraunhofer MEVIS aims to provide image registration to all clinical platforms, ranging from mobile devices to desktop workstations to high-performance clusters. Each has a different scope of application and can profit from more efficient implementation.

Till Kipshagen



MANAGEMENT REPORT 2014

Fraunhofer MEVIS at a Glance

Brief Profile

The Fraunhofer Institute for Medical Image Computing MEVIS (short: Fraunhofer MEVIS) adheres to a clear philosophy: To achieve significant improvements in medical diagnosis and therapy in relevant fields of disease using image-based computer support. At the heart of all research and projects at Fraunhofer MEVIS lie relevant clinical questions, which are addressed by developing and using the technological equipment in the field of medical image computing.

Research at Fraunhofer MEVIS does not merely focus on answering questions that appear interesting on a scientific level; it aims to achieve solutions that reach industrial partners and directly benefit patients involved in clinical routines. The objective of Fraunhofer MEVIS is to attain long-term, substantial improvements in medical treatment.

Clinical Commitment

Research and development at Fraunhofer MEVIS pursue a clinical direction instead of technological or methodological orientations. Work focuses on developing innovative solutions for image-based medical processes and their industrial implementation for clinical use. Identifying and analyzing clinical issues demands a deep understanding of medical research and calls for close cooperation with clinical partners. Fraunhofer MEVIS maintains an international network of over 100 clinical partners. This clinical network is an essential source of target definition and user feedback for evaluating the clinical relevance and feasibility of developed solutions.

Registration of serial sections is a key component in digital pathology. The left is stained with Hematoxylin and Eosin (H&E), the right with Glutamin-synthetase (GS). The GS stain colors central veins in brown, while portal fields are not stained. Thereby, it enables the distinction of the different vascular trees of the liver. The image shows steatosis which has a good contrast under H&E staining. The virtual combination of H&E and GS staining reveals that in this case steatosis is concentrated around portal fields but not around central veins.

Industrial Collaboration

True innovation, the successful launch of solutions onto the market with tangible effect on society, is only possible through close collaboration with industrial partners with the necessary resources and market know-how to fuel the development of new technologies. Fraunhofer MEVIS functions as link between clinicians and industry, aiming to establish solutions for clinical use. Transferring applied research to the industry is a pillar of the institute and a requirement for future research. Partners for cooperation and clients for industrial research and development include large firms and small- or medium-sized ventures in medical technology or related fields such as pharmaceutics.

Certification

Successful introduction of innovative approaches onto the market requires adherence to specific regulations, such as the German Act on Medical Devices (MPG) or the approval guidelines of the United States Food and Drug Administration (FDA). Fraunhofer MEVIS is one of only a select group of research facilities that, in Bremen since 2005 and in Lübeck since 2012, has been certified according to the EN ISO 9001 and EN ISO 13485 quality standards for medical products. This certification lays out well-defined steps for industrial cooperation. In addition, Fraunhofer MEVIS also has experience with CE and FDA approval for clinical environments.

A Complete Innovation Cycle

Together with industrial partners, Fraunhofer MEVIS has established a quality-controlled innovation cycle that spans across applied research and development, clinical prototypes, and certified medical products, which were awarded the German Business Founder Award (Deutscher Gründerpreis) in 2006. A network of clinical partners and numerous research alliances fuels this innovation cycle. Industry partners market the software solutions developed by Fraunhofer MEVIS, whose contribution can range from the delivery of single components to the development of a complete application. This process has generated a number of medical products that are market leaders. Prime examples of this leadership include products for digital screening mammography evaluation, MR mammography, liver operation planning, and tumor progress control.

The MeVisLab Software Platform

The need for an integrated research and development platform for clinical software solutions was recognized at an early stage. The MeVisLab development platform by Fraunhofer MEVIS and MeVis Medical Solutions AG is a tool equally suited for highly flexible development of clinical software solutions and developing products and methods for fields such as image analysis, visualization, and biophysical modeling. The joint use of MeVisLab at Fraunhofer MEVIS and partners in research, medicine, and industry promotes synergy and accelerates development, ensuring engagement between the links of the chain of innovation. This supports the tight technological integration of clinics, research, and industry.

Field of Activity

Work at Fraunhofer MEVIS deals with significant diseases, such as tumors (especially in the breast, liver, prostate, and brain), cardiovascular diseases, neurological diseases, and lung disease. Clinical partnerships have led to numerous patient-specific image-based software solutions to support early detection, diagnosis, and therapy. Many of these software solutions have entered clinical use as research prototypes or medical products. Major focuses of research at Fraunhofer MEVIS include developing algorithms (for quantitative analysis of image data, tumor size measurement, or evaluation of the form and function of an organ, for instance), as well as comprehensive clinical software for applications such as preoperative planning and intraoperative support for therapeutic interventions. Further important fields of activity include visualization, human-computer interaction (HCI), multimodal support, workflow optimization, and novel imaging techniques.

Core Expertise

The future development of medical image computing must address how to bridge the gap between information extracted from medical images beyond the naked eye and the individual clinical reality for each patient. The emerging trends from this investigation are reflected in the core expertise of Fraunhofer MEVIS. The tight integration of classical medical image processing, imaging physics, and biophysical modeling and simulation is unique on the global stage and gives Fraunhofer MEVIS a clear advantage over competitors. This is further enhanced by close clinical partnerships taking place internationally.

Imaging physics: Fraunhofer MEVIS's expertise in physics of medical imaging facilitates analysis and optimization of the complete process, ranging from image acquisition to therapy support. Fraunhofer MEVIS boasts unique expertise and intensive partnerships with industrial partners in developing and optimizing magnetic resonance imaging (MRI) protocols, in particular for perfusion measurement without using contrast agents.

Algorithms and applications: Critical for the development of clinically applicable solutions is the exploration of problem-specific algorithms that meet the demands of daily clinical routines. Fraunhofer MEVIS has gained great international recognition and developed numerous commercial algorithms for segmentation and image registration. Such algorithms have been applied in various clinical software systems.

Modeling and simulation: Modeling and simulating biophysical processes form a central pillar of medical image computing. To support diagnosis and therapy planning, the information visible in acquired image data can be complemented with patient physiology models. Fraunhofer MEVIS has a globally unique, recognized expertise in modeling and simulating thermal ablation processes.

Human-computer interaction: A fundamental advantage that Fraunhofer MEVIS holds over competitors is the tight clinical integration and expertise in visualization, interaction, and user experience engineering (UXE). When developing demonstrators and prototypes, special attention is paid to embedding into the clinical workflow, so that any generated application smoothly integrates into the clinical workflow and can be recognized and appreciated by clinicians as helpful.

Computing and software technology: The MeVisLab rapid-prototyping platform is Fraunhofer MEVIS's central tool for developing algorithms, modules, application prototypes, and complete software assistants for clinical applications. The platform, which has been developed by Fraunhofer MEVIS and MeVis Medical Solutions AG for over 15 years, is the key to efficient software development at Fraunhofer MEVIS and is globally recognized and employed. MeVisLab contains modern image-processing and visualization algorithms and is ready for most modern technologies, such as thin clients and cloud computing.

Intraoperative and intrainterventional support: To implement computer-supported planning data for surgeries and interventions, Fraunhofer MEVIS researches efficient, innovative navigation and interaction processes for the operating room. Augmented reality methods, gesture-based control, and audiovisual communication are being investigated with the aim of minimizing the cognitive demands of the surgeons with the computer.

Image registration: A fundamental shortcoming of current multimodal imaging is the registration of image data on a shared-reference coordinate system. An equally challenging task is registering unimodal image data of an organ during different states of deformation. Fraunhofer MEVIS's Project Group in Lübeck is a global leader in the field of registration. The group has greatly shaped the field over many years and has established remarkable expertise.

Computer-aided detection and diagnosis: Computer-aided detection and diagnosis (CAD) provides software for early diagnosis and decision-making for diagnosis and therapy to support radiologists in interpreting multimodal, multidimensional, and dynamic data. At Fraunhofer MEVIS, intensive work on CAD systems for lung and breast tumor diagnosis has been undertaken in recent years. Object-based image analysis (OBIA), used in CAD, ranks among the primary techniques of Fraunhofer MEVIS's core expertise.

Digital pathology: With the advent of high quality whole-slide scanners plus respective storage capacity, digital pathology has become feasible. We believe that clinical histopathology will be transformed over the next 20 years to almost fully digital, similar to what happened to radiology over the last 20 years. Fraunhofer MEVIS has developed a unique software framework for the automated quantitative assessment of these huge datasets, plus highly accurate deformable image registration technology in order to virtually combine the strengths of complementary tissue stainings.

Project Group for Image Registration

Through the financial support of the State of Schleswig-Holstein and the European Union, the Fraunhofer MEVIS Project Group for Image Registration was established under the direction of mathematician Prof. Dr. Bernd Fischer at the University of Lübeck in April 2010. The internationally renowned project group addresses medical image registration, a key skill in medical image computing, in close cooperation with the Institute of Mathematics and Image Computing (MIC) at the University of Lübeck. The goal of registration is to harmonize medical imagery gathered from different processes (modalities), capture times, or patients, so that this information may be evaluated together.

In July 2013, Prof. Dr. Bernd Fischer passed away following a short, severe illness. The director of the MIC, Prof. Dr. Jan Modersitzki, was appointed director of the Fraunhofer MEVIS Project Group for Image Registration in October 2014.

University Connections

Since its founding as an institute associated with the University of Bremen, Fraunhofer MEVIS has maintained close ties with academia. In 2014, Fraunhofer MEVIS was connected to five universities in Germany, the Netherlands, and the United States through seven professors.

University of Bremen: The support of the Stiftung Bremer Wertpapierbörse helped create an endowed professorship in Department 1 (physics/electrotechnology) in imaging physics to focus on magnetic resonance tomography imaging and spectroscopy. In November 2009, this position was filled by Fraunhofer MEVIS physicist Prof. Dr. Matthias Günther. Since April 2011, Fraunhofer MEVIS has operated its own 3 Tesla MRI scanner at the Technology Park Bremen with Fraunhofer ITWM and the University of Bremen. In January 2014, Prof. Dr. med. Ron Kikinis, a renowned scientist and pioneer in the field of medical image computing, was appointed director of Fraunhofer MEVIS and successor to Prof. Peitgen. Associated with this is a professorship in Department 3 (mathematics/computer science) in medical image computing.

Jacobs University Bremen: Institute director and physicist Prof. Dr. Horst K. Hahn, who has led Fraunhofer MEVIS alongside Prof. Kikinis since 2014, has been adjunct professor of medical visualization since 2007 and full professor of medical imaging at the School of Engineering and Science since 2011. With the support of a private donation by honorary Bremen citizens Conrad and Lotti Naber, another endowed professorship was created in the School of Engineering and Science in mathematical modeling of medical processes. Since the beginning of 2009, this position has been held by Fraunhofer MEVIS mathematician Prof. Dr. Tobias Preußer.

University of Lübeck: Prof. Dr. Jan Modersitzki, a recognized expert in the field of image registration, is professor of mathematics and director of the university's Institute of Mathematics and Image Computing. He was appointed director of the Fraunhofer MEVIS Project Group for Image Registration and successor to Prof. Dr. Bernd Fischer in October 2014.

Radboud University Nijmegen: Since December 2012, Professors Dr. Nico Karssemeijer and Dr. Bram van Ginneken have been formally associated to Fraunhofer MEVIS. They are internationally renowned experts in the field of computer-aided detection and diagnosis (CAD) of breast and lung cancer.

Harvard University: In addition to his duties in Bremen, Prof. Kikinis has continued his professorship at the Harvard Medical School and directorship of the Surgical Planning Laboratory (SPL) in Boston on a reduced scale.

Development of the Institute (1995-2008)

The current Fraunhofer MEVIS institute was founded in August 1995 as MeVis – Center for Medical Diagnostic Systems and Visualization, a non-profit limited liability company (gGmbH). For much of this time, MeVis's sole partner was the Verein zur Förderung der wissenschaftlichen Forschung in der Freien Hansestadt Bremen e.V., a publicly funded organization that promotes scientific research in Bremen. To expand the institute, MeVis received yearly funding from the State of Bremen. Prof. Dr. Heinz-Otto Peitgen was appointed executive director, and an international scientific advisory board oversaw research. In 2006, the institute was renamed MeVis Research GmbH, Center for Medical Image Computing.

Since 1997, MeVis Research has produced several legally and financially independent spin-offs that were consolidated in 2007 into MeVis Medical Solutions AG, a publicly traded company that employs about 150 people. Aside from a few temporary declines in staff due to changes in personnel caused by the founding of a new company, the number of employees steadily increased between the founding in August 1995 and integration into the Fraunhofer-Gesellschaft in January 2009. During this time, the number of employees has increased from 10 to 51 full-time positions.

Affiliation with the Fraunhofer-Gesellschaft

On January 1, 2009, MeVis Research was incorporated into the Fraunhofer-Gesellschaft and renamed Fraunhofer MEVIS, Institute for Medical Image Computing (Institut für Bildgestützte Medizin). Prof. Dr. Heinz-Otto Peitgen was appointed Institute Director. The Advisory Board (Kuratorium) of Fraunhofer MEVIS convened on June 4, 2009, headed by Prof. Dr.-Ing. Erich R. Reinhardt, then the head of medical technology on the board of Siemens AG and current chairman of Medical Valley EMN e.V. in Erlangen. Since early 2009, Fraunhofer MEVIS has been a member of the Fraunhofer Group for Information and Communication Technology (Fraunhofer-Verbund IuK).

In October 2012, Prof. Peitgen departed Fraunhofer MEVIS and former Deputy Institute Director Prof. Hahn succeeded as Interim Institute Director. Prof. Kikinis and Prof. Hahn were appointed new directors of Fraunhofer MEVIS in January 2014 and May 2014, respectively. Since then, Fraunhofer MEVIS has operated under dual leadership. On June 5, 2014, Prof. Dr. Gabor Székely from ETH Zurich was elected new chairman of the Fraunhofer MEVIS Advisory Board and Walter Märzendorfer from Siemens Healthcare its vice chairman.

During the transitional phase of five years, the parent institute in Bremen and the project group in Lübeck have received funding from the States of Bremen and Schleswig-Holstein and have been co-financed by the European Regional Development Fund (ERDF). The institute in Bremen was evaluated positively by an international review board in May 2013 and has received regular basic funding of the Fraunhofer-Gesellschaft since January 2014. In May 2014, the project group in Lübeck was also evaluated positively and will receive Fraunhofer's regular basic funding by mid 2015.

Operating and Organizational Structures

Fraunhofer MEVIS's interdisciplinary focus incorporates medicine, science, and industry, reflecting the institute's operating principles and organizational structure. Researchers are not bound to strict, hierarchically organized work groups; they function in a flexible work environment that consists of strategic teams each targeting a medically defined domain or technological focus which together dynamically adapt to the demands of research and development.

This matrix of domains and focuses is the basis for the creation of project teams. According to the demands and affiliation of each project, Fraunhofer MEVIS researchers may belong to multiple domains, focuses, or project teams. Members of domains and focuses elect coaches who coordinate work and meetings. Domains and focuses are important vehicles for exchanging expertise, developing new project ideas, and ultimately shaping the strategic building blocks of the institute.

This form of collaboration promotes cooperation between researchers for current projects and facilitates putting synergies into practice. It fosters the exchange of application-specific expertise and allows researchers to introduce their own multidisciplinary expertise for the benefit of the institute as a whole. The networked organizational structure of Fraunhofer MEVIS is illustrated in the adjacent figure.

The Heads of the Institute are:

- Prof. Dr.-Ing. Horst K. Hahn (Institute Director)
- Prof. Dr. Ron Kikinis (Institute Director)
- Dipl.-Betrw. Thomas Forstmann (Head of Administration)

The Heads of the Institute are assisted in operational tasks by the extended institutional management. The small committee (Kleines Gremium) includes (in addition to the Heads of the Institutes):

- Prof. Dr. Jan Modersitzki, Dr. Nils Papenberg, Dr. Stefan Heldmann, Dr. Janine Olesch (Project Group for Image Registration)
- Prof. Dr. Matthias Günther (MR Imaging)
- Prof. Dr. Tobias Preußer (Modeling & Simulation)
- Dr. Stefan Kraß (Clinical Partners, Industry)
- Dr. Markus Lang (Industry, Contracts, Personnel)
- Dr. Guido Prause (Publicly Funded Research, PR)

Additionally, the large committee (Großes Gremium) includes an employee representative (see below) as well as:

- Bianka Hofmann (Corporate Communication)
- Dr. Jan Klein (Scientific and Technical Council)
- Dr. Jan-Martin Kuhnigk (Software, IT)
- Dr. Andrea Schenk (Equal Opportunity)
- Dr. Stephan Zidowitz (Certification, QM)

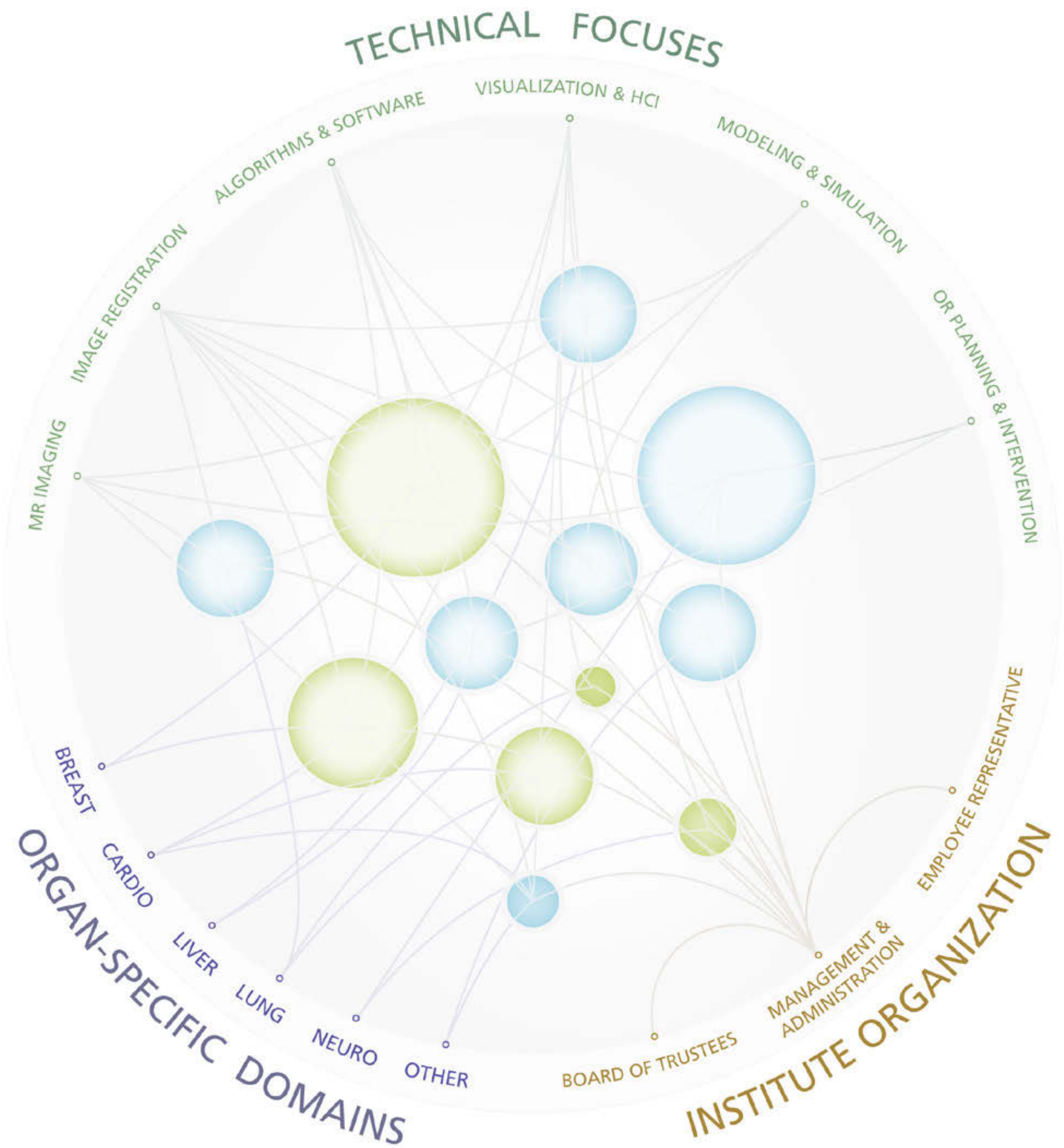
Office management tasks (IT, personnel, accounting, etc.) are undertaken by the administration, which also make up the secretary's office:

- Roswitha Hornung, Karin Entelmann (Bremen)
- Anja Pawlowski, Kerstin Sietas (Lübeck)

Each year, four employee representatives are elected from the staff, excluding management. These employee representatives function as liaisons and mediators when needed.

The Advisory Board of Fraunhofer MEVIS is composed of seventeen members with backgrounds in research funding, business, science, and medicine and advises the management in issues of scientific focus and industrial application.

In 2014 Fraunhofer MEVIS introduced a new leadership model for scientific colleagues ('mentees'). All experienced members of MEVIS are now entitled to act as 'mentor' or 'co-mentor', and can take over direct leadership responsibilities.


TECHNICAL FOCUSES
VISUALIZATION & HCI
ALGORITHMS & SOFTWARE
MODELING & SIMULATION
IMAGE REGISTRATION
OR PLANNING & INTERVENTION
MR IMAGING
EMPLOYEE REPRESENTATIVE
BREAST
CARDIO
LIVER
LUNG
NEURO
OTHER
BOARD OF TRUSTEES
MANAGEMENT & ADMINISTRATION
ORGAN-SPECIFIC DOMAINS
INSTITUTE ORGANIZATION

Advisory Board

The Fraunhofer MEVIS Advisory Board met in Bremen on June 5, 2014 for the sixth time. Dr. Alexander Kurz, Executive Board Member for Human Resources, Legal Affairs and IP Management of the Fraunhofer headquarters in Munich, gave a talk concerning the current state of affairs of the Fraunhofer-Gesellschaft. Institute directors Prof. Dr. Horst Hahn and Prof. Dr. Ron Kikinis reported on developments in the focus and structure of the institute and outlined medium-term plans and prospects.

The 2014 Advisory Board meeting was related to a restructuring plan. Prof. Dr. Gabor Székely from ETH Zurich was elected new Chairman and Mr. Walter Märzendorfer from Siemens AG new Vice Chairman of the Advisory Board. The former Chairman Prof. Dr.-Ing. Erich R. Reinhardt resigned his membership along with Prof. Dr. med. Hans-Peter Bruch, Dr. Rainer Jansen, Prof. Dr. Ron Kikinis, Prof. Dr. med. Klaus Jochen Klose, and Prof. Dr. med. Maximilian Reiser.

Newly appointed members of the Advisory Board included Prof. Dr. med. Jörg F. Debatin (GE Healthcare), Prof. Dr. med. Mathias Prokop (Radboud University Medical Center Nijmegen), Prof. Dr. Kerstin Schill (University of Bremen), and Dr. Ralf Schumacher (Roche Diagnostics). During the reporting period, the Fraunhofer MEVIS Advisory Board consisted of seventeen individuals.

Chairman

Prof. Dr. Gábor Székely
Image Science Division
ETH Zurich

Vice Chairman

Walter Märzendorfer
Siemens AG, Forchheim

Research Funding

Dr. Steffen Lüsse
Ministry of Science, Economy, and Traffic
State of Schleswig-Holstein, Kiel

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Department of Scientific Planning and Research Promotion

Industry

Prof. Dr. med. Jörg F. Debatin
GE Healthcare, Chalfont St Giles, UK

Dr. Bernd Gewiese
Bruker BioSpin GmbH, Rheinstetten

Marcus Kirchhoff
MeVis Medical Solutions AG, Bremen

Prof. Dr. Hans Maier
BGM Associates, Berlin

Dr. Ralf Schumacher
Roche Diagnostics GmbH, Penzberg

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Radboud University Medical Center
Nijmegen, NL

Prof. Dr. med. Ulrich Sure
Department of Neurosurgery
Essen University Hospital

Science

Prof. Dr. Jürgen Hennig
Division of Diagnostic Radiation,
University Medical Center Freiburg

Prof. Dr. Willi A. Kalender, Ph.D.
Institute of Medical Physics,
University of Erlangen-Nuremberg

Prof. Dr. med. Dipl.-Phys. Heinz-Peter Schlemmer
Department of Radiology
German Cancer Research Center, Heidelberg

University of Bremen / Jacobs University

Prof. Dr. Jens Falta
Institute of Solid State Physics,
University of Bremen

Prof. Dr. Kerstin Schill
Faculty of Mathematics / Computer Science
University of Bremen

Dr. Alexander Ziegler-Jöns
Science & Technology Transfer
Jacobs University Bremen

Image Caption: Attendees of the sixth assembly of the Fraunhofer MEVIS Advisory Board in Bremen on June 5, 2014.

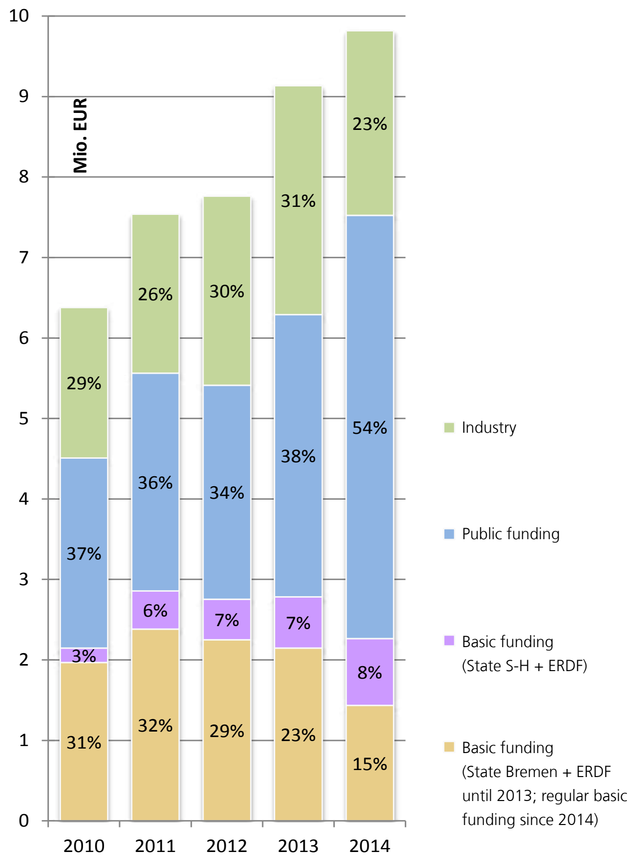
The Institute in Figures

Budget and Earning Trends

In 2014, after completing its transitional phase (2009-2013), Fraunhofer MEVIS in Bremen received Fraunhofer's regular basic financing for the first time provided by the Federal Republic and Federal States of Germany, the so-called 90:10 financing. In 2014, the Project Group in Lübeck was still in its transitional phase and will switch to 90:10 financing during 2015.

2014 was marked by further growth. Compared to the previous fiscal year (PFY), earnings of the entire institute (Bremen and Lübeck) rose by +8% (PFY +18%) to 9 818 thousand euro (T€). Industrial and other earnings decreased by -19% compared to the previous fiscal year (+21%). In comparison to the previous fiscal year, basic financing of the entire institute (2 264 T€) experienced a decline of -19% (PFY +1%). Returns from publicly funded projects rose strongly by +50% from the previous fiscal year (PFY +32%).

The operating budget (OB) in Bremen grew by +15% (PFY +6%) in 2014, whereas the investment budget (IB) decreased by -50% (PFY +127%) after a significant increase in the previous fiscal year due to costs of the MRI scanner. In sum, the overall budget of 8 400 T€ in Bremen has experienced a growth of +9% (PFY +12%). In Lübeck, the overall budget of 1 418 T€ decreased marginally by -1% (PFY +64%).



Total earnings in Bremen and Lübeck for the period 2010 to 2014.

Overall Budget in T€:

	2010	2011	2012	2013	2014
OB:	6 162	6 981	7 401	8 357	9 404
IB:	218	559	360	776	414
Total	**6 380**	**7 540**	**7 761**	**9 133**	**9 818**

Development of Budget Bremen in T€:

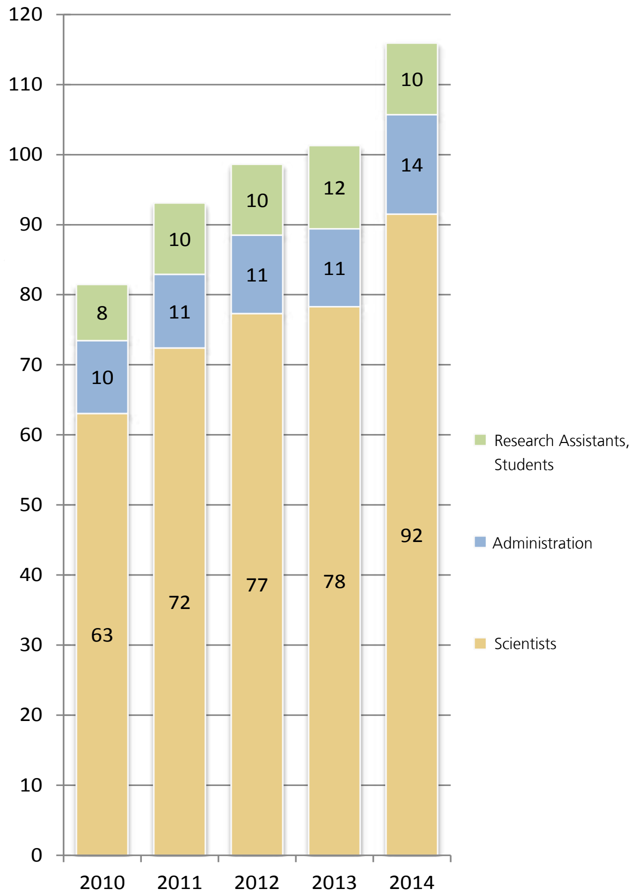
	2010	2011	2012	2013	2014
OB:	6 002	6 535	6 574	6 991	8 047
IB:	195	468	311	706	353
Total	**6 197**	**7 003**	**6 885**	**7 697**	**8 400**

Development of Budget Lübeck in T€:

	2010	2011	2012	2013	2014
OB:	160	446	828	1 366	1 357
IB:	23	91	49	70	61
Total	**183**	**537**	**877**	**1 436**	**1 418**

Human Resources

2014 experienced a significant increase in personnel. The number of researchers rose by approximately 14 positions, or +17% (PFY + 1%). The number of staff in the administration increased by +28% to approximately 14 full-time positions after stability in the three previous fiscal years. The number of research assistants experienced a decrease of -14% (PFY+18%). In total, Fraunhofer MEVIS in Bremen and Lübeck generated approximately 15 new full-time positions in 2014.



Human resources development (full-time equivalent positions at year's end) in Bremen and Lübeck in the period 2010 to 2014.

The Fraunhofer-Gesellschaft

Research of practical utility lies at the heart of all activities pursued by the Fraunhofer-Gesellschaft. Founded in 1949, the research organization undertakes applied research that drives economic development and serves the wider benefit of society. Its services are solicited by customers and contractual partners in industry, the service sector and public administration.

At present, the Fraunhofer-Gesellschaft maintains 66 institutes and research units. The majority of the nearly 24,000 staff are qualified scientists and engineers, who work with an annual research budget of more than 2 billion euros. Of this sum, around 1.7 billion euros is generated through contract research. More than 70 percent of the Fraunhofer-Gesellschaft's contract research revenue is derived from contracts with industry and from publicly financed research projects. Almost 30 percent is contributed by the German federal and Länder governments in the form of base funding, enabling the institutes to work ahead on solutions to problems that will not become acutely relevant to industry and society until five or ten years from now.

International collaborations with excellent research partners and innovative companies around the world ensure direct access to regions of the greatest importance to present and future scientific progress and economic development.

With its clearly defined mission of application-oriented research and its focus on key technologies of relevance to the future, the Fraunhofer-Gesellschaft plays a prominent role in the German and European innovation process. Applied research has a knock-on effect that extends beyond the direct benefits perceived by the customer: Through their research and development work, the Fraunhofer Institutes help to reinforce the competitive strength of the economy in their local region, and throughout Germany and Europe. They do so by promoting innovation, strengthening the technological base, improving the acceptance of new technologies, and helping to train the urgently needed future generation of scientists and engineers.

As an employer, the Fraunhofer-Gesellschaft offers its staff the opportunity to develop the professional and personal skills that will allow them to take up positions of responsibility within their institute, at universities, in industry and in society. Students who choose to work on projects at the Fraunhofer Institutes have excellent prospects of starting and developing a career in industry by virtue of the practical training and experience they have acquired.

The Fraunhofer-Gesellschaft is a recognized non-profit organization that takes its name from Joseph von Fraunhofer (1787–1826), the illustrious Munich researcher, inventor, and entrepreneur.

Chronicle 2014

January 1
Integration of Fraunhofer MEVIS in Bremen into the basic financing of the Fraunhofer-Gesellschaft.

Professor Ron Kikinis is appointed Institute Director of Fraunhofer MEVIS and a professorship in medical image computing at Department 3 (mathematics / computer science) at the University Bremen.

Start of the EU-funded TRANS-FUSIMO project (Clinical Translation of Patient-Specific Planning and Conducting of FUS Treatment in Moving Organs) coordinated by Fraunhofer MEVIS.

February 19
Fraunhofer MEVIS presents current work on neurosurgical planning at the Berlin kick-off for Science Year 2014, 'The Digital Society'. Visitors included German Federal Minister of Research Prof. Johanna Wanka and the President of the Fraunhofer-Gesellschaft, Prof. Reimund Neugebauer.

April 2
Evaluation of the Fraunhofer MEVIS Project Group for Registration in Lübeck. The evaluation commission unanimously recommends integration into Fraunhofer's basic financing.

May 1
Professor Horst Hahn is appointed Institute Director of Fraunhofer MEVIS. He simultaneously holds a full professorship in medical imaging at Jacobs University Bremen. Prof. Hahn and Prof. Kikinis direct Fraunhofer MEVIS in dual leadership.

June 1
Start of MR image acquisition for the National Cohort (NAKO), a long-term study of 200,000 subjects, the broadest of its kind in Germany to date.

June 4
Open House at Fraunhofer MEVIS on the occasion of the new dual leadership.

June 5
Sixth meeting of the Fraunhofer MEVIS Advisory Board (Kuratorium).

July 2–3
Fraunhofer MEVIS is present at the Medizin Innovativ - MedTech Pharma 2014 conference with a booth in the Nuremberg Convention Center.

October 10
Memorial symposium at the University of Lübeck in honor of Prof. Dr. Bernd Fischer (1957–2013), the founder and former director of the Fraunhofer MEVIS Project Group for Image Registration.

November 30 – December 5
Fraunhofer MEVIS showcase for research and commercial partners at the 100th Scientific Assembly and Annual Meeting of the Radiological Society of North America (RSNA) in Chicago, USA.

Awards 2014

Germany's Digital Brains

As part of the Science Year 2014 – The Digital Society, the German Informatics Society (GI) selected 39 men and women who represent a new generation of digital thinkers and doers. These 'digital brains' from business, science, and culture show the demands of the future and the digital excellence that Germany has in store. The Society selected Prof. Dr. Horst Hahn as one of these creative brains.

Fraunhofer TALENTA Grants

Three employees received a grant of the Fraunhofer TALENTA program for female scientists. Sabrina Haase started with a TALENTA speed-up grant in January 2014, and Andrea Schenk and Anja Hennemuth have been awarded with two of the first twenty TALENTA excellence grants in 2014. The TALENTA program supports outstanding Fraunhofer scientists in MINT topics with personal and educational funding for their career.

ISMRM Summa Cum Laude Award

Federico von Samson-Himmelstjerna received the Summa Cum Laude Merit Award 2014 at the Joint Annual Meeting of the ISMRM-ESMRMB in Milan.

MedVis Award

Dr. Frank Heckel was awarded 2nd place at the Karl-Heinz Höhne MedVis Award 2014 for his work on interactive editing of automatically generated tumor segmentations in CT data for chemotherapy monitoring. The award was bestowed at the Eurographics Workshop on Visual Computing for Biology and Medicine (EG VCBM) in Vienna.

MICCAI Challenge on Liver Ultrasound Tracking

Fraunhofer MEVIS successfully contributed three unique algorithms to the Challenge on Liver Ultrasound Tracking (CLUST) at the MICCAI 2014 conference in Boston.

Koenderink Award

Dr. Nils Papenberg received one of the most prestigious awards in the field of machine vision at the European Conference on Computer Vision (ECCV) in Zurich. The prize is awarded every two years and honors publications issued in the last decade that have proven to be of outstanding value for research and industry.

CURAC Mobility Stipend

David Black was awarded a mobility stipend by the German Society for Computer- and Robot-Assisted Surgery (CURAC).

German High Tech Champions Award

Fabian Zöhrer received the distinguished German High Tech Champions Award in Chicago at RSNA, the world's largest radiology conference. The award was bestowed for a software method that can improve early detection and diagnosis of breast cancer. Zöhrer developed the software with fellow computer scientist Dr. Joachim Georgii and Prof. Dr. Horst Hahn.

Academic Publications 2014

Journal Articles

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Impressum

Authors

Stefan Braunewell
Cristoffer Cordes
Thomas Forstmann
Matthias Günther
Horst Hahn
Markus Harz
Anja Hennemuth
Jochen Hirsch
Bianka Hofmann
Markus Hüllebrand
Ron Kikinis
Till Kipshagen
Stefan Kraß
Markus Lang
Jan Hendrik Moltz
Guido Prause
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Illustrations

Christoph Brachmann
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Bianka Hofmann
Olaf Klinghammer
Guido Prause

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Fraunhofer MEVIS
Universitaetsallee 29
28359 Bremen
Germany
+49 421 218 59112
info@mevis.fraunhofer.de
www.mevis.fraunhofer.de