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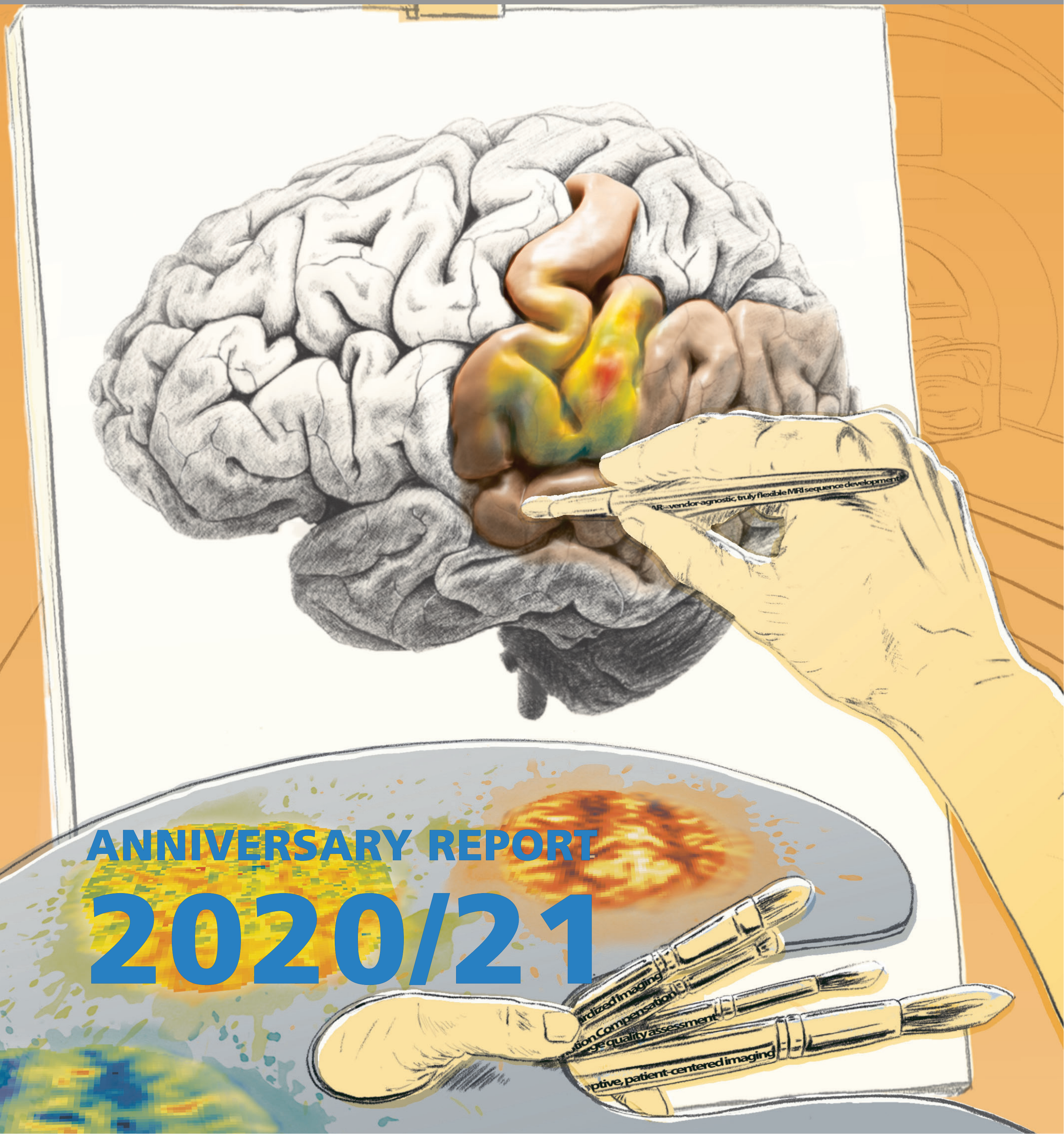

ANNIVERSARY REPORT 2020/21

FRAUNHOFER MEVIS

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Cover image caption: Fraunhofer MEVIS develops flexible solutions to generate robust physiological imaging parameters that support clinical diagnosis and decision making.

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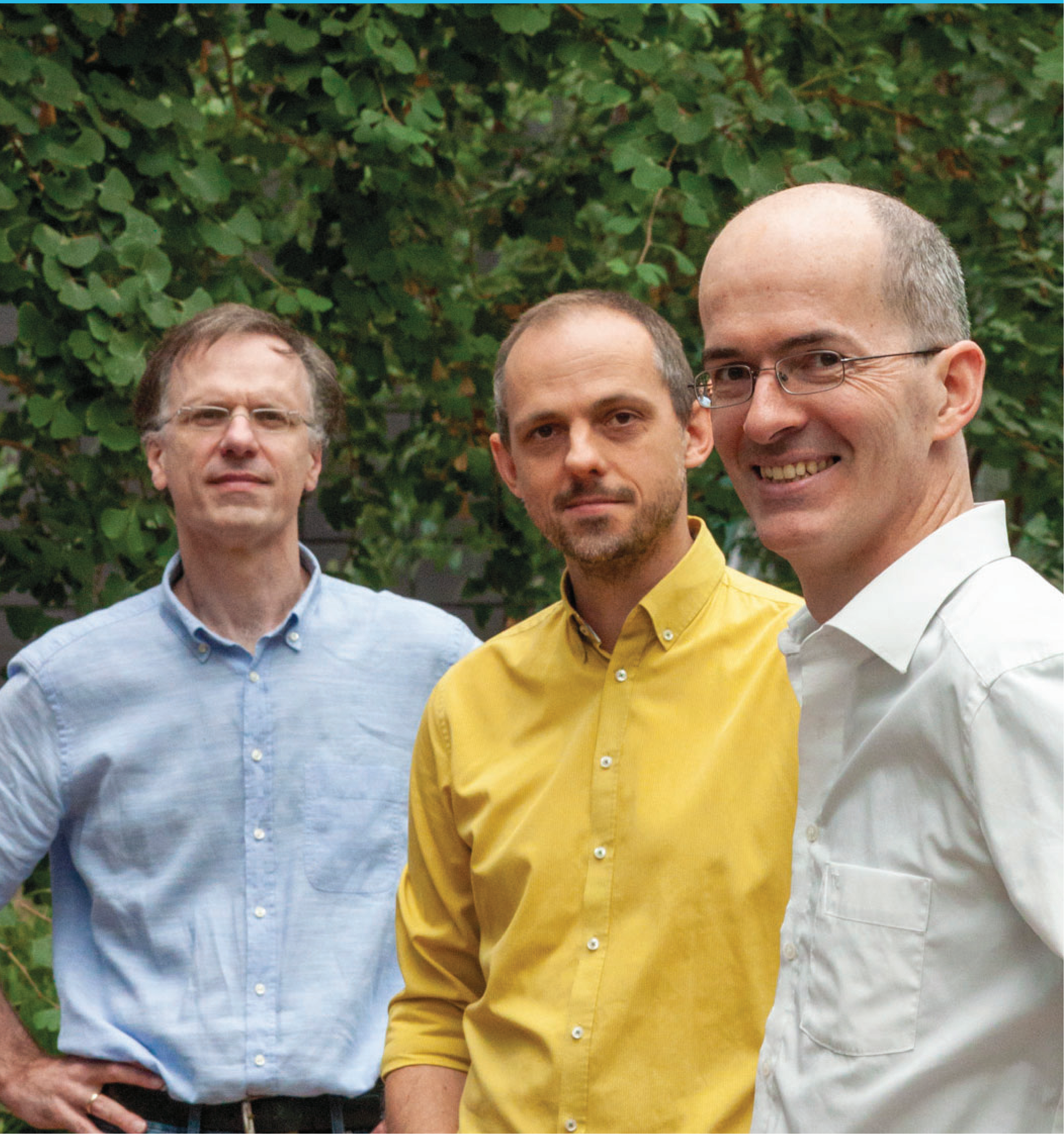

THE DIGITAL TRANSFORMATION IN HOSPITALS AND MEDICAL PRACTICES

The Fraunhofer Institute for Digital Medicine MEVIS develops innovative software solutions for more precise diagnoses and more effective therapies. The possibilities are as varied as the challenges: Artificial intelligence and self-learning algorithms will bring enormous advancements to the clinical routine in hospitals and medical practices. Simultaneously, these solutions call for new structures, for example, in data privacy and interdisciplinary cooperation.

»To develop new methods, we think in terms of partnerships, networks, and platforms. We cannot master these challenges alone, which is why we collaborate with a number of outstanding companies and university hospitals. This allows us to build a bridge between what is now known as data science and biomedical knowledge. We do this openly and interactively, in order to master the digital transformation of medicine together with our partners.«
Horst Hahn, Fraunhofer MEVIS

»Most of today's medical data is gathered in digital form, including MR and CT images, laboratory values, or genetic data,« says Horst Hahn, institute director of Fraunhofer MEVIS. »However, these data have not yet been sufficiently connected with each another, meaning that not all of the information contained within can be used.« Fraunhofer MEVIS is working on software-based systems that can help accomplish this, including software platforms that refine MRI and ultrasound diagnoses, optimize minimally invasive therapies, or provide targeted assistance to determine the best medication. The goal is precision medicine personalized to each individual patient.

The journey towards this goal is filled with challenges. The glut of available medical data and the growing number of therapy options offer new opportunities, but also contribute to the growing complexity of everyday medical life that must be managed. »Computers can help manage this complexity,« Hahn emphasizes. »Using methods from artificial intelligence (AI), for example, we want to achieve medical care that can act with more precision, integration, and efficiency.«

Today's oncologists, for instance, are hardly able to memorize all available knowledge regarding the detailed differences between different tumor types. A digital support system will accompany them in the future: Based on self-learning pattern recognition, such a system could, for example, detect similar past cases according to unusual disease patterns. Valuable information could then be extracted: What treatments were used at the time, and what were the results?

Detecting hidden patterns

Medical AI systems should be able to analyze numerous clinical parameters simultaneously, including blood values, image data, and ECG measurement data. The algorithms are likely to detect patterns that, because of their highly complex nature, are inevitably invisible to the naked eye. These patterns may improve, for example, the early detection of certain tumors and thereby increase the chances of recovery.

High-quality data is the main prerequisite for data-driven methods to function reliably. »Garbage in, garbage out,« is how deputy institute director Matthias Günther sums it up. »Even the best algorithms can't turn low-quality data into pure gold.« It is also important to monitor image acquisition automatically, for example, during an MRI scan to detect and correct imaging errors as quickly as possible. Fraunhofer MEVIS has already developed algorithms that promise exactly this.

A further challenge is that different clinics and equipment manufacturers often collect data according to varying standards. »This causes problems, for example, when comparing image data within a multicenter study,« explains Günther. »This is why we are advancing methods to standardize such processes and ensure image quality at the time of image acquisition.« Data privacy must be guaranteed by methods such as decentralized learning: Patient data should not leave the clinics; the algorithm should come to the data and be trained on it.

Our Institute Leadership: Institute Director Prof. Dr.-Ing. Horst Hahn and Deputies Prof. Dr. Tobias Preusser and Prof. Dr. Matthias Günther (from right to left).

The digital patient model

Carefully handling data is fundamentally essential for the digital patient model, a concept that likely will play a significant role in the future. »Ideally, everything we know about a particular patient flows into this mathematical model,« says Tobias Preusser, deputy institute director of Fraunhofer MEVIS, »This might include different image data, various lab values, and DNA genotypes and phenotypes.« This computer model then acts as a sort of digital twin: To identify the best treatment, clinicians can play through various therapy scenarios virtually.

»For example, this could help evaluate whether a patient is a candidate for chemotherapy,« said Preusser, »or even a combination therapy. The evaluation of therapy options on the basis of a virtual patient model has the potential to spare the patient from unnecessary risks and side effects.« It is also plausible to use digital patient models in clinical studies, for instance, when developing devices or drugs.

In some cases, this might eliminate the need to perform an experiment on animals. »A digital model of the entire patient is still a dream for the future,« says Preusser. »However, we can already model individual organs such as the liver, parts of the heart, and some joints for planning operations.«

»With all these new tools it is important that it is not the machine that makes the decision,« emphasizes Horst Hahn. »Making a decision must always be reserved for medical professionals and their patients.« The statements made by AI must, therefore, always be as transparent and comprehensible as possible, and sources of error and uncertainties in the statements must be clear. »One thing seems evident,« Hahn believes. »The use of AI systems will change the structures of medicine.« The various disciplines are likely to come closer together. To exploit this new technology, some hospitals are already considering establishing departments for the new discipline of artificial intelligence.

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AN OUTLOOK INTO THE FUTURE

ON THE TRAIL OF IMPORTANT LIFE PROCESSES

Ultrasound and MRI are among the most important imaging procedures in medicine. The Fraunhofer Institute for Digital Medicine is developing software solutions that optimize image acquisition and simplify tracking physiological functions.

An MRI scanner can create non-invasive 3D images from inside the body. Generally, the device acquires still images. However, this technology can do much more: it can make vital processes visible, such as the flow of blood into the finest of brain vessels. »Physiological imaging can sometimes help detect diseases earlier than a conventional MRI scan,« says MEVIS researcher Daniel Hoinkiss. »For example, a stroke initially manifests itself as a disruption in the brain's blood supply and only later as a structural change in a conventional MRI image.«

Physiological imaging could also uncover both neurological diseases such as Alzheimer's and Parkinson's as well as tumors at an early stage. The earlier the diagnosis, the better the likelihood that a treatment succeeds. Physiological MR imaging has, however, only been employed in the clinical routines of a few hospitals due to the difficulty of operation and the susceptibility to errors. Physiological imaging is much more complex than a conventional MRI scan. Prior to each examination, specialized personnel are required to set various parameters and adapt them to each individual patient.

Fraunhofer MEVIS wants to overcome this hurdle. The goal is to make physiological imaging as easy to acquire as standard MR imaging to increase accessibility for routine diagnostics. »The personnel only need to press a button, and the software automatically adapts the MR sequence to the patient,« explains Hoinkiss' colleague Nora-Josefin Breutigam. Describing their vision, she says, »Afterwards, all that remains is to wait until the image is acquired.«

»One problem in MR imaging is the lack of standardization. Until now, each manufacturer has employed its own control software for its devices, making it cumbersome to transfer new measurement technology from one manufacturer to another. We are working on a platform called gammaSTAR, with which control software can be developed independently of manufacturers and transferred to different systems. This should also ease conducting clinical studies at several centers using different devices while still being able to make robust comparisons between the results. Because the platform supports dynamically adjusting the MRI hardware during measurement, it is especially beneficial for pursuing our goals in physiological imaging while facilitating use on different devices.«

Daniel Hoinkiss, Fraunhofer MEVIS

An algorithm that compensates for movement

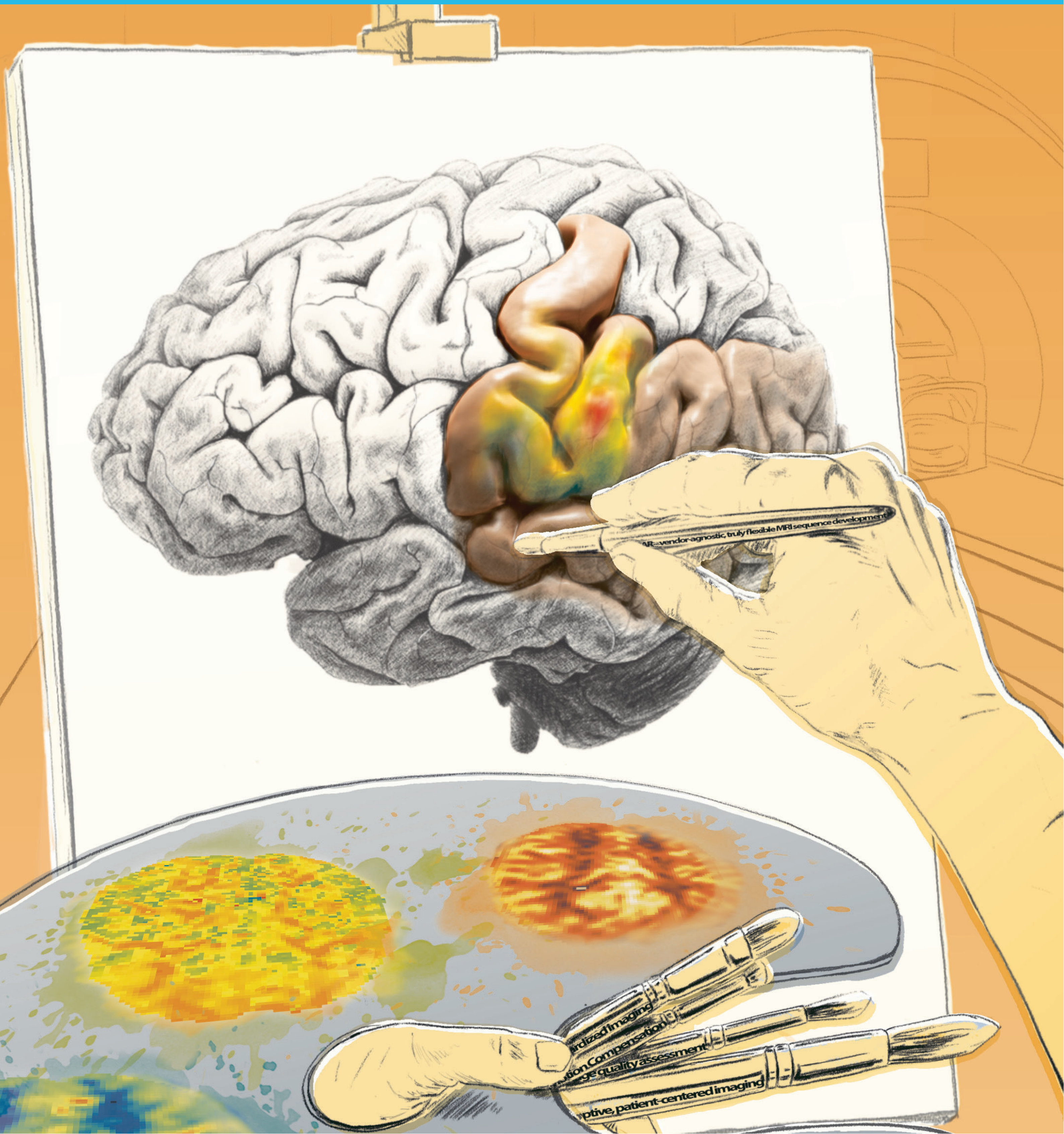
A combination of several innovative methods should facilitate this. One method should solve the following problem: Image acquisition inside the scanner can take up to several minutes. Most patients inevitably move during this time, which unsurprisingly interferes with image acquisition. »We want to counteract this with an adaptive technique that continuously compensates for this movement,« explains Hoinkiss. »If the software recognizes, for example, that the patient slipped one millimeter to the side, it corrects the MRI scanner so that it acquires the same part of the body as before.«

The experts pay particular attention to MRI blood flow measurement, which does not rely on using a contrast agent. In this method, blood in the neck is marked magnetically. After this blood reaches the brain, an MRI scan is initiated. Comparing this with a reference measurement allows visualization of blood flow into the brain in the time period between marking and recording. The timing of the MR images plays a major role in this technique; it is important to seize the exact moment when the marked blood is distributed in the brain. »This happens differently for each person,« explains Breutigam. »This is why we are developing software that ensures that the MRI scanner doesn't select the wrong moment.«

The researchers are also developing an algorithm that automatically suppresses irrelevant signals. Observing physiological processes requires identifying extremely small changes in the signal. Therefore, it is essential to suppress types of tissue that aren't involved. The new algorithm is designed to do exactly this, thereby emphasizing the relevant signals even more clearly.

Fast ultrasound

Physiological imaging is also gaining increasingly significance



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in another procedure: ultrasound. A physician performing an ultrasound needs special training and a lot of experience to operate the ultrasound equipment optimally. Fraunhofer MEVIS is planning systems to ease operation of this technology, particularly for young specialists. »Software will analyze the ultrasound images in real time and determine, for example, whether the image contains errors,« explains MEVIS physicist Sven Rothlübbers. »This should then be shown to the operator.«

The researchers at Fraunhofer are also refining ultrasound technology itself. They are developing a method to measure the temperature of tissue during image acquisition. This is valuable for cancer treatments in which the tumor is destroyed by applying heat. A further field of research is 3D ultrasound image acquisition. Vast amounts of data have to be handled here, resulting in fairly lengthy recording times. »We are working on self-learning procedures that generate high-quality images based on only a few input data,« says Rothlübbers. »This could significantly accelerate the image acquisition process.«

Algorithms like these could also be beneficial when using ultrasound with contrast agents. During image acquisition, a contrast agent is administered, which travels through blood vessels and appears on the image with high contrast. »The speed at which it becomes light and dark again says a lot about what is happening,« explains Sven Rothlübbers. »This could, for example, make tumors and cysts in organs such as the liver or kidney more visible and distinguishable.«

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Fraunhofer MEVIS develops flexible solutions to generate robust physiological imaging parameters that support clinical diagnosis and decision making.

IMPROVING INDICATORS FOR TUMOR DIAGNOSIS

Biomarkers are often indispensable for accurate diagnoses. The Fraunhofer Institute for Digital Medicine MEVIS is working on adaptive algorithms that make the search for new biomarkers much easier. This can provide physicians with valuable support in choosing the best possible therapy.

Biomarkers make up an important building block of diagnostics. One common example is the cholesterol level in blood, which can suggest an increased risk of cardiovascular disease. Biomarkers also play a significant role in pathology, the microscopic examination for example of suspected tumor tissue samples. If particular cell types with certain combinations of properties are present, this can be considered a meaningful indicator that ideally reveals which subtype of tumor is present. This lets physicians select a targeted treatment that is effective for each individual patient.

In clinical practice, however, this accurate procedure does not always work. A study from 2018, for example, revealed that 44 percent of cancer patients in the United States should be considered for immunotherapy, a special type of tumor treatment. In reality, however, this treatment was only effective in 12 percent of patients, meaning that many were treated in vain. »To provide more targeted therapy in the future, we need to be able to subdivide tumor types much more precisely than at the present,« says MEVIS researcher Johannes Lotz. »We need to discover the biomarkers that deliver this differentiation.«

Detecting such biomarkers demands extensive clinical studies. The adaptive AI systems of the future will assist in this search. »The computer analyzes digitalized tissue sections and looks through them for patterns,« says Lotz's colleague Henning Höfener when describing the strategy. »This enables it to find new biomarkers.« The software must be trained with as many sets of high-quality data as possible, otherwise the search for patterns will be unsuccessful. This creates a problem: The more precise the differentiation between different tumor subtypes, the fewer patients exhibit a certain subtype and the fewer data sets are available for training and analysis.

Our vision is to develop data-driven methods to capture the fundamental cellular features considered in modern histomorphological diagnostics. In this way, we aim to accelerate the development of better algorithms for clinical and research purposes.

The best of two worlds

Another difficulty: »The appearance of digital tissue sections can vary significantly from laboratory to laboratory,« explains Lotz. »This makes it difficult for the computer to detect existing patterns in the images reliably.« These problems can hardly be overcome using previous AI methods, in which the algorithms sift through vast quantities of pixels. That's why the MEVIS team is attempting a new strategy and is taking a look at some of the tried-and-true ways in which humans work. »Experienced pathologists have seen thousands and thousands of tissue images and derive the essential laws from them,« explains Höfener. »Unlike AI, a handful of images is typically sufficient for an accurate diagnosis.«

»Chemotherapy regularly has severe side effects. With the new biomarkers discovered by AI, it could be possible to predict how a tumor disease would progress without additional chemotherapy. This could help assess whether such a therapy is suitable for each individual case.«
Henning Höfener, Fraunhofer MEVIS

The MEVIS team wants to bring the best of both worlds together. Their plan is to train the artificial intelligence as if it were a pathologist, using many tissue images unrelated to a specific inquiry. Thanks to this »basic training,« the AI acquires knowledge about general characteristics and relations, so-called tissue descriptors. With their help, the machine can describe and classify the images. »If the algorithm then encounters a specific problem, it can use tissue descriptors to find correlations. Even with relatively few data, this could predict, for example, the success of a certain therapy,« says Höfener.

The project is still in its beginning phase, but Fraunhofer MEVIS is well prepared to master it successfully. »We have a lot of experience training adaptive algorithms and programming computer-aided diagnostic tools,« emphasizes Henning Höfener. »In cooperation with our clinical project partners, we can select the data we need for initial algorithm training.«

AI accelerates automatic detection

These biomarker algorithms will benefit the research departments of pharmaceutical companies, but also university workgroups. The approach promises additional applications, however. For example, tissue descriptors could be used for segmentation, the automatic recognition and measurement of an image's tissue structures. »The descriptors also reduce the amount of training data required in this case,« says Höfener. »This could significantly accelerate adaptation of the segmentation algorithm.«

Content-based image retrieval could also benefit from this method. »Many are familiar with a similar feature on Google, where an image can be uploaded and similar ones are displayed,« explains Johannes Lotz. »For medical images, however, this is not yet as reliable.« The MEVIS experts hope that the descriptor concept could lead to substantial advancements. They envision a system that allows physicians who encounter unusual findings to search databases for similar images to check their diagnoses and discover which therapies have or have not worked in the past.

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GUIDEPOST FOR THE BEST CHOICE OF TREATMENT

A diagnosis has been made. Now it is up to clinicians, together with their patients, to find a suitable treatment. However, as more and more treatment choices are becoming available, the most suitable one isn't always the most obvious choice. The Fraunhofer Institute for Digital Medicine MEVIS is developing AI-based support systems to facilitate decision-making and pave the path towards finding the optimal treatment.

Operate or wait? Chemotherapy or not? Stay on the current medication or change to another? These decisions constitute the everyday routine in clinics and medical practices. These decisions are, however, not always easy to make: »A treatment decision usually depends on a variety of factors,« says Fraunhofer MEVIS researcher Andrea Schenk. »What image data is available? Does the patient have a pre-existing condition? What are our treatment options? What do the corresponding guidelines recommend?« Making these decisions is challenging because medical progress is constantly increasing both the amount of data available and the number of treatment choices.

This is where CDS (clinical decision support) systems can help. Ideally, these decision support systems characterize the patient as an individual digital model incorporating all available data and current guidelines. The software can simulate and compare various treatment approaches. This gives physicians important clues as to which treatment is most effective or gentle for the patient. »Until now, only basic CDS systems have been available that are limited to specific subdomains,« explains Schenk's colleague Markus Wenzel. »Now, we are working on a broader solution that will incorporate and unify data from an wide range of sources.«

Filling gaps in the guidelines

The core notion is that novel systems should act individually for each patient instead of according to a relatively rigid scheme. A guideline might, for instance, recommend that a patient with breast cancer undergo a mastectomy. In contrast, a CDS system fed with extensive image and laboratory data of the patient and the results of recent clinical studies might reach a different conclusion and recommend breast-preserving radiotherapy for better results.

»Guidelines can never cover all cases and, thus, inevitably have gaps,« explains Wenzel. »We aim to fill these gaps with the help of intelligent modeling.« An important element of this is segmentation, for which software can, for example, automatically detect the size and location of a tumor on an MR image. Segmentation forms the foundation for creating an individual patient model.

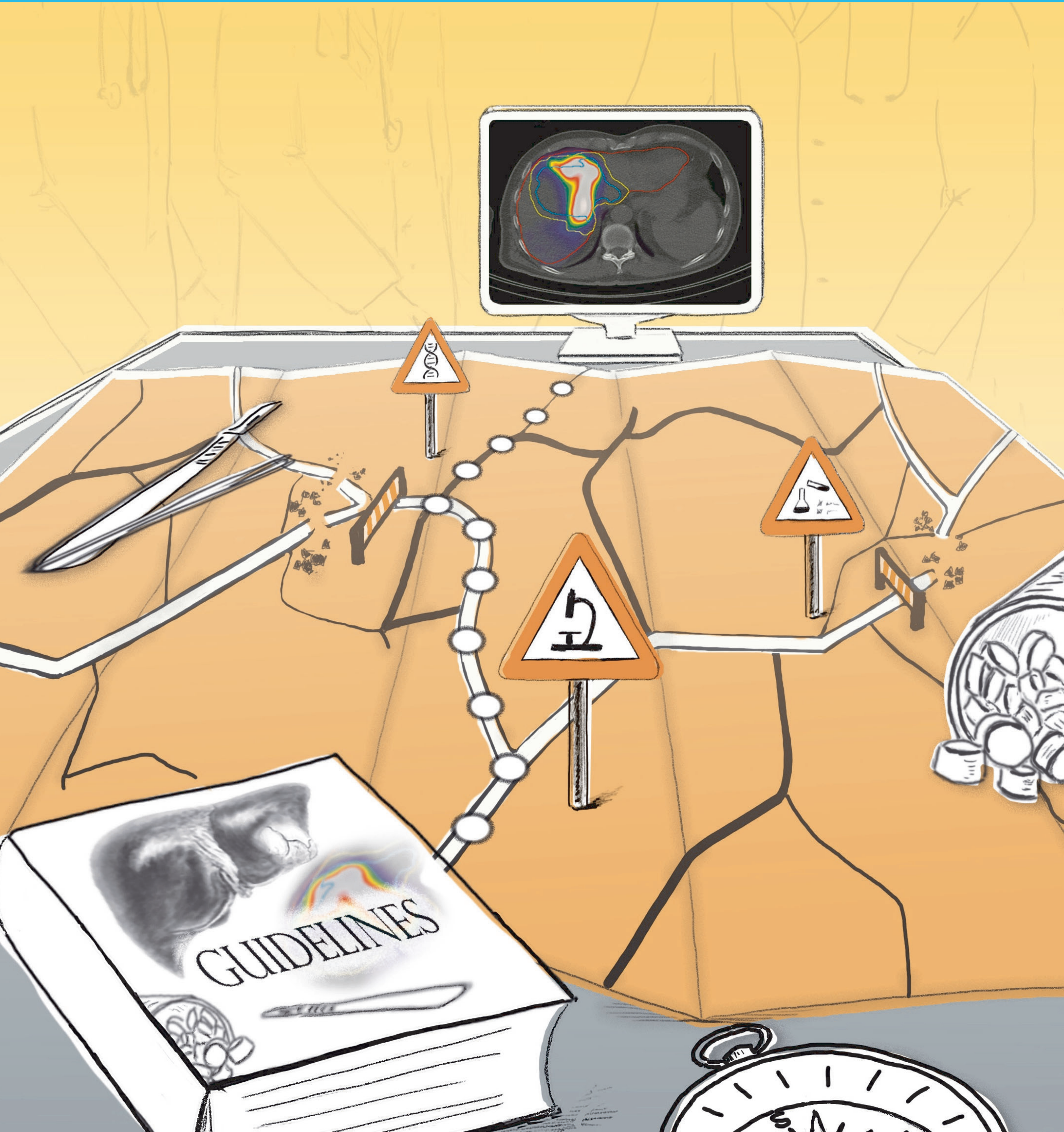
»We can simulate the success or failure of a planned liver intervention or tumor sclerotherapy based on using this model as a basis,« explains Andrea Schenk. »We have already achieved a lot of groundwork in these areas, which we can integrate into future systems.« After all, Fraunhofer MEVIS is not in the position to build a complete CDS system alone. Instead, the institute will deliver core components and work alongside a tight network of research partners, companies, and professional associations.

»CDS systems could also be employed to gain new medical insight from data that is already collected during the clinical routine. This would supplement common clinical studies and ultimately help improve treatment guidelines.«
Andrea Schenk, Fraunhofer MEVIS

Transparent algorithms

Future CDS systems will include additional elements, such as adaptive algorithms, to detect cases in medical databases that progressed similarly. This comparison could provide the attending physician important information: Which treatment was successful in this specific case? Which were less effective? It is also important to involve patients in this process. »The recommendations of a CDS system should not only be intelligible for doctors. They should also be communicated to the patient,« says Andrea Schenk.

This applies in particular to the use of AI algorithms, where it is essential that conclusions don't appear to come out of a black box. They should be transparent and comprehensible for


GUIDELINES

the user. »The human being must remain at the console, so to speak,« stresses Markus Wenzel. »We view CDS systems as tools for managing ever-increasing complexity to even be able to support all involved parties during multidimensional decision making. Using such systems gives us hope that physicians will have more time for their patients in the future.

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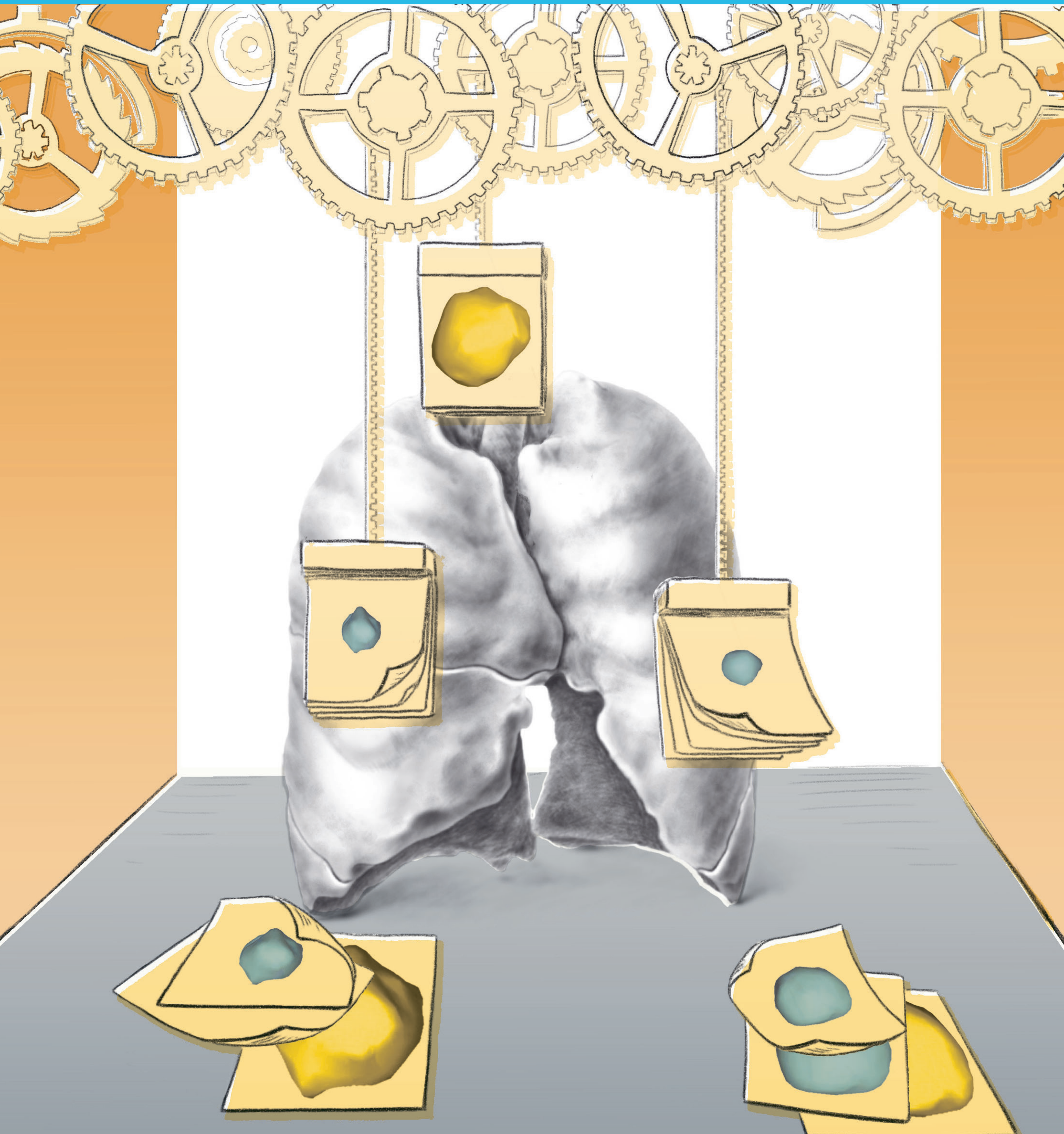
Fraunhofer MEVIS develops AI-based support systems to facilitate integrative decision-making and pave the path towards finding the optimal treatment.



MONITORING TUMOR THERAPY MORE PRECISELY

Cancer patients generally need to attend regular check-ups, which help determine how the patient responds to a new treatment. The Fraunhofer Institute for Digital Medicine MEVIS is working on a method supported by AI to carry out follow-up checkups more quickly and accurately.

A patient has been receiving chemotherapy for some time. Now his doctor wants to know how well the drug has performed. Did the tumor shrink as hoped? Would it be better to switch to another medication? To determine this, a CT scan is typically made after three months and compared with the image from the onset of treatment. Until now, this has been performed with the naked eye supplemented by fairly rudimentary electronic aids that measure tumor diameter. Fraunhofer MEVIS is developing an automated procedure to achieve before-and-after comparisons, thus saving time and producing more accurate findings.

»Because our system measures tumors more precisely, scheduled follow-up examination dates could possibly be performed earlier. It might be possible to perform them as early as one month after the beginning of therapy instead of three months, which is now the case. The advantage is, if a medication does not respond as anticipated, it would be possible to change to a more promising drug at an earlier stage than currently possible.«
Jan Hendrik Moltz, Fraunhofer MEVIS

Today, comparing old and new pictures is rather complex. To avoid missing any newly formed metastases, specialists have to sift through three-dimensional CT data sets slice by slice - a time-consuming process. Another shortcoming, according to MEVIS researcher Jan Hendrik Moltz, is that »it is relatively imprecise to determine only the diameter of a tumor. Tumors and metastases are three-dimensional objects. A change in diameter does not necessarily reflect the relevant change in size: how the volume of the tumor has transformed as result of the therapy.«

A better way to compare pictures

The team is working on an automated solution to evaluate the therapeutic response with more speed and accuracy. Researchers want to use a method called registration to facilitate image comparison. The computer can superimpose identical image sections in two different images for direct comparison: Clicking on a certain point in the new image automatically marks the corresponding position in the old image.

This lets personnel more easily detect whether metastases have vanished, or new ones have formed. The system will automatically visualize differences in the images, for example, by marking or highlighting them. »Fraunhofer MEVIS is in a great position when it comes to registration,« says Moltz. »Radiologists are often amazed at how well it works.«

The second step, measuring tumor volume precisely and automatically, is more demanding. For this, accurate segmentation is required. The computer should be able to recognize what is and isn't a tumor in the CT image. Such methods have been available for some time, but until now have usually required human intervention, limiting their practical application in hospitals and doctor's practices. »Deep learning technologies should bring critical progress in this area,« says Moltz. »We hope to prepare the system for the clinical routine.«

An AI that recognizes tumors

To do so, the experts train a segmentation algorithm using extensive CT data sets. This contains detailed information about the appearance of tumors and metastases on the image and how they vary from surrounding tissue. Moltz and his colleagues also hope to integrate knowledge gained from previous work. »We are very experienced in segmentation,« says the computer scientist. »This sets us apart from groups that are only now beginning and employ purely data-based approaches.«

Initially, the Fraunhofer team wants to concentrate on the lung and liver, two organs that are especially relevant in oncology. Over the long term, however, the algorithm should be able to identify metastases throughout the body reliably and measure them precisely. The research group will also try to dis-

Artificial intelligence helps monitor changes during the course of a tumor therapy.

cover parameters from the segmentation in addition to tumor volume. These could include, for example, clues about tumor tissue composition and help describe changes in the tumor, thus providing supplementary information about the therapy response.

An initial prototype to demonstrate the registration is likely to be completed in a year. In five years, the software is expected to provide automatic tumor segmentation for organs such as the liver and lungs.

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TARGETED NAVIGATION AND PRECISE MOTION CONTROL

Minimally invasive interventions play a central role in medicine, seen in applications including radiotherapy, heart catheters, and keyhole surgery. The Fraunhofer Institute for Digital Medicine MEVIS is researching methods to improve minimally invasive treatments significantly.

Surgery isn't always about scalpels and open wounds. Sometimes it is possible or even necessary to employ minimally invasive methods, of which there are many varieties. During keyhole intervention, the surgical wound is made as small as possible, after which endoscopes help look inside the body and perform the operation. Some tumors can be destroyed with thin electrical needles inserted from the outside. In cardiovascular diseases, physicians navigate catheters through blood vessels, for example, to widen constricted coronary arteries. In addition, methods such as radiotherapy or focused ultrasound do not involve surgical incisions at all. For these methods, radiation or sound waves enter the body from outside and focus on a tumor to destroy it as fully as possible. Ideally, the surrounding healthy tissue remains intact.

»Minimally invasive methods take an approach of doing as little damage as possible while accomplishing the therapy goal,« says Jan Strehlow, computer scientist at Fraunhofer MEVIS. However, these gentler methods pose a challenge: During the procedure, physicians have no direct view of what is occurring in the patient. They depend on images from imaging techniques, such as X-rays or ultrasound, for both executing the procedure and monitoring the results.

Fiber optics help navigate

An example: a doctor performing a catheter intervention in the coronary vessels must X-ray their patient almost continuously. Only by using this »X-ray video,« combined with the administration of a contrast medium, can the doctor be sure that the tip of the catheter is guided correctly towards the target. This is no simple task, however, because the current three-dimensional catheter position is only shown in 2D on the X-ray image. Moreover, the method is accompanied by a considerable dose of radiation resulting from the large number of X-rays. These pose a burden not only for the patients, but also for the personnel exposed to this radiation daily.

Fraunhofer MEVIS is working on methods to reduce radiation and simplify navigation. In one of these methods, the catheter is combined with a special glass fiber. When laser light is guided into these fibers, the fiber reflects different colors of the light depending on how the fiber is bent. The spectrum of the reflected light can thus be used to calculate the curvatures along the fiber.

The vision: During the procedure, curvature sensor values are compared with a digital model of the patient's vascular system obtained beforehand using MRI. »We can determine the position in the vascular system that best explains the measured catheter curvatures,« says Strehlow. This allows the physician to see the catheter moving through the vascular labyrinth on a monitor – in real time and in 3D. »We have successfully evaluated our method in a silicone model of part of a patient,« reports Strehlow. »Now we want to test it on animal models and continue development.« One conceivable application is more precise and gentler navigation in neurology, for example, to treat aneurysms.

»Our long-term goal is to combine our new procedures into one software system. This would relieve doctors by supporting them before, during, and after surgery. Ultimately, this would increase precision and safety for minimally invasive methods.«
Jan Strehlow, Fraunhofer MEVIS

Algorithm compensates for breathing

A further challenge is minimally invasive treatment of organs that move with the heartbeat and respiration, such as liver and lungs. »With focused ultrasound for liver cancer, you have to compensate for the movements of the patient so that the ultrasound waves always hit the tumor and not the surrounding tissue,« explains Fraunhofer researcher Michael Schwenke. In some cases, the patient lies during treatment in an MRI scanner that takes several images each second. This makes it possible to

track liver movement with each breath – but only partially and with a delay.

To improve this procedure, Fraunhofer MEVIS is developing an algorithm to predict the liver's position in upcoming moments based on MR or ultrasound images. »We are currently transferring the technology that we successfully developed for focused ultrasound to other applications such as radiotherapy or needle-based intervention,« says Schwenke. »For example, we have already created a kind of traffic light for liver biopsies that shows personnel the patient's current breathing state.« Furthermore, the team is working on software to compensate larger patient movement, such as body rotation.

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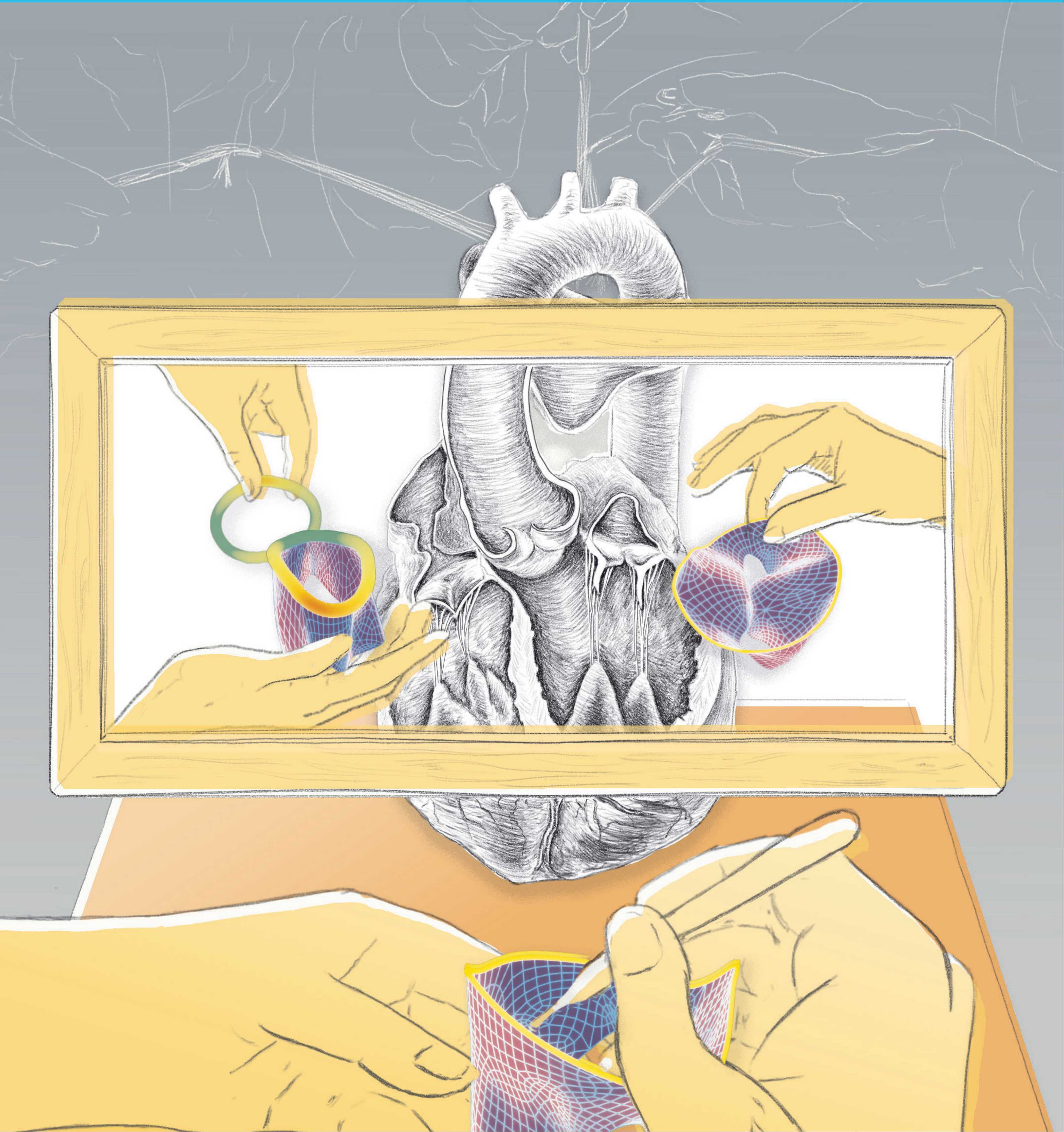
Our motion compensation as well as our catheter navigation combine a patient model with real-time sensor data to assess the therapy situation.



PRECISE PLANNING FOR HEART SURGERY

Heart valve operations are often very complex and have to be prepared with great precision. The Fraunhofer Institute for Digital Medicine MEVIS, the German Heart Center Berlin, and the Charité are developing an assistance system that will ease planning interventions by using virtual reality. In the future, patients are also likely to benefit from this new technology.

Surgery is often necessary when a heart valve no longer closes properly. In these operations, special rings or threads, for example, are sewn into the inlet or outlet of the heart chamber that the valve is supposed to close. They enable the valve leaflets to connect again. Some operations are still performed on an open heart, but patient-friendly minimally invasive procedures are increasingly being used.

»Heart valve surgery can be very complex, often combining several measures,« says MEVIS researcher Anja Hennemuth, a professor at the Institute for Computer-Assisted Cardiovascular Medicine (ICM), a joint facility of Charité and the German Heart Center Berlin. »Often, the team has to make many quick, ad hoc decisions during surgery.« Thorough planning of the procedure must take place to avoid potential mistakes and minimize risk to patients.

»Cardiac patients should also benefit from our concept during discussions with the physician before an operation. Heart valve operations are often complex, and it isn't always easy to comprehend what is happening. We are hopeful that our digital heart model will be able to clearly explain what therapy options are available to patients and what they mean.«
Anja Hennemuth, Fraunhofer MEVIS

This is where Fraunhofer MEVIS aims to support medical professionals. The institute is developing an AI-supported assistance system that adheres to guidelines to optimize the planning and execution of heart valve surgery and thereby improve operation quality. Specifically, the team will be able to simulate the surgery realistically on the computer even during preliminary discussions. To choose the best possible strategy, the experts can test various alternatives. They can help discover, for example, which type of ring should be used and at which exact location it should be inserted.

With image-based anatomical models we can simulate and compare different therapy strategies for the cardiac valves.

An AI that analyzes heart valve movement

The new assistance system is based on moving images, for example, from a CT or MRI scanner. These portray the heart of a patient in action and can uncover, for example, when the mitral valve, through which blood flows into the heart, no longer closes correctly. »We can extract an anatomical model of the patient from this image data using computer graphics methods,« Hennemuth explains. »This digital model doesn't just display the heart; it also shows how the valves open and close again, like in a 3D movie.« Artificial intelligence plays a crucial role in creating this model. Learning algorithms can recognize individual structures in the image data, analyze the heart valve movement quickly, and transfer them to the digital heart model.

The digital model can then be observed using AR/VR glasses: the beating heart floats in 3D directly in front of the user and can be seen from different angles. It can also be displayed on a conventional screen and manipulated using a mouse. This is practical, for example, for experts joining the meeting using teleconferencing. The team can use this model during a preliminary meeting to simulate the intervention in advance. Specialists can, for example, insert virtual sutures at different locations or attach rings of different sizes. They can determine which of the actions would have the most beneficial effect on heart valve movement.

Support in the operating room

The new MEVIS concept, however, goes even further – right into the operating room, where images of the virtual and real heart can be displayed side by side or even superimposed during the procedure. This lets the team see the planned operation literally before their very eyes.

MEVIS scientists have already developed and tested building blocks for this innovative concept alongside their project partners. They generated a database of currently available valve rings and compared their model with results from real interventions. A follow-up project called MINIMAKI began in March 2021. »Here, we aim to merge the individual elements,« explains Anja Hennemuth. »We're also working on streamlining 3D interactions so that medical professionals can use the new assistance system as intuitively as possible.«

One of the challenges: Some personnel and patients find using AR/VR glasses to be annoying and disturbing. The glasses can, for example, obscure the facial expressions of those in front of them. Fraunhofer MEVIS is researching these aspects in collaboration with medical ethicists as part of the new project. »Fortunately, AR/VR glasses are becoming lighter and more comfortable to wear,« Hennemuth emphasizes. »We're also working on a version that can hand off a session to a tablet or computer.« The first complete version of the new assistance system should be ready in two to three years. Soon afterwards, it could start being used in clinics and make it easier for both doctors and patients to prepare for heart valve surger.

Listen to the audio podcast

ONE PLATFORM, MANY TOOLS

Programming AI is a complicated process. Huge amounts of data need to be collected, reviewed, and evaluated. Our research group on »Collaborative AI in Healthcare« is developing a platform that integrates all key steps and eases collaboration between programmers and clinicians.

Artificial intelligence (AI) is becoming increasingly important in medicine. Adaptive algorithms can now recognize organs in CT or MR image data with more and more accuracy and determine whether tumors are benign or malignant. This promises new possibilities for the clinical routine. For example, diagnostic assistants can often streamline laborious, routine tasks and simplify a hospital's workflow. In addition, treatment planning algorithms could generate clues about a patient's tolerance for a certain drug.

However, developing such AI systems is challenging. The software must be trained with as much high-quality data as possible. If a program must reliably recognize and accurately measure a specific region of the liver on MR images, it needs to be trained with a vast amount of image data annotated by clinicians onto which the liver has already been outlined. Even though several programming tools exist to accomplish the involved tasks, they are often not well integrated. Fraunhofer MEVIS is, thus, developing a collaborative AI platform that unifies all essential tools and allows the main players - programmers and physicians - to work together. »Our platform should integrate everything into one system,« explains MEVIS computer scientist Hans Meine. »Everyone involved can log in to the platform and complete all of their tasks.«

»Our collaborative platform should be as simple to use as possible. Any action that affects data should always be traceable: Who entered the data? Who verified it? Who decided that some data should be excluded? This quality assurance process is an important aspect of our platform.«
Hans Meine, Fraunhofer MEVIS

Integrated quality assurance

It all begins with data handling. Nowadays, exporting data from one program and importing it into another is a tiresome, manual task. The new platform is intended to automate and, thus, simplify these processes. As with professional photo management software, it will collect and catalog data sets and present them clearly.

The data can be assessed (automatically when possible) according to their quality, and images with poor quality can be filtered out. Staff can add comments to each data set, such as what is visible on a CT scan and how pathological changes could become noticeable. Doing so incorporates important medical knowledge, allowing the computer to iteratively refine its learned skills.

»One example is segmentation, which is, for instance, when an algorithm attempts to detect specific areas of the lung automatically,« explains Bianca Lassen-Schmidt, one of Meine's colleagues. »If a clinician notices that the segmentation was not sufficiently successful, he or she can improve it manually.« The corrected image is then fed back into the program to train and improve the algorithm for more accurate results. »Of course, we aim to ensure that the software doesn't become worse,« says Lassen-Schmidt. »This can be avoided by verifying it regularly using a test data set.« Only after the algorithm passes this test will it adopt the learned changes, thereby fulfilling an important quality assurance requirement.

Training at multiple clinics

Another challenge: If an algorithm is trained with data from only one specific clinic, it might only function there, because different clinics use varying equipment and imaging protocols. Even for an identical clinical impression, data sets can vary subtly. This can be more confusing for AI than for humans. For an algorithm to work at multiple clinics, it is desirable to train it using data from as many hospitals as possible. This is complicated, however, by data privacy requirements, which often prohibit patient data from leaving the hospital.

»We are investigating how to train an algorithm using data from multiple clinics without requiring that data ever leaves the premises,« explains Bianca Lassen-Schmidt. The strategy

involves training the algorithm in Clinic A and then continuing in Clinic B. The algorithm then returns to Clinic A to refine the process. Because the software only »carries« learned patterns and not patient data out of each clinic, data privacy requirements are respected.

»We have already developed most of the individual components of our AI platform in-house at Fraunhofer MEVIS,« says Hans Meine. »We are now in the process of combining them into a complete package to test with other partners, for instance, to perform clinical studies.« In the long term, the collaborative platform might even help different clinics investigating similar topics to work more closely together. »For medical research,« believes Bianca Lassen-Schmidt, »this could make a great impact.«

Listen to the audio podcast

Fraunhofer MEVIS provides an integrated toolkit for worldwide collaborative development of AI solutions.


Medizin
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DIGITAL SOVEREIGNTY AND SCIENTIFIC LITERACY FOR THE BROADER PUBLIC

Interactive, aesthetic, and participatory public engagement and science communication: towards an accessible and diverse research and development landscape. The Institute's scientists are committed to raising awareness about how digital medicine and related STEM sciences influence healthcare. They develop experiential SciArt projects to stimulate critical dialog and ownership of new technologies, reach new audiences and foster a diverse future R&D landscape. The digital extension of human decision-making processes is not perfect and has its limits just as much as purely human interactions. It is a matter of uniting the specific capabilities of both worlds and adapting technological processes to human needs and abilities. Human-centered digitalization can explain, visualize and help manage complexities. Our concern is to make these new procedures understandable and accessible in our science communication. We also address topics artistically, utilizing or uniting digital medical image data, anatomical-medical illustration, and volume renderings to develop visuals and illustrate the R&D performed at the Institute. Our focus is on diverse, life-long education, collaborative production, and scientifically inspired art. Laypersons and experts are invited to get involved, learn, and exchange ideas eye-to-eye with the scientists. Engagement is a two-way process involving attention and interaction for mutual understanding and benefit. The aims are:

- making the outcome and impact of R&D accessible and stimulating critical dialog within society
- fostering diverse and equal ownership of future technology
- bolstering digital sovereignty for cooperating partners, universities, schools, employees, the media, and the broader public
- creating meaningful interactions between diverse players in society and STEM scientists in digital medicine
- shaping the future of digital medicine with the next generation of scientists
- promoting »first-in-family« academics
- supporting evidence-based discussions by learning and co-creation to build confidence in digital medicine and related STEM sciences

»The public engagement at the Institute is driven by the question of how we can create contemporary formats to engage people in digital medicine. The goals are to build emotional, positive engagement and self-directed learning with the required STEM sciences and promotion of a diverse research and development landscape.«
Bianka Hofmann, Fraunhofer MEVIS

R&D Engagement and Science Communication: New ways to learn more about digital medicine together with scientists and software developers.

Example: Artist residency STEAM Imaging III – Into the MRI tube for art's sake

During her residency at Fraunhofer MEVIS, media artist Eli Joteva created a remarkable installation: To obtain the material for her digital artwork, the Bulgarian lay down in an MRI scanner for hours. The result: a digital installation called »IntraBeing.« It shows oversized organs and highly complex webs of nerves that move meditatively and mysteriously right before the viewer's eyes.

The third artist residency, which Fraunhofer MEVIS is organizing together with Ars Electronica in Linz and the International Fraunhofer Talent School Bremen, is once again being held in cooperation with the Walle School Centre in Bremen. For the first time, the UCLA ArtSci Center in Los Angeles is also involved. The title of the program is »STEAM Imaging« – STEAM stands for the linking of science, technology, and mathematics with other disciplines, such as the world of art. The starting point of the residency is to bring artists together with scientists and school students to transcend disciplinary boundaries, develop flexible forms of learning and collaboration, and teach skills to use new technologies effectively and critically. The residency allows artists to engage in intensive exchange with MEVIS experts and to link their work with the latest scientific methods and approaches. An integral part of this is the joint development of the STEAM online course for young people. Based on the unusual alliance of art and science, it breaks new ground in approaching scientific and technical topics at school.

Bulgarian media artist Eli Joteva lives in the United States and has been tackling science-related themes for some time: she incorporates influences from quantum mechanics and neurophysics into her work and uses sophisticated imaging techniques such as infrared cameras and laser scanners to create her digital installations. »I'm very inspired by the mysteries of the invisible, such as how forces and vibrations outside our perception affect us,« she describes. »That's why I try to use imaging techniques to look into spaces we can't perceive with our senses.«

At the STEAM imaging residency, she was fascinated by the possibility of being able to take a deep, detailed look inside the body and process it artistically. The basis for this were images taken with an MRI scanner – an imaging technique that uses strong magnetic fields to deliver extremely detailed and, at the same time, body-friendly 3D images from inside a person. »I have always been interested in the complex ecosystems inside the human organism and have often used my own body in my work,« Joteva says. »That's why I was excited to be able to take MRI data of my body and work with it.«

An important element of the residency is a STEAM course for students. Joteva designed it together with the developers of the residency program, Bianka Hofmann and Sabrina Haase, and their colleague Hanne Ballhausen. For the conception, the Fraunhofer MEVIS team met in internal workshops to break up the planned scientific and technical teaching content and integrate it in a new way. The course is designed around objects that play a direct or indirect role in the otherwise digital everyday work of the experts: a skeleton and a phantom, i.e., a physical model for research purposes. Then the specific interests and competencies of the artist were incorporated. The course was held in English and online. On ten evenings, it dealt with topics such as »Analog and Digital Simulations for the Body« and »What Gets Lost in the Digital World?« The young people had the opportunity to have their own hands-on experiences, which were also carried over into the lessons at the Walle School Center. »For example, I showed them how to scan objects from their surroundings and create 3D models from them, which they can then share with others via the internet in augmented reality,« Eli Joteva tells us. »The students really enjoyed it – the feedback, anyway, was very positive!«

For her artwork development, Joteva was particularly taken with an MRI method called DTI that can be used to map the shape and also the behavior of nerve fibers. Normally, this method is used for brain images. Joteva had the idea of using it for other parts of the body, especially the chest, pelvis, and feet. However, due to the pandemic, it was not possible for her to travel to Bremen and acquire the images there. Instead, she was able to use an MRI scanner from MEVIS research partners at the University of California in Los Angeles LONI.

The scans proved to be an ordeal: for a total of eight hours, spread over two days, Joteva had to lie down in the scanner's narrow tube, remain there, and keep holding her breath so as not to move. »And this despite the fact that I suffer from claustrophobia,« the Bulgarian tells us. »There were many moments when I wanted to press the button so they would get me out. But in the end, I endured it for the sake of the art.«

Numerous online sessions with Fraunhofer MEVIS experts followed. Eli Joteva learned how and with which software tools the image data could be processed and interpreted. »Without this incredible support, the project would not have been possible,« she enthuses. »But I also noticed that the in-depth engagement with an artist definitely fired up the people at MEVIS to push the limits and possibilities of what they do. It was a very inspiring process.«

Based on the processed image data, Eli Joteva created a room-sized installation using 3D graphics software. »IntraBeing,« as the artwork is called, shows the alienated, oversized organs from Joteva's body surrounded by highly complex meshes of nerve fibers. The structure is in constant, meditative motion – streams of hydrogen atoms and magnetic fields that are invisibly connected to the organs. »The behavior of these hydrogen atoms cannot be predicted because they are constantly docking to and from other atoms,« the artist describes. »This scientific uncertainty fascinates me – it shows that when we penetrate the body, we always discover something we don't understand.«

IMPACT STORIES

SOFTWARE IMPROVES RADIATION THERAPY

Until now, tumor treatment with X-rays has usually followed a set schedule. Software from the Fraunhofer Institute for Digital Medicine MEVIS can significantly accelerate treatment sessions. It also helps adjust radiation planning more precisely to therapeutic progress. Since 2020, the program has been successfully used as part of a product of the medical technology company Varian.

Radiation therapy is one of the pillars of cancer treatment. It involves bombarding the tumor with strong, focused radiation, usually X-rays. It destroys the cancer cells and makes the tumor shrink and, in ideal cases, disappear. However, one treatment session is not enough; the radiation must be repeated during daily sessions over several weeks.

»When possible, it is important to hit only the tumor and to spare the surrounding healthy tissue as much as we can,« says MEVIS researcher Stefan Heldmann. »That's why the tumor is hit from several directions, not just one.« Only when the beams arrive from different directions and meet in the tumor does this method reach its full effect. The healthy tissue along the path is only slightly affected.

»Until now, radiation therapy lasting several weeks mostly follows the original radiation plan. Our image registration software creates the prerequisite for adaptive treatment, adjusting it to changing circumstances, such as when a patient loses weight during the course of therapy.«
Nils Papenberg, Fraunhofer MEVIS

To make the therapy, which lasts several weeks, as effective as possible, careful preparation is required. Based on a CT scan of the patient, the physicians create a precise radiation plan with the help of complex mathematical models and extensive computations. However, the patient does not always lie in the same position during the different sessions. In addition, a patient's anatomy may change during therapy, for example due to weight loss, or might depend on daily fluctuations, such as how full the bladder is. In addition, organ motion during breathing can also complicate treatment.

Precise registration

To ensure that the radiation reaches its target during each session, the patient is scanned by a special X-ray scanner during treatment. The medical staff can compare these control images with the plan to then correct the position on the scanner bed, for example. If necessary, the original plan will be adjusted to account for weight loss, which can change the location of the tumor in the body.

To improve and accelerate comparison of planning and control images, Fraunhofer MEVIS has developed special software that has been used in an industry partner's product since 2020. This software performs so-called image registration, which automatically compares the planning and control image with each other. One major challenge during registration is that the control images have a significantly lower image quality than the CT image taken for planning.

»Based on this automatic image matching, our software can transfer the planning data to the control image,« explains MEVIS researcher Nils Papenberg. »This makes it easier to see, for example, how much a safe distance to an adjacent organ is being kept.« Until now, medical staff has had to transfer the planning data to the control images largely by hand during the session – often a time-consuming task. The MEVIS software can now do this automatically and with great accuracy.

The graphics card sets the pace

A major challenge during development has been speed. While the image registration software is running, doctors and patients must wait for the results before starting treatment. MEVIS' industrial partner Varian had targeted a maximum computing time of 90 seconds. Through clever programming, the MEVIS experts initially managed to achieve it in 30 seconds. When they then implemented their system on a fast graphics card (GPU), they were able to reduce the computing time to just a few seconds, which is advantageous for clinical practice.

During treatment, the physicians must only check the result of the image registration and adjust it when necessary. As a result, the duration of the radiation session is shortened for all involved. »We started by developing the mathematical fundamentals,« Heldmann recalls. »From that mathematical basis, we then shifted towards developing an algorithm that eventually became quality-assured software for Varian.«

As a result, MEVIS software helps with adaptive radiotherapy: radiation planning that optimally adjusts to changing conditions over the course of several weeks of treatment. To improve this capability, Fraunhofer MEVIS has been constantly developing the software. »It is designed to employ various input parameters to determine and precisely compute the sum of the radiation doses to which patients have been exposed during the course of therapy,« explains Papenberg. Based on such dose images, physicians can more accurately assess, for example, whether the tumor received the intended dose of radiation. As a research project, MEVIS experts have already been able to run such algorithms. Now they are in the process of transferring these programs into practice.

NAVIGATOR FOR TUMOR THERAPY

During thermoablation, a needle is inserted into the body to destroy a tumor with microwaves or laser light. The Fraunhofer Institute for Digital Medicine MEVIS has developed pioneering assistance software that automatically and accurately finds the optimal puncture site.

Thermoablation is a minimally invasive procedure to treat cancer. A needle is inserted into the body and placed in or near the tumor. Energy flows through the needle in the form of microwaves, laser light, or high-frequency alternating current. This energy heats the cells of the tumor to such an extent that they die and, if the therapy is successful, the lesion disappears. This fairly gentle treatment is now employed for a wide variety of types of cancer, including liver and kidney tumors, as well as prostate, breast, and lung cancer.

The primary requirement for therapeutic success is that the needle is positioned as precisely as possible. Only when it is correctly inserted can enough tumor cells be killed, necessitating careful procedure planning. High-quality images, usually generated by a CT or MRI scanner, are used for this purpose. The physicians mark the exact point where the needle must be placed. The procedure itself also takes place under imaging. This is the only way to check whether the needle reaches the desired target.

In practice, however, this poses a substantial challenge: images used for planning are not updated daily and in some cases are several weeks old. In addition, patients might lie slightly differently in the scanner during the procedure than during the planning scan, as it is impossible to achieve the same position twice.

As a result, »It is very difficult to match the current image with the planning images - the doctors see the planning image on one monitor and the current image on another and have to match both images mentally,« explains MEVIS researcher Christian Rieder. »This requires specially trained and experienced professionals, and that's why such thermal ablation treatments have so far been offered by fairly few centers.«

»Until now, we've been able to use our software to help plan interventions and subsequently assess their success. With the new system, we can now support the intervention itself«.
Torben Pätz, Fraunhofer MEVIS

Automatic image matching

To support specialists during this challenging task, Fraunhofer MEVIS has developed navigation software for a novel robotic system to be offered by a medical device company in the future. The software can compare the planning image with the current image and calculate the exact insertion point for the needle. The robot then positions a guide sleeve at this location, through which the medical professionals can insert the needle and perform the thermal ablation. »The goal of this robotic system isn't to replace the physician and place needles in humans fully autonomously,« emphasizes Rieder's colleague Torben Pätz. »It's designed to transfer the doctor's plan to the current situation; the robot helps find the planned puncture site reliably.«

The software is provided with the planning image, including the planning data, as well as the images taken during the current procedure. Based on this information, the program performs a so-called image registration. Despite different image sections and viewing angles, organs and tumors on the old and new images are brought into congruence. The software can then transfer the planning data, in this case the intended puncture site, from the old to the new image and relocate the guide sleeve to the right location. »One challenge was that merging this information has to occur relatively quickly,« says Pätz. »In addition, our program must be able to match two-dimensional X-ray images with three-dimensional images from a CT scanner.«

Perceptible simplification

Currently, the robotic system is in the approval phase, whereas the MEVIS software has already passed the quality assurance process and is qualified as a medical device component. »We began initial research work in 2015 and have now been able to successfully transfer the results into clinical practice,« Torben Pätz is pleased to report. The system can noticeably simplify applying thermal ablation, so that in the future, more clinicians may be able to master it and more centers offer it. »And patients could also benefit,« says Christian Rieder. »Until now, this therapy hasn't always generated the desired effect. Thanks to our system, the needle can be placed more precisely, which could increase treatment success.«

The new system is based on a technological core called SAFIR (Software Assistance for Interventional Radiology), which also offers other interesting features. For example, Fraunhofer MEVIS is working on modifying the software for real-time motion images, such as those generated by ultrasound devices. This could target organs that move during breathing and for which patients have had to hold their breath during treatment

BETTER NETWORKING THANKS TO MEVIS SOFTWARE

The large-scale RACOON project focuses on digitally linking all radiology departments at German university hospitals to advance COVID-19 research. The Fraunhofer Institute for Digital Medicine MEVIS has developed a central software element for this purpose, helping to facilitate and accelerate joint research projects.

The first corona wave rolled through Germany in the spring of 2020 and revealed many shortcomings in the German healthcare system, especially in terms of digitalization. For example, the radiology departments at the country's university hospitals were inadequately networked with each other, which complicated, for instance, the joint development of AI algorithms for research. To improve the situation and conduct joint research on COVID-19, the collaborative RACOON project was launched in 2020, with Fraunhofer MEVIS as a project partner alongside 36 university hospitals.

»RACOON may also improve future research into rare diseases in which a single clinic might record only a few cases annually. Usually, no solid research can be conducted with very low case numbers. But with RACOON and our SATORI software, image data from all German university hospitals is available for research. This will greatly benefit patients in the future.«
Bianca Lassen-Schmidt, Fraunhofer MEVIS

»In the past, there have been numerous technical and regulatory obstacles to collaboration between clinics,« explains MEVIS researcher Bianca Lassen-Schmidt. »One problem is that, due to privacy concerns, medical recordings are often not permitted to leave the hospital.« This is just one obstacle to the development of new AI algorithms. These algorithms can, for instance, automatically identify tiny tumors in CT images. They only function reliably, however, if they are trained using as much image data as possible. The more hospitals that make their image data available for software development, the better the results.

To jump start the RACOON network, the Technical University of Darmstadt, the German Cancer Research Center (DKFZ), mint medical GmbH, and Fraunhofer MEVIS developed special techniques. Lassen-Schmidt and her team at Fraunhofer MEVIS have been developing the SATORI software platform for several years. It is capable of 'segmenting': automatically recognizing different parts of the lung in the images. After the researchers presented their AI software to the project management, it quickly became clear that it was an ideal fit for RACOON.

Optimized training for AI algorithms

With RACOON, the goal is to teach MEVIS' segmentation software to detect the disease features typical of COVID-19. »This can then be used to automatically identify the size and distribution of the affected areas in the lungs,« explains Lassen-Schmidt. »This is important information to better understand the disease.« The team set an ambitious goal for training the AI. To train the software with as much image data as possible, CT images from all German university hospitals were to be used. To accomplish this, it was vital for the experts at each hospital to use SATORI to examine the images and mark the disease features present in each case - the prerequisite for successfully training the AI.

However, the challenges proved to be great: for example, clinics operate varying CT scanners. Some produce images with relatively coarse resolution, others at a much finer resolution. »It wasn't as standardized as you might imagine,« says Lassen-Schmidt. »In some cases, comparing images was like comparing apples and oranges.« To solve the problem, the working group had to adapt the algorithms and make them compatible.

Data protection concerns brought additional difficulties. German federal states and even individual hospitals interpret the regulations differently. »The hospitals had to coordinate with each other and agree on a common data protection policy,« says Bianca Lassen-Schmidt. »That was an additional challenge, but it worked out very well.« In the end, the situation was resolved in such a way that, as a rule, the actual data remains at the hospitals and all that leaves are the algorithms trained there.

Better patient care through research results with increased validation

A RACOON server with the SATORI software is now installed at each of the participating university hospitals. Around 2800 lung

CT scans have been completely segmented and marked with the necessary disease characteristics. This provides Germany with a comprehensive dataset that can be used to train AI algorithms to assist in COVID-19 research. »Now research can take place at a much higher level,« Lassen-Schmidt emphasizes. »Clinical hypotheses can now be tested on larger patient populations, providing more valid results and ultimately better patient care.«

This new infrastructure will also facilitate other scientific projects that are significant for COVID-19 research. In the future, experts might not only work with lung images, but also with images of the heart and brain, for example. After all, the coronavirus also attacks these organs. There are also plans to analyze images of children with the disease. One of the aims here is to investigate possible long-term consequences of COVID.

FRAUNHOFER MEVIS AT A GLANCE

BRIEF PROFILE

Fraunhofer MEVIS is dedicated to the development of software and IT solutions to overcome the rapidly growing complexity in healthcare in order to achieve improved patient outcomes with higher efficiency and fewer risks and side effects. The work is focused on the mission areas Precision Diagnostics, Precision Interventions and Collaborative Health Data Research. The commitment to responsible research and innovation as well as transdisciplinary lifelong learning runs through all scientific fields of activity.

Clinical commitment

Research and development at Fraunhofer MEVIS is guided by a clinical direction instead of being technologically or methodologically driven. Our work focuses on developing innovative solutions for computer-assisted 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 our partners. Fraunhofer MEVIS maintains an international network of over 100 clinical partners. This clinical network is an essential source to understand user needs and to evaluate the potential clinical value and feasibility of developed solutions.

Strategic considerations

The roots of Fraunhofer MEVIS lie in the creation, quantitative analysis, and interactive exploration of medical image data in their specific clinical context. We believe that medical imaging shall no longer be regarded as a field on its own. Instead, image features must be quantitatively correlated to available clinical information in order to discover new relevant knowledge. Fraunhofer MEVIS is uniquely positioned by combining a deep understanding of clinical procedures and problems with a mastering of the technological value chain – from imaging physics and data generation to algorithm and platform development to validation, product certification, and clinical implementation.

We have built substantial expertise and a good reputation in the deep learning and artificial intelligence (AI) arena. This enables us to successfully cope whith the rapidly growing complexity in all diagnostic and therapeutic domains. While many groups worldwide are active in the field of medical AI, Fraunhofer MEVIS is one in a few that covers the complete process of knowledge generation such that AI will eventually become a powerful clinical tool in hospitals and medical practices. Solutions based on our collaborative and modular software platforms are used likewise in multi-centric clinical trials and pharmaceutical research. Below, we briefly describe the building blocks needed to fulfill our mission.

Industrial collaboration

True innovation, the successful launch of solutions onto the market with tangible impact, 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 the link between clinicians and industry, aiming at technological advancement for clinical use. Transferring applied research to the industry is a pillar of the institute and a basis 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, pharmaceutics, and related fields.

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 a small group of medtech research facilities worldwide that, in Bremen since 2005 and in Lübeck since 2012, has operated a quality management system according to the EN ISO 13485 (Medical Devices) standard with a special focus on implementing a software development process in compliance with IEC 62304. The establishment of these quality management systems with the scope on design, development and production of software for medical products lays out well-defined steps for industrial cooperation and enables Fraunhofer MEVIS to provide market-ready solutions for commercial partners in the strongly regulated medical device market. In addition, Fraunhofer MEVIS also has experience with CE and FDA approval of software solutions for clinical environments.

Software platform

Fraunhofer MEVIS has initiated and developed a family of versatile, modular web-enabled software platforms that enable our partners and ourselves to build new solutions faster and to better adapt to new challenges. The *»MeVisLab«* development platform by Fraunhofer MEVIS and MeVis Medical Solutions AG is a tool for rapid prototyping, flexible development of clinical software solutions as well as 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. This supports the tight technological integration of clinics, research, and industry. MeVisLab provides a modular interface to 3D Slicer, a software platform for the analysis and visualization of medical images and for research in image-guided therapy. Slicer is a free, open source software available on multiple operating systems and extensible via plugins for adding algorithms and applications.

Additional platforms and frameworks target specific application areas. Among those are *»Histokat Web«* serving at multicentric research, development and validation of solutions in the field of computational pathology, as well as our deformable image registration library *»RegLib«* used for multimodality, intraoperative, and follow-up image matching and motion correction. The modular software platform *»QuantMed«* supports quantitative medicine to enable more reliable, accurate, and efficient clinical decisions.QuantMed offers support along the way: creating reference training data, training and validating deep learning models, and deploying the results into your quantitative diagnostic software. *»SATORI«* is a core component of our AI collaboration toolkit and a web frontend for curating medical data. The platform for reader studies can be highly customized through extensions that can be quickly developed with MeVisLab. Moreover, Fraunhofer MEVIS has developed the remote deep learning framework *»RedLeaf«* as an extension of MeVisLab, that allows for modular, distributed and reproducible pattern recognition on large medical datasets.

Business areas

Our four business areas align with our strategic directions as described above and focus on specific market segments and related industrial customers. A range of services and solutions can therefore be tailored and developed for these customer groups.

The planning and support of surgical and minimally invasive procedures, which has been a key focus of Fraunhofer MEVIS since its founding, is developed in the business area *»Image-Guided Therapy«*. A particular challenge here is to provide the operating physician all relevant information at the time he/she needs it. Customers are mainly hardware vendors that span a wide range of products from implants like valves and stents to catheters and needles, treatment devices like robots, focused ultrasound systems or linear accelerators (linacs), as well as navigation devices.

The business area *»Diagnostic Software«* is centered around the clinical challenge to ensure optimal therapeutic decisions and improved early detection, incorporating the constantly growing amount of multidisciplinary data on the one hand and the efficiency pressure for faster processing on the other. The customers in this segment are imaging device vendors, clinical IT companies, and specialized image analysis providers.

Within the area of diagnostic software, we have defined a specific business area around *»Computational Pathology«* as a field with special potential for growth, considerable technological development, and not least for becoming a game-changer in the field of precision medicine due to the enormous amount of information encoded in the digitized tissue sections. Customers are manufacturers and providers of digital pathology equipment, biotech companies, laboratories, as well as healthcare IT integrators. Our key focus is in modular pattern analysis and virtual multi-staining based on highly accurate deformable image registration, thereby building on existing digital pathology platforms.

The business area »*Clinical Trials and Pharma*« emerged from the field of analysis software for image-based studies, combined with our web-based software platform developments, and is being expanded to a comprehensive range of services for the industry and for larger research consortia. Customers are pharmaceutical companies, contract research organizations (CROs), service and software providers for image analysis as well as researchers in hospitals, laboratories, and industry.

Additional business activities open up the potential for exploitation of the existing expertise in the field of imaging physics. We aim at bundling the offers of other areas of competence for the customer group of medical imaging device manufacturers. In magnetic resonance imaging (MRI), we offer our expertise to develop dedicated sequences for research, clinical and commercial customers.

Technology and translation

The following scientific and supporting core competences form the pillars of our work in research, technology, and translation.

The process of creating medical images is addressed by our core competence »*Imaging Physics*«. This spans from improving image acquisition and creating new physiological information to automated motion tracking and quality assessment. The goal is to integrate image acquisition and post-processing to an optimized image analysis pipeline. Since April 2011, Fraunhofer MEVIS is operating an own 3 Tesla MRI scanner for research and clinical studies.

The core competences »*Cognitive Medical Computing*« and »*Clinical Decision Support*« revolve around the extraction of information from medical images and other medical data. The previous technological focus of image processing has been extended to non-imaging data and, therefore, to the challenge of incorporating a broad range of relevant clinical information. The main goals are to maintain and expand our competence in the automatic extraction of quantitative information in imaging and other big data scenarios and in efficient interactive solutions for decision support systems as well as for planning and support systems in image-guided therapy. In this context, data-driven approaches such as machine learning, especially deep learning, are becoming increasingly important. At Fraunhofer MEVIS, machine learning is successfully applied for image segmentation as well as tissue and cell classification, among other things.

With our core competence »*Image Registration*« we aim at harmonizing images from different modalities, capture times, or patients, in order to evaluate the combined information. Fraunhofer MEVIS provides applicable image registration with a focus on robust, reasonable, accurate, and computationally highly efficient solutions.

Our core competence »*Modeling and Simulation*« enables us to incorporate knowledge of biophysical and biomedical processes to enhance the information within medical images. In addition to application driven developments, we perform basic research to enhance the technological capabilities. A particular focus for the next years will lie on validation of simulation results, in order to gain acceptance by industrial partners and physicians.

The capability of providing high quality, modular, reusable software components, efficient and well-integrated software applications and flexible deployment is developed and encapsulated in the core competence »*Custom Software Solutions*«.

The anchoring of Fraunhofer MEVIS in digital medical technology and the focus of its research activities towards clinical benefits are strengthened through the core competence »*Clinical Expertise*« and will be further developed as a long term USP.

A goal of our »*Science Communication*« is to create projects, exhibits, movies and workshops in which scientists contextualize their expertise and research in a broader sense and become inspired to relate facts, empirical data, and science to humanities, social realities, and values.

Links to academic institutions

In addition to the network of clinical partners, Fraunhofer

MEVIS maintains a strong network of technological and academic partners. In the reporting period, Fraunhofer MEVIS was connected with eight universities in Germany, the Netherlands, and the United States through twelve professorships:

- University of Bremen: Prof. Günther, Prof. Kikinis
- Jacobs University Bremen: Prof. Hahn, Prof. Preußer
- University of Applied Sciences Bremerhaven: Prof. Rascher-Friesenhausen
- University of Lübeck: Prof. Modersitzki
- Charité, TU Berlin: Prof. Hennemuth
- RWTH Aachen: Prof. Kießling, Prof. Merhof, Prof. Schulz
- Radboud University Nijmegen: Prof. van Ginneken
- Harvard Medical School, Brigham and Women's Hospital: Prof. Kikinis

From its first days, Fraunhofer MEVIS maintains strong ties to the universities in the State of Bremen. The directors of the institute hold professorships at the University of Bremen and the Jacobs University Bremen. Further close cooperation exists through professorships in the fields Imaging Physics, Modeling and Simulation, and Medical Technology. The University of Bremen and Fraunhofer MEVIS intensified their partnership in computer science education through a new study focus Medical Computing.

With financial support of the State of Schleswig-Holstein and the European Union, the Fraunhofer MEVIS Project Group for Image Registration was established at the University of Lübeck in April 2010. The internationally renowned group addresses the core competence of state-of-the-art medical image registration in close cooperation with the Institute of Mathematics and Image Computing (MIC) at the University of Lübeck. Since July 2015, the project group is part of the Fraunhofer MEVIS mother institute in Bremen.

Since 2012, Fraunhofer MEVIS pursues a strategic partnership with the Diagnostic Image Analysis Group (DIAG) at the Radboud University Medical Center in Nijmegen, the Netherlands, an internationally renowned center of excellence for Computer-Aided Diagnosis (CAD).

In April 2017, Fraunhofer MEVIS opened a new site in Berlin with close links to the German Heart Center, the Charité – Universitätsmedizin, and the Technical University Berlin. Fraunhofer MEVIS researcher Anja Hennemuth was appointed professor for image-based therapy support at the Institute for Imaging Science and Computational Modelling in Cardiovascular Medicine.

In 2018 Fraunhofer MEVIS established a strategic cooperation with the Institute of Experimental Molecular Imaging (ExMI) at the RWTH Aachen headed by Prof. Fabian Kießling. In close collaboration with the Comprehensive Diagnostic Center Aachen (CDCA), particular attention is paid to projects in the field of OMICS data. This includes the development of automated and standardized workflows for the detection, segmentation, and extraction of biomarkers in the fields of radiomics and quantitative pathology.

In March 2020, Prof. Kikinis left Fraunhofer MEVIS to take up the prestigious »B. Leonard Holman Endowed Professorship of Radiology« at Harvard Medical School in Boston.

Our new name, the 25th anniversary, and the new building in Bremen

Exactly ten years after joining the Fraunhofer-Gesellschaft, on January 1, 2019, the former Fraunhofer Institute for Medical Image Computing MEVIS changed its official name to Fraunhofer Institute for Digital Medicine MEVIS (Fraunhofer-Institut für Digitale Medizin MEVIS). The new name, in short still Fraunhofer MEVIS, underscores the institute's mission to drive the transformation of tomorrow's digital, integrated precision medicine through systematic computer support.

August 2020 marked the 25th anniversary of the founding of the MEVIS research center at the University of Bremen, the

Fraunhofer MEVIS' new institute building, the »Workshop of Digital Medicine,« accommodates up to 210 workplaces on a usable floor space of 2600 m². The building located on the campus of the University of Bremen is funded in equal parts by the Federal Republic of Germany, the Federal State of Bremen, and the European Commission (ERDF).

forerunner of today's Fraunhofer Institute for Digital Medicine MEVIS. In a seven-part campaign between October 2020 and May 2021, Fraunhofer MEVIS informed its cooperation partners and the public about concrete application scenarios and key work objectives of the institute with a focus on integrated diagnostics and precision therapy.

In May 2021, Fraunhofer MEVIS' new institute building building on the campus of the University of Bremen was completed and occupied after a construction period of 2.5 years. As a »*Workshop of Digital Medicine,*« the building is to be perceived as a driver of digital change in the healthcare sector. digital transformation in the healthcare sector and create space for encounters and discussions on the topic of digital medicine.

Brief history

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) at the University of Bremen. The founder Prof. Dr. Heinz-Otto Peitgen was appointed executive director, and an international scientific advisory board oversaw research. To expand the institute scientifically and economically, MeVis received a fixed basic funding from the State of Bremen. 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 of MeVis Research increased steadily from 10 to 51 full-time positions by the end of 2008.

On January 1, 2009, MeVis Research was incorporated into the Fraunhofer-Gesellschaft and renamed Fraunhofer Institute for Medical Image Computing MEVIS (Fraunhofer-Institut für Bildgestützte Medizin MEVIS). 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, at that time CEO of the Healthcare Sector of Siemens AG.

In April 2010, 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 July 2013, Professor Fischer passed away following a short severe illness. The director of the MIC, Prof. Dr. Jan Modersitzki, was appointed new director of the Fraunhofer MEVIS Project Group for Image Registration in October 2014.

In October 2012, MEVIS founder Prof. Peitgen retired after heading the institute for 17 years and his former deputy Prof. Dr.-Ing. Horst K. Hahn succeeded as Interim Institute Director. From May 2014, the institute was jointly headed by Prof. Hahn and Prof. Ron Kikinis, MD. After Prof. Kikinis moved to Harvard Medical School in March 2020, Prof. Hahn is the sole director of the institute. His deputies are Prof. Dr. Matthias Günther and Prof. Dr. Tobias Preußer.

During the transition phase of five years, the parent institute in Bremen (2009–2013) and the project group in Lübeck (2010–2014) have received funding from the States of Bremen and Schleswig-Holstein and have been co-financed by the European Regional Development Fund (ERDF). The mother institute in Bremen and the project group in Lübeck were positively evaluated by international review boards in May 2013 and 2014. They are under regular basic funding of the Fraunhofer-Gesellschaft since January 2014 and July 2015, respectively.

Since its integration into the Fraunhofer-Gesellschaft, Fraunhofer MEVIS has been a member of the Fraunhofer Group for Information and Communication Technology (Fraunhofer-Verbund IuK). In 2021, Fraunhofer MEVIS switched to guest status and joined the newly established Fraunhofer Group for Health Research (Fraunhofer-Verbund Gesundheit) as one of six founding members.

OPERATING AND ORGANIZATIONAL STRUCTURES

Fraunhofer MEVIS' interdisciplinary orientation is reflected in the institute's operating principles and organizational structure. Researchers are not bound to strict, hierarchically organized working groups, but act in a flexible network.

Three categories of strategic topics shape this network, with dedicated experts forming the nuclei of activities: organ- or disease-related clinical domains, technological core competences, and customer-oriented business areas.

Project teams are put together with team members from different technological and clinical credentials. This form of dynamic collaboration promotes cooperation and fosters cross-training, beneficial both to the individuals and to the institute as a whole.

Internal communication is governed by transparency and cooperation. Access to information is only restricted insofar as required by confidentiality agreements with customers or by legal constraints – otherwise sharing of information is encouraged and expected at all levels and is actively aided by exchange forums such as the social Wiki-based intranet (Confluence), morning meetings for all staff members, and an active information policy by the leadership. Initiative by all staff members also beyond their current work assignment is highly encouraged.

To improve management, organization, and staff development, Fraunhofer MEVIS established a mentoring system. Management responsibility is extended to a group of experienced staff members who act as mentors or co-mentors for mentees. Responsibilities of the mentors include the professional development of the mentee, the coordination between the goals of the institute and the mentee, as well as the identification and addressing of potential conflicts and problems.

Fraunhofer MEVIS introduced a structure of organizational entities (OEs) each with a responsible OE manager (OEV). The main objectives of the OE structure are:

- clear allocation of responsibilities,
- delegation of project budgets, and
- strengthening of strategic focus.

The OEVs are by default mentor for the respective OE members. The mentees can freely choose their OE as well as the co-mentor. OEVs as well as additional colleagues bear specific strategic responsibility to the institute, especially for business areas and core competences. Alloced budgets must be explicitly used for appropriate strategic objectives. Objectives and budgets are coordinated by the OEVs in consultation with the institute directors and the financial management.

Overall responsibility for the institute is organized in a central leadership and administration structure. The heads of the institute are:

- Prof. Dr.-Ing. Horst K. Hahn (Institute Director)
- Prof. Dr. Matthias Günther (Deputy)
- Prof. Dr. Tobias Preußer (Deputy)
- Dipl.-Betrw. Thomas Forstmann (Head of Administration)

The heads are assisted in operational and strategic tasks by the OEVs and six leadership committees for human resources (LH), valorization (LV), research (LR), finance (LF), quality management (LQ), and IT security (LS).

The Advisory Board (Kuratorium, cf. next section) advises the management of Fraunhofer MEVIS in issues of scientific focus, strategic orientation, and clinical as well as industrial translation.

Three male and three female persons of trust are elected by the staff to function as liaisons and mediators when needed. In addition, two female equal opportunity officers are elected to promote and ensure balanced participation and diversity.

The guiding principle of Fraunhofer MEVIS' diversity management is to value the diversity of all employees. The aim is to create a working environment in which all employees have fair opportunities for participation and development – irrespective of their ethnic origin, gender, religion and ideology, disability, age or sexual identity.

ADVISORY BOARD

Fraunhofer MEVIS is actively supported by its Advisory Board (Kuratorium) which is composed of persons with backgrounds in medicine, science, business, and research funding. It advises the management of Fraunhofer MEVIS in issues of scientific focus, strategic orientation, and clinical as well as industrial translation.

Due to the corona pandemic, in 2020 and 2021 the annual meeting of the Advisory Board could not take place in presence but as an online event. Beyond their usual role as advisors, the members of the Advisory Board have been actively involved in the strategy process 2020/21 of Fraunhofer MEVIS in several workshops and interviews.

Six members of the Advisory Board retired by rotation during the reporting period: Prof. Dr. Craig Garner in 2020 – Walter Märzendorfer, Astrid Lurati, Prof. Dr. Jürgen Hennig, Prof. Dr. Gábor Székely, and Dr. Ursula Niebling at the end of 2021. The president of the Fraunhofer-Gesellschaft and the directors of Fraunhofer MEVIS thanked them for their great effort and dedication. In the reporting period, the Advisory Board consisted of the following persons:

Chairs

Prof. Dr. Hans Maier (since 2009)
formerly Bayer Schering Pharma AG, Berlin

Walter Märzendorfer (2009–2021)
formerly Siemens Healthineers, Forchheim

Medicine

Prof. Dr. med. Ruth Knüchel-Clarke (since 2019)
Institute for Pathology, RWTH Aachen

Astrid Lurati (2018-2021)
Executive Board, Charité – Universitätsmedizin, Berlin

Prof. Dr. med. Mathias Prokop (since 2014)
Radboud University Medical Centre, Nijmegen, The Netherlands

Science

Prof. Dr. Craig Garner (2017-2020)
German Center for Neurodegenerative Diseases (DZNE)
Charité – Universitätsmedizin, Berlin

Prof. Dr. Dr. h.c. Jürgen Hennig (2009-2021)
Medical Physics, University Medical Center, Freiburg

Prof. Dr. Gábor Székely (2009-2021)
Image Science Division, ETH Zurich

Business

Stefan Widensohler (since 2019)
Krauth Invest GmbH & Co. KG, Hamburg

Dr. Christoph Zindel (since 2019)
Siemens Healthcare GmbH, Forchheim

Universities

Prof. Dr. Jens Falta (since 2010)
Dean of Faculty Physics / Electrical Engineering, University of Bremen

Prof. Dr. Kerstin Schill (since 2014)
University of Bremen / Hanse-Wissenschaftskolleg, Delmenhorst

Dr. Alexander Ziegler-Jöns (since 2010)
Science & Technology Transfer, Jacobs University Bremen

Research funding

Dr. Ursula Niebling (2009-2021)
Bremen Senator of Science and Ports, Bremen

Dr. Bernd Roß (since 2019)
Ministry of Education, Science and Culture, Kiel

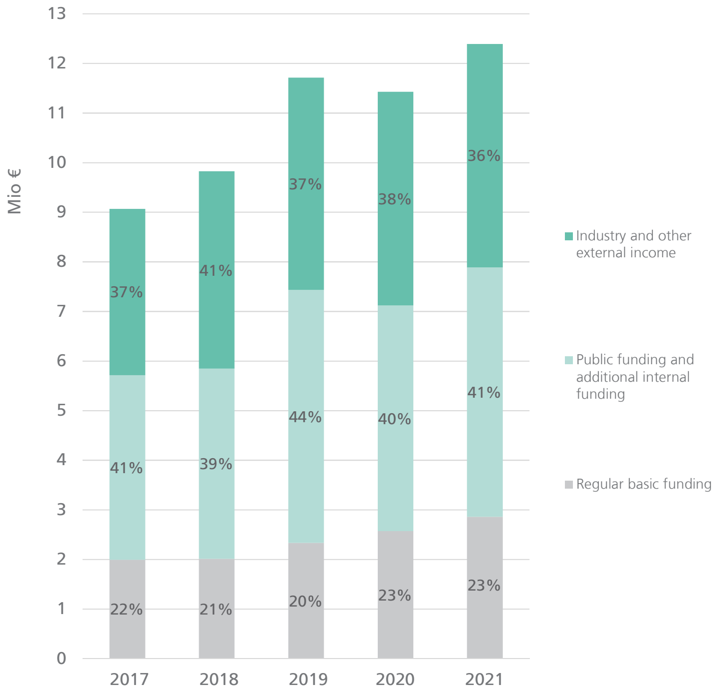
THE INSTITUTE IN FIGURES

Budget and earning trends

Despite the difficult conditions caused by the corona pandemic, the earnings in 2020 and 2021 maintained at the level of 2019. Due to an unexpected project, the completion of a technical upgrade of our MRI scanner, the investment budget in 2021 increased significantly to 947 T€ compared to the previous fiscal years (587 T€ in 2019 and 122 T€ in 2020).

Industry revenues remained at a level above 37% of the total budget (4 308 T€ in 2020 and 4 505 T€ in 2021). This is mainly due to our strategic work base with Siemens and Varian. Earnings from public and internal sources decreased by about -10% compared to an exceptionally strong value in 2019 (5 099 T€), but still represent about 40% of the total budget.

In the reporting period, our basic funding grew steadily by about +10% p.a. compared to the respective previous fiscal year. Thanks to the successful results in 2020 and 2021, the institute's reserve could be significantly increased.



Earnings in million euros in the period from 2017 to 2021.

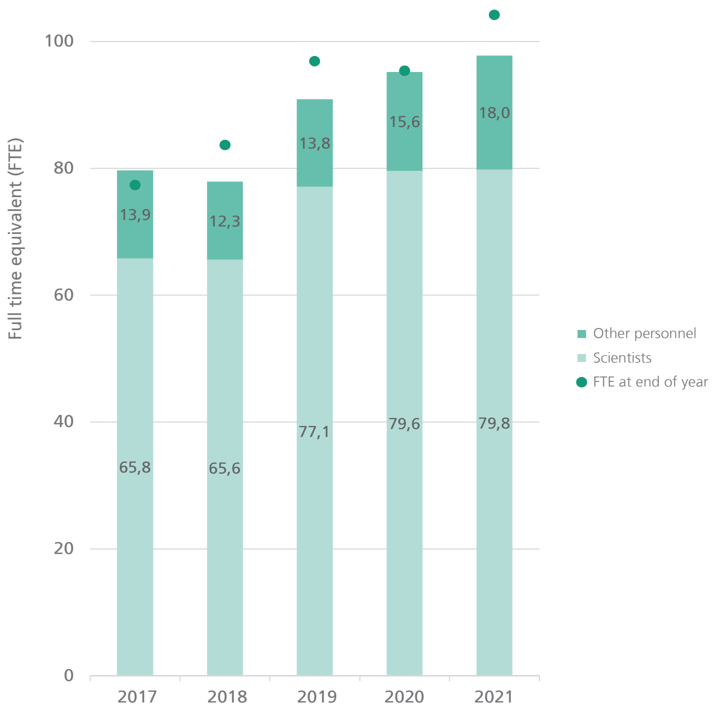
Operating Budget (OB), Investment Budget (IB) and Total Budget in T€:

	2017	**2018**	**2019**	**2020**	**2021**
OB:	8 567	9 577	11 126	11 306	11 448
IB:	500	251	587	122	947
Total:	**9 067**	**9 828**	**11 713**	**11 428**	**12 395**

Human ressources

The overall average number of persons employed by Fraunhofer MEVIS rose continuously in 2020 and 2021. This is due to a good project situation and a corresponding effort to acquire new staff. The number of scientists and the overall number of employees under contract increased by +4.3 full-time equivalents (FTE) in 2020 and +2.6 FTE in 2021 compared to the respective average of the previous fiscal year.

The high value at the end of 2021 (104.2 FTE or +8.8 FTE compared to 2020) indicates a dynamic increase in staff, due in part to the new institute building and the introduction of a new ERP system. We expect further personnel growth in 2022.



Development of employment figures for scientists and other personnel shown as annual average FTE between 2017 and 2021. The dots indicate the staff FTE at the end of the year.

Full-time equivalents as annual average (avg FTE) and at the end of the year (eoy FTE):

	2017	2018	2019	2020	2021
avg FTE:	79.7	77.9	90.9	95.2	97.8
eoy FTE:	77.4	83.7	96.9	95.4	104.2

THE FRAUNHOFER-GESELLSCHAFT

The Fraunhofer-Gesellschaft based in Germany is the world's leading applied research organization. Prioritizing key future-relevant technologies and commercializing its findings in business and industry, it plays a major role in the innovation process. It is a trailblazer and trendsetter in innovative developments and research excellence. The Fraunhofer-Gesellschaft supports research and industry with inspiring ideas and sustainable scientific and technological solutions and is helping shape our society and our future.

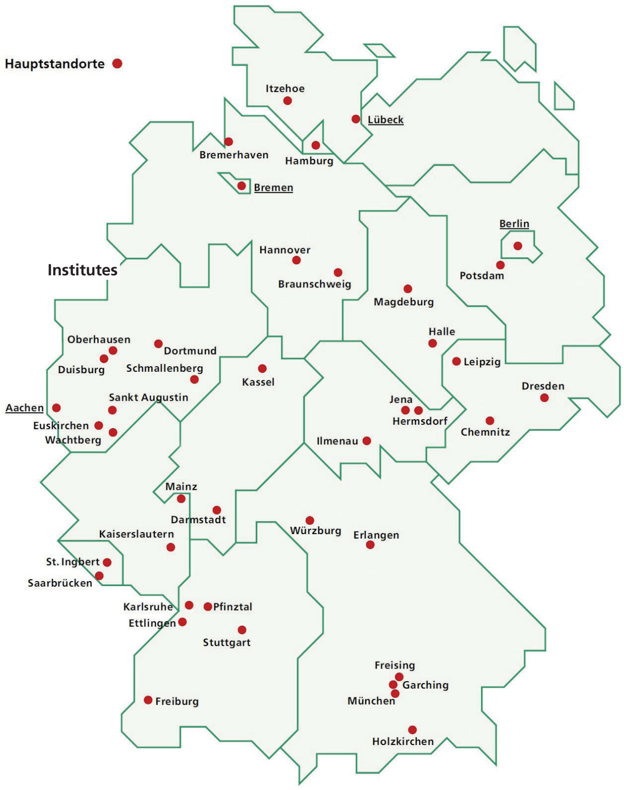
The Fraunhofer-Gesellschaft's interdisciplinary research teams turn original ideas into innovations together with contracting industry and public sector partners, coordinate and complete essential key research policy projects and strengthen the German and European economy with ethical value creation. International collaborative partnerships with outstanding research partners and businesses all over the world provide for direct dialogue with the most prominent scientific communities and most dominant economic regions.

Founded in 1949, the Fraunhofer-Gesellschaft currently operates 76 institutes and research units throughout Germany. Over 30,000 employees, predominantly scientists and engineers, work with an annual research budget of €2.9 billion. Fraunhofer generates €2.5 billion of this from contract research. Industry contracts and publicly funded research projects account for around two thirds of that. The federal and state governments contribute around another third as base funding, enabling institutes to develop solutions now to problems that will become crucial to industry and society in the near future.

The impact of applied research goes far beyond its direct benefits to clients: Fraunhofer institutes enhance businesses' performance, improve social acceptance of advanced technology and educate and train the urgently needed next generation of research scientists and engineers.

Highly motivated employees up on cutting-edge research constitute the most important success factor for us as a research organization. Fraunhofer consequently provides opportunities for independent, creative and goal-driven work and thus for professional and personal development, qualifying individuals for challenging positions at our institutes, at higher education institutions, in industry and in society. Practical training and early contacts with clients open outstanding opportunities for students to find jobs and experience growth in business and industry.

The prestigious nonprofit Fraunhofer-Gesellschaft's namesake is Munich scholar Joseph von Fraunhofer (1787–1826). He enjoyed equal success as a researcher, inventor and entrepreneur.



Locations of Fraunhofer Institutes in Germany. In 2020/21, Fraunhofer MEVIS had major sites in Bremen (headquaters), Lübeck, Berlin and Aachen plus additional offices in Hamburg, Heidelberg, Nijmegen and Boston.

THE YEARS 2020/21

CHRONICLE

2020

January 13-14
Strategy workshop in Bremen with the chairmen of the Fraunhofer MEVIS Advisory Board Prof. Dr. Hans Maier and Walter Märzendorfer.

February 15-20
Fraunhofer MEVIS attends the SPIE Medical Imaging Conference in Houston, Texas with a conference chair, four oral presentations, two courses on Deep Learning, and a live demonstration.

February 28-29
Two-day institute retreat at the seminar hotel Kunze-Hof close to the Jade Bay in Lower Saxony.

March 1
Prof. Dr. Ron Kikinis leaves Fraunhofer MEVIS after six years of dual leadership. Since then, Prof. Dr.-Ing. Horst Hahn is the sole director of the institute with the deputies Prof. Dr. Matthias Günther and Prof. Dr. Tobias Preußer.

March 9
The Senator for Science and Ports, Dr. Claudia Schilling, pays her inaugural visit to Fraunhofer MEVIS.

March 12
A COVID-19 task force is established at Fraunhofer MEVIS. All business trips are cancelled and employees are advised to work mobile or in their home office.

March 26
Girls' Day activities offered by Fraunhofer MEVIS in Bremen and Lübeck.

April 17
Kick-off for the strategy process 2020 with six successive ideation workshops on breakthrough targets.

May 25
Institute director Horst Hahn gives the opening lecture on »How artificial intelligence is changing radiology« at the opening event of the 101st German Radiology Congress.

June 24
For the ninth time, partners from science and industry discuss hot topics in medical technology at the Lübeck Summer Academy (LSA), co-organized by Fraunhofer MEVIS.

July 14
The mayor of Bremen, Dr. Andreas Bovenschulte, visits the construction site of Fraunhofer MEVIS' new institute building on the campus of the University of Bremen.

August
25th anniversary of the founding of the research center MEVIS at the University of Bremen, the forerunner of today's Fraunhofer Institute for Digital Medicine MEVIS.

August 10
The artist in residence program »STEAM Imaging III« begins with Eli Joteva, a Bulgarian intermedia artist and researcher based in Los Angeles, USA.

September 9-13
Fraunhofer MEVIS is part of the 41st Ars Electronica Festival with a virtual guided tour and a panel at the Institute's MRI Lab alongside with Marshmallow Laser Feast (MLF).

October 6
Fraunhofer MEVIS starts an information campaign on the occasion of its 25th anniversary. It presents the institute's main work objectives, which are intended to help shape the future of digital medicine.

October 21
Marshmallow Laser Feast and Fraunhofer MEVIS as scientific partner co-operate on the installation »The Tides Within Us«,

the initial part of the Human Nature exhibit at York Mediale 2020, before launching in full at the Coventry City of Culture with »Observations on Being« from June to August 2021.

November 9
Virtual strategy meeting with participation of the Fraunhofer MEVIS Advisory Board (Kuratorium).

November 29 – December 5
Fraunhofer MEVIS presents itself with a virtual booth at the first purely virtual Annual Meeting and Exhibition of the Radiological Society of North America (RSNA).

2021

February 12
Fraunhofer MEVIS is among the winning teams of the call for »Ideas & Innovation« of the InnoHealth USA 2021 campaign.

April 22
Girls' Day activities offered by Fraunhofer MEVIS in Bremen and Lübeck.

May 4-5
Move into Fraunhofer MEVIS' new institute building »Workshop of Digital Medicine« in Bremen.

May 15-20
Fraunhofer MEVIS is well represented at the virtual Annual Meeting & Exhibition of the International Society for Magnetic Resonance in Medicine (ISMRM).

June 18
Virtual open house for the inauguration of the new institute building of Fraunhofer MEVIS in Bremen.

June 16
For the tenth time, partners from science and industry discuss hot topics in medical technology at the Lübeck Summer Academy (LSA), co-organized by Fraunhofer MEVIS.

July 14
Jury meeting for the competition »Kunst am Bau« for the new institute building in Bremen.

September 15
Virtual meeting of the Fraunhofer MEVIS Advisory Board (Kuratorium).

September 27
Launch of the AI Center for Health Care in the U Bremen Research Alliance.

November 9-10
Fraunhofer MEVIS Strategy Audit 2021 takes place as hybrid meeting in Bremen.

November 15
Fraunhofer MEVIS welcomes LA-based Turkish media artist in residence Zeynep Abes to »STEAM Imaging IV«.

December 1
Winter Workshop 2021 of the Medical Imaging with Deep Learning (MIDL) Foundation, co-organized by Fraunhofer MEVIS.

December 8-10
Artist Daniele Dell'Eva installs the sculptures of his artworks »Menschskulptur« and »Three Clouds« in front of and inside the new institute building in Bremen as part of the »Kunst am Bau« competition.

December 13
Fraunhofer MEVIS' 3T MRI scanner is updated from Siemens MAGNETOM Skyra to Vida Fit.

HIGHLIGHTS

Fraunhofer MEVIS at SPIE Medical Imaging 2020

Computer-aided diagnosis, artificial intelligence and navigation of vascular catheters – these are the topics Fraunhofer MEVIS presented at the »Medical Imaging« conference of the International Society for Optics and Photonics (SPIE), which took place in Houston, Texas, from February 15 to 20. Institute director Horst Hahn co-chaired the four-day conference »Computer-Aided Diagnosis«. MEVIS researchers Markus Wenzel and Florian Weiler offered practical workshops for students, scientists, and engineers on the topics »Introduction to Medical Image Analysis Using Convolutional Neural Networks« and »Adversarial Networks: From Architecture to Practical Training«. Sonja Jäckle received a student paper award for her presentation

New leadership at Fraunhofer MEVIS

Prof. Ron Kikinis, former head of Fraunhofer MEVIS, has accepted a prestigious appointment at Harvard Medical School in the USA. In March 2020, he assumed the »B. Leonard Holman Endowed Professor of Radiology«. This endowed professorship is one of the highest academic honors at the renowned medical school and is only awarded to researchers who are world leaders in their field. Since March 1, 2020, Prof. Dr.-Ing. Horst Hahn has been the sole director of the institute, and his deputies are Prof. Dr. Matthias Günther and Prof. Dr. Tobias Preußer. For the past six years, Prof. Hahn and Prof. Kikinis had formed a dual leadership.

Opening lecture at German Radiology Congress 2020

Institute director Prof. Horst Hahn gave the opening lecture on »How artificial intelligence is changing radiology« at the opening event of the 101st German Radiology Congress, followed by a discussion round. Due to the dynamic development of the COVID-19 pandemic, the 101st German Radiology Congress, originally planned to take place in Leipzig from May 20 to 23, was transformed into the digital training and information program RÖKO DIGITAL.

25th anniversary of the Founding of Fraunhofer MEVIS

August 2020 marks the 25th anniversary of the founding of the MEVIS research center at the University of Bremen. This evolved into today's Fraunhofer Institute for Digital Medicine MEVIS with over 120 employees in Bremen, Lübeck, Berlin, and Aachen. This was a fitting reason to observe the future of the possibilities of digital medicine and concrete application scenarios. The anniversary year was accompanied by articles, audio podcasts, images, and moving images about key issues and essential work targets with which Fraunhofer MEVIS wants to help shape the future of digital medicine. The digital extension of human decision-making processes is not perfect and has its shortcomings just as much as purely human procedures. It is a matter of uniting the specific capabilities of both worlds and adapting technological processes to human needs and abilities. Human-centered digitalization can visualize, explain, and help manage this complexity. With this anniversary campaign, the Institute's R&D Engagement team addressed important work topics artistically, bringing medical image data, anatomical-medical illustration, and volume renderings together to illustrate the Institute's R&D to a broader public.

Artist in residency with Eli Joteva

The artist in residence program »STEAM Imaging«, an interdisciplinary exploration of digital medicine and the human body, has been carried out for the third time. This time, jointly hosted with Ars Electronica in Linz, Austria, in collaboration with the International Fraunhofer Talent School Bremen, and the UCLA ArtSci Center, Los Angeles, USA. The artist in residence was Eli Joteva, a Bulgarian intermedia artist and researcher based in Los Angeles, USA. The concept of her artwork entitled »IntraBeing« was guided by the questions: What lies within the bounds of being? How do our physical bodies and their virtual representations affect one another? The remote residency, and the course following, included encounters during 2020 connecting the artist, Fraunhofer MEVIS scientists, and school students from Schulzentrum Walle in Bremen. The artist's work was also featured at the Ars Electronica Festival in Linz in September 2021.

Moving into the »Workshop of Digital Medicine«

After more than six years of planning and construction, the new building of Fraunhofer MEVIS on the campus of the University of Bremen was completed in May 2021. The building with its rounded geometry and curved white façade consists of three interlocking structures whose basic shape is inspired by nerve cells. With a usable floor space of approx. 2,600 m², it accommodates up to 210 workplaces on four floors. The spatial concept of office, seminar and meeting rooms, as well as technical rooms and individual laboratory areas, offers both retreats for concentrated work and open areas for communication and collaboration. As a »Workshop of Digital Medicine,« the building is to be perceived as a driver of digital change in the healthcare sector and create space for encounters and discussions on the topic of digital medicine. To celebrate the inauguration, the institute openend its doors in an online event on Friday, June 18.

Launch of the »AI Center for Health Care«

A virtual »AI Center for Health Care« has been established in the U Bremen Research Alliance (UBRA), a collaborative environment between the University of Bremen and twelve non-university research institutes including Fraunhofer MEVIS. For this purpose, the state of Bremen provides funds that are awarded to forward-looking projects in the UBRA. Artificial Intelligence (AI) is of critical relevance, especially with regard to health care research. The goal of the U Bremen Research Alliance is therefore to establish an »AI Center for Health Care« as a virtual institute of cooperation across institution boundaries. Fraunhofer MEVIS director Prof. Dr.-Ing. Horst Hahn is spokesman of the lead project »Artificial Intelligence« in the UBRA and one of the initiators of the project.

MRI scans for early detection of Alzheimer's disease

Reliable and feasible early detection of Alzheimer's disease is the goal of DEBBIE, an international joint project under the EU Joint Programme – Neurodegenerative Disease Research (JPND). It is coordinated by the Fraunhofer Institute for Digital Medicine MEVIS in Bremen, which has received national funding from the Federal Ministry of Education and Research (BMBF) for its work. In this project, MRI images shall uncover the extent to which the blood-brain barrier loses function before the first symptoms of Alzheimer's disease appear. To speed up development, Fraunhofer MEVIS has enhanced their own 3T MRI scanner (from Siemens MAGNETOM Skyra to Vida Fit) to allow much more effective cooperation with clinical partners.

»The Tides Within Us« at SIGGRAPH Asia 2021

Fraunhofer MEVIS presented as a research partner, jointly with Marshmallow Laser Feast (MLF), and York Mediale »The Tides Within Us« at SIGGRAPH Asia 2021 Art Galleries. The artwork is an ongoing exploration into the world beyond the limits of our senses at the intersection of art, science, and technology; where does the living body begin, and where does it end? By peering under our skin we reveal the tidal rhythms of oxygen flowing through the branching ecosystem of the human body. The aim is to challenge notions of boundaries between us human beings and our environment. Fraunhofer MEVIS teamed up with MLF, one of the world's leading immersive art collectives, and presented the work last year in collaboration with York Mediale, an international new media arts charity that celebrates York as the UK's first and only UNESCO Creative City of Media Arts the cross-sectoral project.

The enhanced 3 Tesla research scanner for magnetic resonance imaging jointly used by University of Bremen and Fraunhofer MEVIS in Bremen.


SIEMENS
Healthineers
MAGNETOM Vida Fit
A BioMatrix System

AWARDS

2020

2nd Place at SPIE Student Paper Award

Fraunhofer MEVIS scientist Sonja Jäckle is awarded with the runner-up of the Image-Guided Procedures, Robotic Interventions, and Modeling Student Paper Award for her submission »3D catheter guidance including shape sensing for endovascular navigation« at SPIE Medical Imaging in Houston from February 15-20.

Magna Cum Laude Merit Award at ISMRM

The Fraunhofer MEVIS team around Daniel Hoinkiss receives Magna Cum Laude Merit Award for the contribution »Event-Based Traversing of Hierarchical Sequences Allows Real-Time Execution and Arbitrary Looping in a Scanner-Independent MRI Framework« at virtual ISMRM from August 8 to 14.

Winner of CUBDL Challenge at IUS

The Fraunhofer MEVIS team around Sven Rothlübbers wins shared first place in the Challenge on Ultrasound Beamforming with Deep Learning (CUBDL). The challenge was part of the virtual IEEE International Ultrasonics Symposium (IUS) in Las Vegas from September 7 to 11.

Certificate of Merit Award at ESMRMB

The Fraunhofer MEVIS team around Daniel Hoinkiss receives Certificate of Merit Award for the contribution »Guidewire Tracking Based on Passive MRI Markers for MR-Guided Endovascular Interventions« at virtual ESMRMB from September 30 to October 2.

Cum Laude Award at ESMRMB

The Fraunhofer MEVIS team around Daniel Hoinkiss receives Certificate of Merit Award for the contribution »Exchange time as a proxy measure of blood brain barrier integrity – A two-stage estimation« at virtual ESMRMB from September 30 to October 2.

Gorter Price

Mareike Buck wins third place of the Gorter Price for contribution »Modellierung des Strömungsverhaltens von Blut mittels Arterial Spin Labeling« at the annual meeting of the German Chapter of the ISMRM.

Fraunhofer IUK ICT Dissertation Award

André Homeyer wins second place of the Fraunhofer IUK ICT Dissertation Award for his submission »Automated analysis of necrosis and steatosis in histological images – Practical solutions for coping with heterogeneity and variability«.

Highly Cited Researcher

Professor Fabian Kießling is for the second time in a row in the list of highly cited researchers in the »Cross-Cield« category for interdisciplinary researchers who have significant influence on several research fields and areas beyond their own field of work.

2021

Winner of InnoHealth

Fraunhofer MEVIS is among the winning teams of the call for Ideas & Innovation of the InnoHealth USA 2021 campaign. Nine Research-SME-Tandems and their innovative projects are invited to join the Matchmaking Tour USA and the Idea2Project Workshop.

Second place for Live Demo at SPIE

The Fraunhofer MEVIS team around Sven Kuckertz wins second place for their computer-aided diagnosis live demonstration »Fully automated monitoring of lesion evolution over time in multiple sclerosis« at virtual SPIE Medical Imaging in San Diego from February 15 to 19.

Best Poster Award at BVM

Student Carina Tschigor awarded with Best Poster Award for her contribution »Deep Learning-Based Surface Reconstruction from Binary Masks« at virtual BVM Workshop in Regensburg from March 7 to 9.

Magna Cum Laude Award at ISMRM

The Fraunhofer MEVIS team around Daniel Hoinkiss receives Certificate of Merit Award for the contribution »Joint Estimation and Correction of Motion and Geometric Distortion in Segmented 3D Arterial Spin Labeling« at virtual ISMRM from May 15 to 20.

Honorary Mention at STARTS Prize

The cross-sectoral project »The Tides Within Us« receives Honorary Mention at the STARTS Prize 2021 which annually recognizes groundbreaking projects at the interface of science, technology and the arts that have the potential to contribute to economic and social innovation.

Outstanding Reviewer Awards at MIDL

Fraunhofer researchers Alessa Hering and Hans Meine receive Outstanding Reviewer Awards at Medical Imaging with Deep Learning (MIDL) in Lübeck from July 7 to 9.

2nd Place at MIDL Audience Award

Fraunhofer MEVIS researchers Alessa Hering and Jan Moltz win second place at MIDL 2021 Audience Award for best long oral presentation for their presentation »Whole-Body Soft-Tissue Lesion Tracking and Segmentation in Longitudinal CT Imaging Studies« at the MIDL in Lübeck from July 7 to 9.

North German Future Prize for Artificial Intelligence

Andrea Schenk receives the »Norddeutscher Zukunftspreis für Künstliche Intelligenz« during the AI Week in Lübeck from November 15 to 19, 2021. The prize donated by the Junge GmbH recognizes her work in AI-based liver surgery planning.

Highly Cited Researcher

Prof. Dr. med. Fabian Kiessling is recognized by Clarivate as a Highly Cited Researcher 2021 in the Pharmacology and Toxicology category. This is the third consecutive year he has been on the Highly Cited Researcher list.

SCIENTIFIC PUBLICATIONS

Journal articles 2020

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