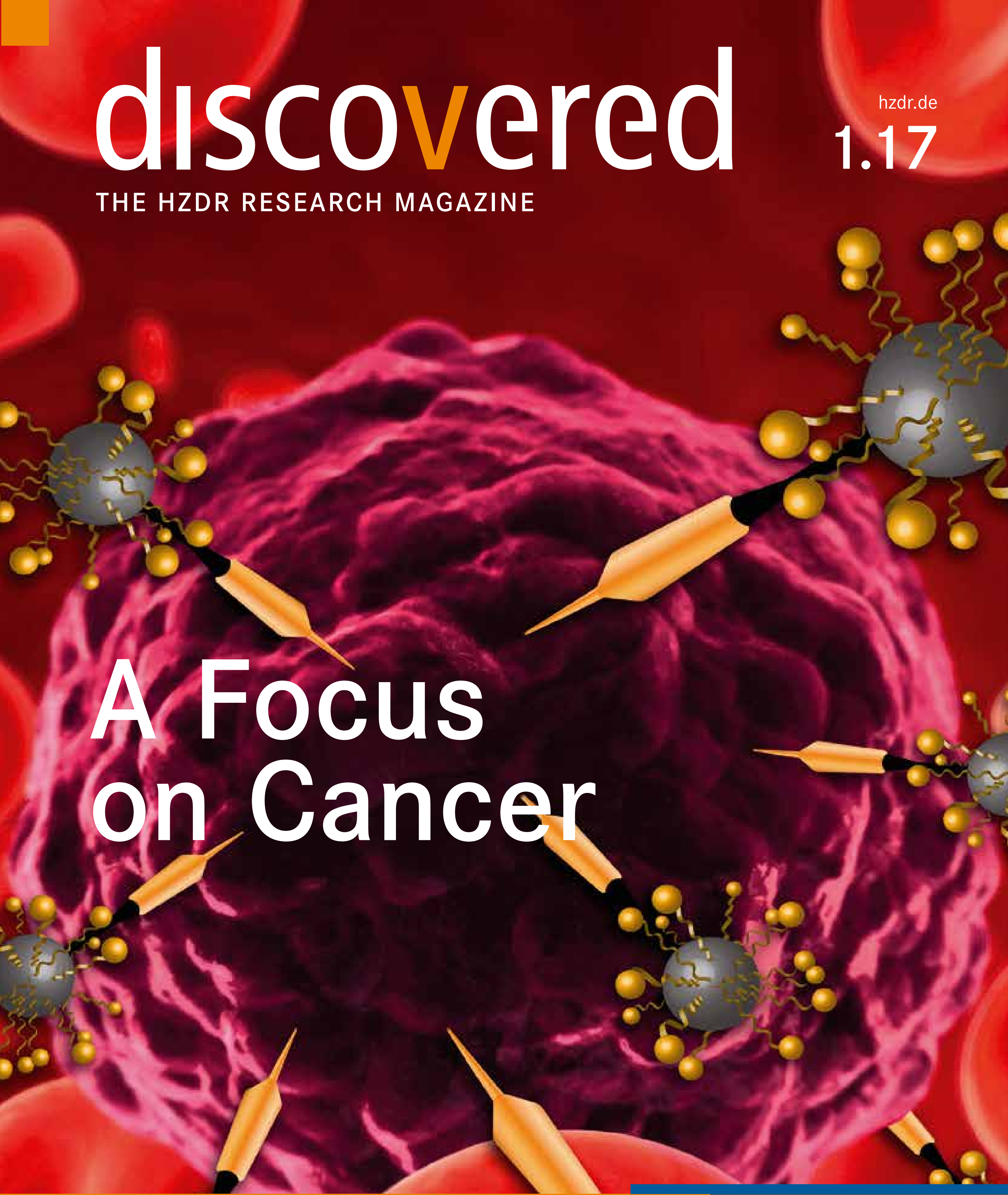
hzdr.de
1.17

discovered

THE HZDR RESEARCH MAGAZINE



A Focus on Cancer

How to simulate a giant planet in the lab
HZDR physicists study new state of matter

"Turn right for the tumor"
A vision of the operating room of the future

A glimpse into the black box of flow
The wind tunnel bubble column connection

HZDR
HELMHOLTZ
ZENTRUM DRESDEN
ROSSENDORF

Dear readers,

You may well have noticed when you opened the cover that this edition of "discovered" looks a bit different from its predecessors. As the old saying goes, nothing is as constant as change, so we have updated the look of our magazine. The focus of content is, however, still on our research which aims to find solutions to the pressing issues of our age. One of the major challenges is the battle against cancer. Together with national and international partners, HZDR researchers are investigating new approaches to detecting, characterizing and treating tumors.

Cooperation – not just between different locations, but also across disciplinary boundaries – plays a crucial role. In collaboration with the German Cancer Research Center in Heidelberg, Carl Gustav Carus University Hospital and the Medical Faculty at TU Dresden, for instance, we recently laid the foundations for the National Center for Tumor Diseases in Dresden. This is where the operating room of the future is to be created, where computers assist surgeons with their work.

Scientific work can sometimes feel like a Sisyphean task. New insights and successes trigger new questions and challenges at the same time. Take proton-based cancer therapy that also generates neutrons. Exactly how many and what they do is something physicists want to find out. Chemists and biologists, on the other hand, want to investigate why cancer stem cells develop during radiotherapy and how they can be prevented. So, constant change is a central motif of research, as well.

I look forward to receiving your questions, comments and suggestions and hope you enjoy reading this edition of "discovered".

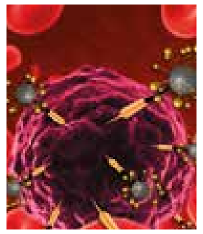
Christine Bohnet
Department of Communications and Media Relations at HZDR

Content

Portrait

Source: NASA

Research



Cover Picture: HZDR researchers are working on nanoparticles that should make the task of diagnosing cancer easier. Their aim is to combine all the elements that are needed to trace diseased cells in these ultrasmall particles. In addition to tumor-seeking entities, they should contain a radionuclide and a special dye. The idea is that the surface of the nanoparticles should be modified so that they mostly accumulate at the tumor, making it possible to image the diseased area both by PET scan and intraoperatively using fluorescence. Source: Composing – Michael Voigt / Werkstatt X | Sebastian Kaulitzki / Fotolia | media_ag / Fotolia

Publication:
J. A. Barreto et al., in Advanced Materials, 2011 (DOI: 10.1002/adma.201100140)

Title A Focus on Cancer

Panorama – HZDR News

Healing rays

How many friends do you have? More than 20? If so, there is a strong possibility that at least one of them has already suffered from cancer. Currently, some four million people in Germany have experience of living with a tumor caused by uncontrolled cell growth. Since the 1970s, the absolute numbers of new cases have almost doubled. In the last two or three decades, however, the chances of survival have increased significantly as well – evidence of progress in diagnostics and treatment. In their fight against this insidious disease, HZDR researchers mainly put their trust in radiation – one of the central pillars of cancer therapy. In the case of proton therapy, for example, the tumor is targeted with charged particles to damage the genetic material. Together with Dresden University Medicine, physicists at HZDR are investigating methods for tracing the course taken by the rays and considering approaches to reduce the size of the enormous facilities needed to generate the particles.

For many years, chemists and biologists at the research center have been developing radioactive drugs which can dock onto the cancer cells. Using imaging methods like positron emission tomography it is possible in this way to determine the location and properties of tumors. The drugs could be also transported directly into the tumor to irradiate it from inside. While demographic change means the number of people with cancer is likely to continue increasing in the coming years, thanks to this kind of research, so is also increasing the number of people who will overcome the disease.

Publication:
M. Patra et al., in Chemical Society Reviews, 2016
(DOI: 10.1039/c5cs00784d)

Source: istockphoto.com / Spectral-Design, wildpixel, svisio

Research Highlights

RAW MATERIALS

Bacteria as Miners

In flotation, a routine procedure to process ores, finely ground rock is mixed with water and additional substances. As shown in the illustration, the desired resources attach to air bubbles introduced in the liquid. So far, this process has required the use of chemicals. Researchers at the Helmholtz Institute Freiberg for Resource Technology at HZDR and the Universidad de Chile are now working on replacing these chemicals with bioactive substances derived from bacteria. The plan is to get these substances to attach to the ores, collecting the metals copper and molybdenum while holding back unwanted minerals. This could render the method far more ecological.

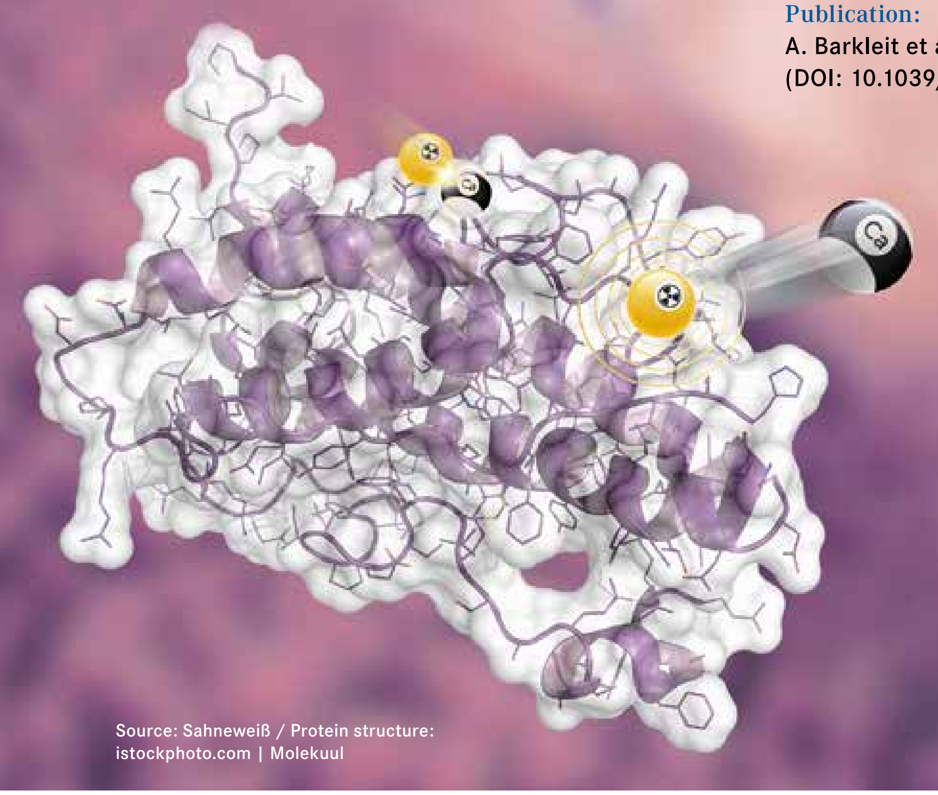
Source: 3D Kosmos

RADIOECOLOGY

Molecular Billiards

Highly toxic radioactive substances such as actinides can attach to digestive tract proteins very fast and tightly, as radiochemists from Rossendorf found out when they examined the protein alpha-amylase. This enzyme, produced by the salivary glands and the pancreas, breaks down the sugars in our food. If actinides enter the human body via food and drink, for instance if the environment is radioactively contaminated, calcium in the protein could be replaced by the actinides, which allows the radioactive substance to spread through the organism. The study provides valuable information on the molecular interaction between the actinides and human proteins.

Publication:
A. Barkleit et al., in Dalton Transactions, 2016
(DOI: 10.1039/C5DT04790K)



Source: Sahneweiß / Protein structure: istockphoto.com | Molekuul

CANCER RESEARCH

Tiniest Trojans

Chemists from Rossendorf have succeeded in coating tiny nanoparticles of iron oxide with a zwitterionic layer, resulting in a neither positive nor negative surface charge of these minute particles, which measure no more than five nanometers. This is an important step towards using particles in the fight against cancer, because in contrast to nanoparticles which are stabilized with coating agents such as polyacrylic acid - the most widely used substance - this new method will form almost no protein corona around the particle. The particles can therefore travel to the tumor almost unnoticed by the human immune system. Combined with radioactive markers, this method will enable physicians to visualize diseased cells using imaging technologies. The method might even be used for radiating cancer cells.

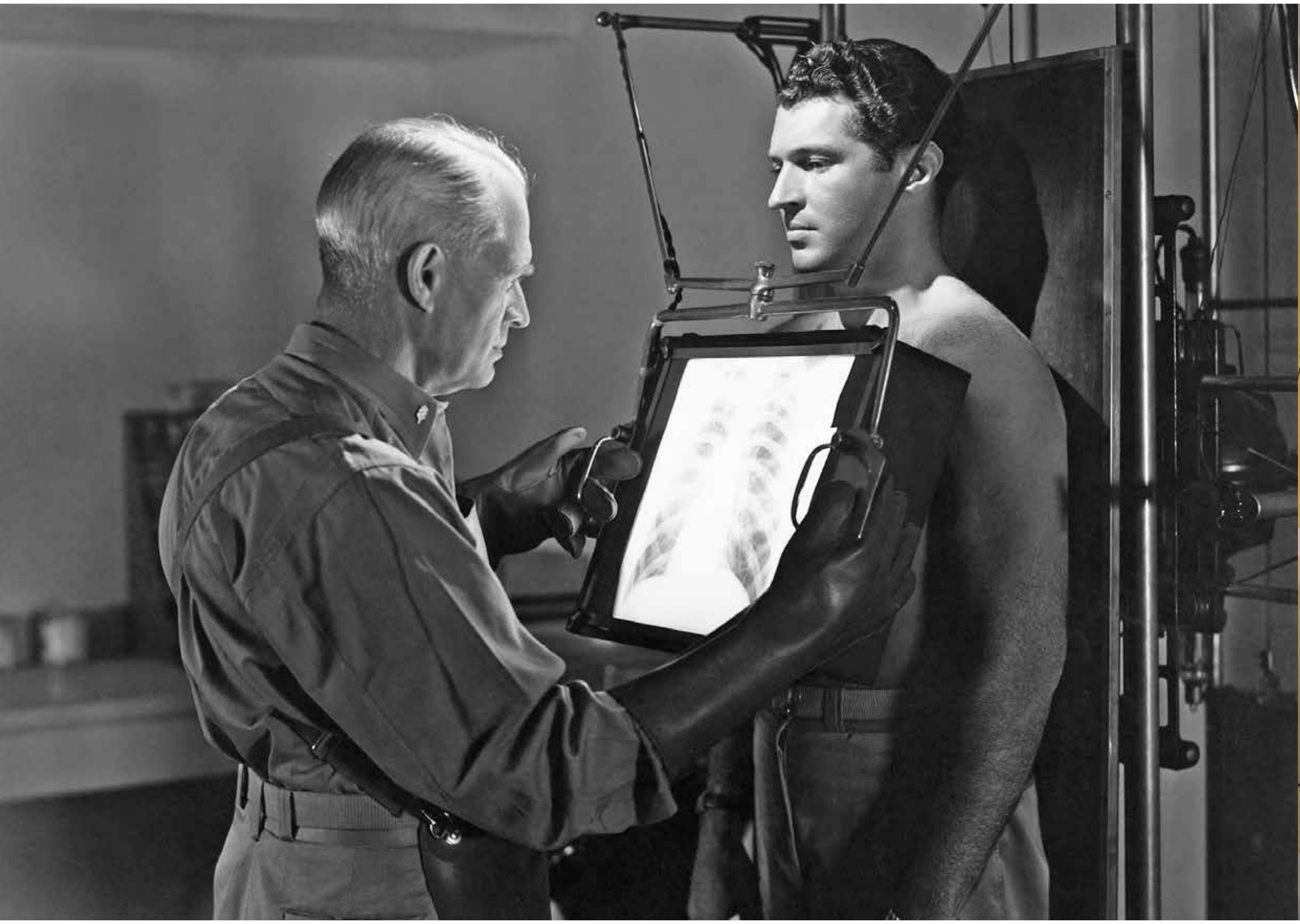
Publication:
K. Pombo-Garcia et al., in ChemNanoMat, 2016
(DOI: 10.1002/cnma.201600233)

QUANTUM PHYSICS

Superfluid – and yet solid

Physicists at the University of Augsburg and the Dresden High Magnetic Field Laboratory have discovered clues indicating that materials can be solid and superfluid at the same time – or, as scientists call it, supersolid. The scientists exposed a compound of manganese, chrome and sulfur to a high magnetic field and low temperatures, which made the spin, i.e. the magnetic moment, of the manganese and chrome atoms align in a special order. The manganese spins can align parallel, antiparallel or in any other direction relative to the magnetic field, which can be described as superfluidity. The chrome spins, on the other hand, remain parallel to the field. This triggers an unusual, almost constant magnetization between circa 25 and 48 Tesla.

Publication:
V. Tsurkan et al., in Science Advances, 2017
(DOI: 10.1126/sciadv.1601982)



Rapid progress: Just a few decades divide the beginnings of imaging using X-rays from modern procedures such as positron emission tomography. Source: Everett Collection / shutterstock (left) / F. Bierstedt (right)

A clear view of cancer

Irradiating cancer cells is like walking a tightrope: If doctors assign too big an area to treatment, they risk damaging healthy tissue. If they are too circumspect, they are in danger of missing part of the tumor, which can lead to relapse. Radiooncologist Esther Troost therefore works on imaging methods that provide physicians with more detailed information – an important basis for tailoring radiation therapy to the needs of the individual patient.

_ Text . Nadine Querfurth

November 1895: Physicist Wilhelm Röntgen discovers X-rays. The ability to look inside a patient from the outside revolutionizes medicine. Inspired by Röntgen's rays, Henri Becquerel, Marie Curie and Ernest Rutherford experiment with radioactive elements. In 1907, their potential for cancer therapy was recognized by the British inventor Alexander Graham Bell. He was convinced that there is no reason why "a tiny fragment of radium should not be inserted into the very heart of the cancer". He had no idea of the dangers involved for doctors and patients. Since those days, there have been massive improvements in radiation protection and the targeted precision of radiotherapy, especially in the last few years. "Even just fifteen or twenty years ago, our planning was two-dimensional. To calculate the radiation dose, we looked at the patient as a container filled with distilled water – a so-called water phantom," Esther Troost remembers. "With the aid of millimeter paper and X-rays we calculated what dose had to go where."

Today, doctors use state-of-the-art imaging that allows them to view the tumor and surrounding organs potentially at risk for their radiation planning. The software delivers three-dimensional images. "We have now reached a stage where we can even take into account the movement of tumors – we think of it as the fourth dimension," Troost explains. The professor of image-guided high-precision radiotherapy heads a division at HZDR's Institute of Radiooncology – OncoRay as well as a research group at the National Center for Radiation Research in Oncology – OncoRay, a joint research platform incorporating Carl Gustav Carus University Hospital, the Faculty of Medicine at TU Dresden and HZDR. Her aim is to develop radiotherapy so that more patients can be healed of their tumors. "My heart beats for translational research, for the speedy, efficient transfer of pre-clinical research to clinical applications." So, in her everyday work, the deputy director of the Department for Radiotherapy and Radiooncology seeks to closely interlink the two fields.

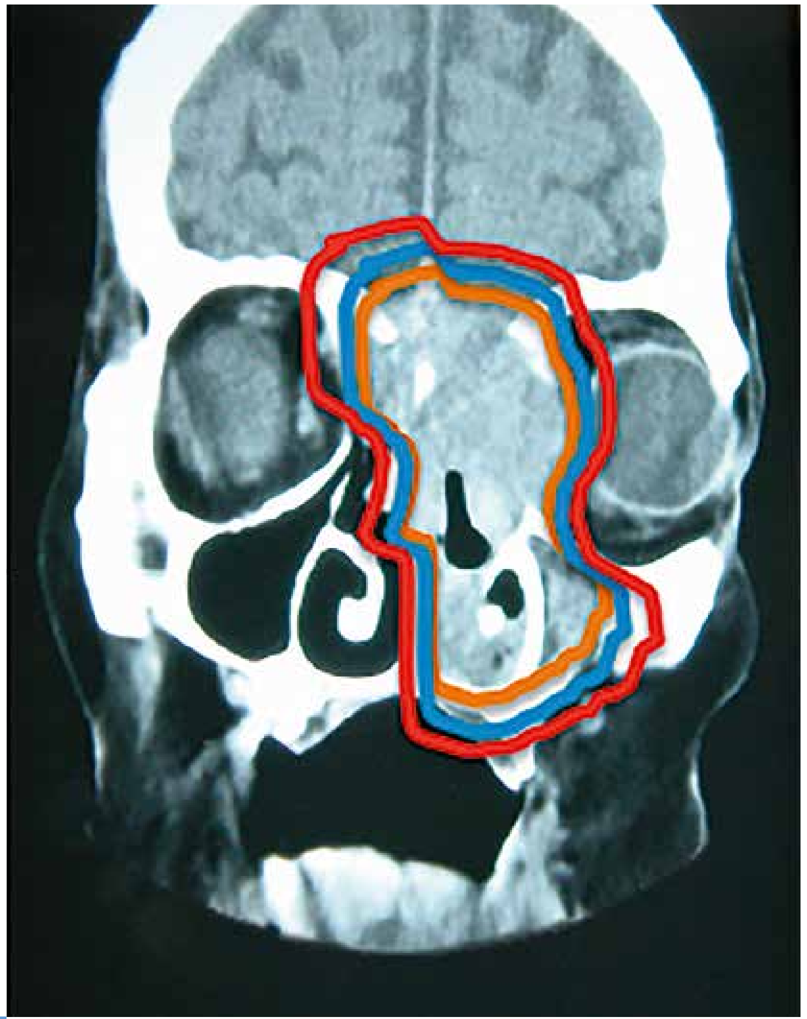
"I'm driven by the desire to ensure that my research results benefit patients in the shortest possible time. We need personal contact to understand which direction our research should take. This helps us pinpoint how we can improve the treatment of tomorrow's patients." Therapy strategies tailored to the individual are the main goal: "We would like to develop precisely the right treatment strategy for individual patients with a specific tumor," the radiation oncologist explains. "At the moment, the prescribed dose works on a one size fits all basis. Specific tumors are treated with a radiation dose found to be effective in randomized clinical studies. This might not be enough for one patient but too much for another. To discover exactly what dosage the individual patient needs and can tolerate would be amazing. I want to use imaging to analyze this and learn from the image data."

Esther Troost routinely produces images for the radiation plan using various imaging procedures – also known as molecular imaging. While on the pictures generated by high-performance computed tomography (CT) the anatomical condition of tumors can be captured well, the metabolic activities of cancer cells cannot. For this purpose, doctors use PET, positron emission tomography. The patient is injected with a radiotracer, a marker which has been laced with a radiolabeled substance, containing, for example, sugar. Because tumor cells usually have a higher metabolism, they accumulate larger amounts. The radiation given off by the radiotracer can be detected and captured in detailed, three- and four-dimensional images. If the results of both procedures are fused, computerized PET/CT images are produced, revealing not only the precise location and size of the tumors but also their metabolic activity.

These parameters deliver important information for radiation planning. One of the major challenges is to determine the target volume as precisely as possible. Physicians refer to it as target volume contouring. The objective is to inflict maximum damage on the entire tumor while avoiding the healthy tissue roundabout. Esther Troost and her team are working on new models for calculating optimum target volumes. Not all imaging procedures are equally fit for purpose. "For target volume contouring," says Esther Troost, "PET imaging has its pitfalls because normal tissue can also be infiltrated by the radiotracer. We have to examine what is supposed to be irradiated very carefully and analyze whether it is really tumor tissue or an inflammatory reaction around the tissue."

If the target volume the doctors contour is too large, there is a danger that the tissue will receive too high a dose of radiation. "We then risk damaging healthy tissue. If the contour is too small, we might not hit the entire tumor and it'll start growing again." Another challenge facing doctors is the fact that the tumor tissue can shrink in the course of therapy. New strategies are supposed to factor in precisely this kind of development. "At present, we use X-rays or CT images during therapy, which both mean the patient is exposed to radiation yet again. That's why we are testing whether we can use magnetic resonance imaging (MRI) instead."

Esther Troost uses new imaging ideas to better characterize and treat tumors. Source: R. Weisflog



Skull base tumor treatment plan: the orange border on the image shows the volume of the tumor. With a margin of typically five millimeters, it is expanded (blue) to the clinical target volume (CTV). In order to compensate for systematic and random errors, doctors expand the CTV further to the planned target volume (red). Source: E. Troost

To produce MRI images, Esther Troost and her colleagues utilize ultra-modern PET/MRI equipment that was moved from HZDR to OncoRay on the campus of Dresden University Hospital at the beginning of 2015. "In comparison with CT, this hybrid imaging delivers far more information about soft tissue," Troost comments. The radiooncologist does not only use the equipment to generate data for target volume contouring but also to visualize damage to healthy tissue after radiotherapy. Imaging, however, does not allow doctors to discern clearly whether tumors with the tiniest capillary extensions are invading the surrounding tissue.

Tracking down the diseased cells

And that is another thing for which Troost would like to establish models. So far, they are based on old data sets with a restricted number of tumor specimens that were removed by operation. "My goal is to find a way of measuring the microscopic spread of a tumor in individual patients. The contributory parameters are probably primary localization – the area where the tumor originally occurred –, the histology and the degree of the tumor, but maybe also biological factors. That's what we're going to look at in the next few years."

The model for predicting infiltration which could inform radiation planning before and possibly during therapy is still very theoretical. At the moment, data from previously published scientific literature are being included in the calculations. "We will underpin this with our own studies on tumor specimens," Esther Troost predicts. "We want to use both the specimens and the various imaging procedures to examine what happens to the microscopic spread of tumors during irradiation. Is the five-millimeter margin that we currently use sufficient? Would two millimeters suffice or do we even need eight millimeters for some patients? These questions are even more important when you are dealing with novel proton particle therapy than they are when using X-ray radiation."

Treatment with accelerated particles has been available for patients at the University Proton Therapy Facility in Dresden since the end of 2014. The centerpiece of the facility is a cyclotron that speeds up the protons to nearly two-thirds the speed of light. Seven hundred tons of equipment is needed to produce the tiny charged particles that are then accelerated and redirected by multiple electromagnets to reach the patient in a precise beam. In comparison with traditional X-ray radiation, proton therapy has crucial advantages for patients: "We can calculate the precise energy charged protons need in order to discharge their dose into the tumor. By a steep drop in dosage we get a zero measurement in the tissue behind," says the radiooncologist. "That's why we can protect healthy tissue so well using protons."

For Esther Troost, who is employed by both the University Hospital and HZDR, OncoRay is not only an attractive research location thanks to its modern equipment. "There are all sorts of additional opportunities for interdisciplinary cooperation," she says approvingly. The proximity of partner institutions, the logistics and the internationality are ideal. "Thanks to all these opportunities, OncoRay is a jewel that conducts very sound research." Ideal pre-conditions for making further advances in radiation therapy.

Contact

_Institute of Radiooncology – OncoRay at HZDR / National Center for Radiation Research in Oncology – OncoRay
Prof. Esther Troost
e.troost@hzdr.de

"Turn right for the tumor"

Enter address, press ok, set off. When we are heading for new destinations by car we usually, quite naturally, rely on navigation devices. The future scenario in the operating room could be quite similar: intelligent assistance systems guiding surgeons reliably and directly to the tumor. Computer scientist Stefanie Speidel of the National Center for Tumor Diseases (NCT) in Dresden develops such approaches using virtual and augmented realities.

_Text . Anna Kraft

Tomorrow's operating room will be jam packed with technology: a robot arm guiding the endoscope, sensors measuring the position of the medical instruments – integrated in a digitally networked system, they all have one overriding function: to pool the flood of data and extract what is useful in the given context. "We are working on delivering the right information at exactly the moment that surgeons need it – nothing more, nothing less," says Stefanie Speidel,

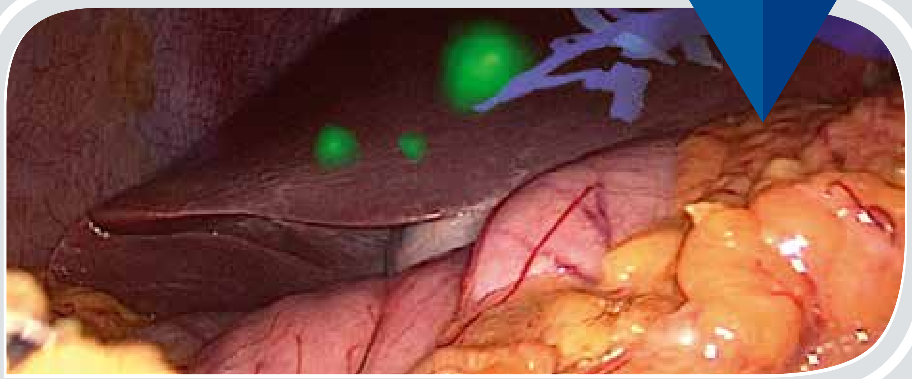
Stefanie Speidel is working on the operating room of the future. Source: A. Wirsig

who became Professor of Translational Surgical Oncology at NCT Dresden in April. "But today, and in future, it'll still be the surgeons who have the responsibility and make the decisions during the operation. We are merely offering them intelligent support for their work."

This kind of support is particularly needed in minimally invasive operations where the surgeon only makes a small incision in the patient's skin and controls the surgery via endoscopic images. The navigation system Speidel and her team are working on adds additional information to the two-dimensional video images, such as a three-dimensional view of the areas that are supposed to be operated or vessels that should not be damaged. Superimposing a computer-generated image on a view of the real world is known as augmented reality. The system can calculate the accurate incision and location of the tumor in the liver, for example, and guide the surgeon through the operation.

Mobile surfaces hamper navigation

In neuro- and orthopedic surgery, where operations are conducted on largely stable structures, comparable systems are already being used. What is new, and particularly difficult, is the development of navigation systems for soft tissue such as the abdominal region. "It is extremely complex to predict tissue deformation," the computer scientist explains. "During surgery, the surface of the organ is changed, not just by the patient's breathing or heartbeat but by contact with instruments. In real time, we have to analyze and image these variations, which are a bit like changing position in a car. To stay with the driving metaphor: What use is a system that merely informs us: 'You should have turned right 300 meters back'."



Directly to the tumor thanks to augmented reality: the three-dimensional representation of the tumors (green) and the vascular tree (blue) are superimposed on the endoscopic image of the liver. Source: KIT

To this end, Speidel combines image data acquired before and during surgery with biomechanical models and develops new programs that can use this information to directly calculate changes in the surface. "Another problem we're working on is predicting complications. It's our aim to be able to provide the surgical team with information like the need for more blood reserves at an early stage." Another goal is to support surgeons by using a robot that guides the endoscope and shows them what the next step should be.

Surgery 4.0 delivers necessary data

One particular challenge Speidel faces is obtaining the necessary data for her research – because standard operating rooms are not equipped with sensors. "That's why I'm really looking forward to the digitally networked operating suite that is being installed in the new NCT building," Speidel explains. "In future, we'll be able to collect a lot of additional data during surgery there." The new NCT building on the site of Dresden University Hospital is due to be completed in 2019 and will provide space for some 200 cancer researchers.

In addition to augmented reality, Speidel investigates innovative solutions in the field of virtual reality. The latter involves computers generating a three-dimensional environment with which the user can interact in an apparently physical way. She is developing special software for data glasses, for instance, which will allow surgeons to view a three-dimensional model of the organ or tissue to be treated before surgery. With a hand movement, the projection can be twisted and turned, as desired. "The data glasses could also be used by tumor boards, experts from different fields who decide on the ideal therapy for a patient, or for training medical students."

Building a bridge between disciplines and locations

Before moving to Dresden, Speidel was a researcher at Karlsruhe Institute of Technology (KIT) and cooperated closely with scientists at the German Cancer Research Center (DKFZ) as well as doctors at Heidelberg University Hospital. At NCT she now enjoys outstanding conditions for driving her interdisciplinary research across sites. "Karlsruhe doesn't have a medical faculty and in Heidelberg there is no engineering – TU Dresden has both. There are close connecting factors to various surgical fields at Dresden University Hospital. Moreover, we want to use the new potential for imaging during surgery, which is being developed at HZDR."

Speidel's work could benefit patients in the foreseeable future. Pilot studies are already testing the data glasses, uploaded with the surgical planning program. In the Dresden operating room of tomorrow, the computer scientist wants to study the navigation system and the use of robots. "I think it's absolutely realistic to envisage these technologies being implemented in clinical practice for certain operations in about ten years' time," Speidel emphasizes. "This, of course, pre-supposes the right kind of collaboration with industry to develop a product from a research prototype." So, that means stepping on the accelerator pedal and heading directly for Surgery 4.0.

Contact

_National Center for Tumor Diseases NCT Dresden
Consortium: Carl Gustav Carus University Hospital, Medical Faculty of TU Dresden, Helmholtz-Zentrum Dresden-Rossendorf, German Cancer Research Center (DKFZ)
Prof. Stefanie Speidel
stefanie.speidel@nct-dresden.de

www.nct-dresden.de

Science defies Sisyphus

Sometimes research seems like a Sisyphean task. In Greek mythology, Sisyphus, King of Corinth, was condemned to keep rolling a heavy stone to the top of a hill. Just as he reaches the top the huge rock rolls down to the bottom again. To scientists, this is all too familiar. Success always throws up new questions and challenges. Unlike Sisyphus, however, researchers do not usually have to start from the valley floor but set out from a higher point than they started from.

_Text . Marcus Anhäuserr

Most people think of science as a straight climb to the summit of knowledge because the media, on the whole, only tend to tell them about the successes. But this arduous path is littered with setbacks – and they are probably more frequent than the big success stories. A mantra common in science says: the path to the top means two steps forward and one step back. New insights constantly generate new questions. New technologies mean new solutions – but also new risks. Just like with medicinal drugs: no benefits without side effects.

In medicine, in particular, reports Mechthild Krause, Director of the National Center for Radiation Research in Oncology – OncoRay and the HZDR Institute of Radiooncology, unforeseen difficulties repeatedly occur when it comes to taking the step from lab to clinical trials: "Preclinical results that initially seem really promising often come back after the first clinical trial peppered with question marks because the results we had hoped for can't be achieved at first." This means analyzing the problems and searching for the causes that got missed originally – experience shows that this is more likely to happen with new approaches than with technologies which have been used for some time.

But even with established methods like proton therapy or classic radiotherapy involving ultrahard X-rays, scientists still encounter new problems or have to deal with questions that nobody has examined carefully enough before. Take Benjamin Lutz who would definitively like to discover precisely how many neutrons with how much energy are actually produced during proton therapy, because the uncharged particles are the problem children of this form of treatment.

The researcher, who focuses on detector physics, stands next to the proton facility in the basement of the OncoRay building looking small and a little bit lost, despite being a broad-shouldered six-footer. That is how massive the gantry frame is, all 120 tonnes of it that stand in the three-storey hall. The giant is reminiscent of the sort of mount that supports a telescope in an observatory. Like a basket, enormous steel girders embrace the device, which will certainly not enable anyone to gaze into the infinity of space; instead, it shoots particles at a cancer tumor as precisely as possible.

Patients have no idea how huge the steel construction is that hides behind the futuristic wall of the treatment room. There the proton beam is funneled into a tapered nozzle. Thanks to the steel gantry, it can be maneuvered precisely over and around the patient lying on a carbon operating table. The mobile structure slowly revolves the nozzle until it reaches the exact position for shooting the protons into the patient's body, fully exploiting one of its strengths: the sharply-defined irradiation of the tumor tissue, down to the last millimeter, without affecting the tissue behind it.

The search for uncharged particles

In contrast to classic X-ray radiotherapy, the proton beam can be adjusted so that the particle emits most of its energy within the tumor. The damaging effect of the proton is thus completely released in the tumor tissue. The electromagnetic waves in X-rays, on the other hand, also affect the healthy tissue in front of and behind the tumor because the beam goes right the way through. Nevertheless, proton therapy does harbor the risk of damage, if at a significantly reduced level.

Even after two years of working here and at the Helmholtz-Zentrum Dresden-Rossendorf, Benjamin Lutz is still impressed by the steel construction. But it does, in fact, make his job harder because the physicist focuses on the things that can increase the risk of side effects from proton therapy, such as secondary tumors, just when you thought the cancer had been beaten: neutrons.

These uncharged particles occur when the proton beam wanders around matter, and this happens several times on the flight from particle accelerator to tumor, "right at the beginning, when the beam exits the accelerator vacuum chamber through the exit window," Lutz explains. One crucial point is to be found at the end of the journey taken by the positively charged particles: brass discs in the nozzle with holes in the middle that reproduce the cross-section of the tumor and form the beam so that it is exactly the size of the diseased area. "A comparatively large number of neutrons occur here," says Lutz.

Quite logically, the uncharged particles are, of course, still being generated when the beam reaches the tumor and unleashes its destructive energy. "But they are unavoidable," says Lutz. The problem with neutrons is that in the worst, if very rare case, a new tumor can develop, although researchers believe that the risk is much lower than in classic radiotherapy. Nonetheless, it would be desirable to generate as few neutrons as possible. And to do that, you have to know how many there are in the first place.

How many particles are really generated?

For many years, experts hotly debated the issue of the number of neutrons to which a patient is exposed. In 2006, radiation researcher Eric Hall published a critical essay that caused a sensation in the community. In another article a year later, he presumed to make the much-quoted claim: "Does it make any sense to spend over 100 million dollars on a proton facility, with the aim to reduce doses to normal tissues, and then to bathe the patient with a total body dose of neutrons?" Today, we know that the figures Hall came up with were far too high because the data on the scattering dose he was working with were wrong. Now it is agreed: "Proton therapy always has the edge over photon therapy for example, simply because we get far less radiation scattering," Lutz explains, period.

Unlike Sisyphus, research usually starts out from a higher summit of knowledge, even after setbacks.

Panorama: Composing – Werkstatt X / Michael Voigt | Sisyphos: zhekakopylov / © superiorstocker / Fotolia

Targeting cancer: At the University Hospital's proton therapy facility, doctors can damage tumors precisely. Source: NCT / P. Benjamin

The construction in Dresden is one of a handful worldwide that allow patients to be treated in the gantry (left) and experiments with charged particles to be conducted in a special experimental space (middle). The protons are generated by the ring accelerator (right). Source: OncoRay

With the help of so-called Bonner spheres from the National Metrology Institute, Dresden researchers studied the formation of neutrons in the proton therapy treatment suite. Source: B. Lutz

"But it's not enough simply to know that it's better," Lutz comments. He and his colleagues want to establish precise values, not just out of scientific curiosity but for particularly sensitive cases when children, pregnant women and especially their delicate unborn children have to be treated. "We already had a case like that here," reports Lutz. There are many reasons why claims about the number of neutrons differ so much: "On the one hand, neutrons are very difficult to measure," Lutz explains. As they do not have a charge they cannot be directly traced with ionization-based detectors. "Apart from that, with proton therapy we are entering a field of energy in which research on neutrons hasn't exactly been exhaustive so far."

Thanks to nuclear research, scientists have a pretty good idea what is going on in the field up to 20 mega electron volts. But in proton therapy they are looking at up to ten times that energy. An added complication is that, across the world, nearly all the facilities were developed exclusively for cancer patient therapy, not for research purposes. This is what makes the OncoRay facility in Dresden so special – both purposes are combined. Benjamin Lutz and his team can use a huge room, almost a hall into which the proton beam can be redirected.

It is here that researchers test various configurations such as different materials like brass, plastic or graphite that form the beam in the nozzle in order to determine the frequency of neutrons released along the energy spectrum. To address this particular challenge the Dresden team cooperates with the measuring experts at the German National Metrology Institute (PTB) in Braunschweig. They have special neutron detectors known as Bonner spheres, which have nothing whatsoever to do with the town on the Rhine. They are named for their developer, the US experimental physicist Tom Wilkerson Bonner, who first introduced them in a scientific article in 1960. The spheres contain a sensitive helium-3 counter, a tube in which the neutrons collide with the helium nuclei, indirectly generating ionization, an electric impulse that can easily be counted. The tube on its own, however, only responds to slow thermal neutrons which are found very low down the energy spectrum. For higher energies, the neutrons have to be decelerated to a speed that can be registered by the counter tube. This is where the Bonner spheres come in: they are made of various thicknesses of polyethylene casing. "Parts of the polyethylene have much the same composition as water. Instead of oxygen, we have carbon: H_2C instead of H_2O – which means that the neutron also collides with the hydrogen and, on average, loses fifty per cent of its energy. The thicker I make it, the more I can decelerate it," explains Lutz.

Measured down to the last detail

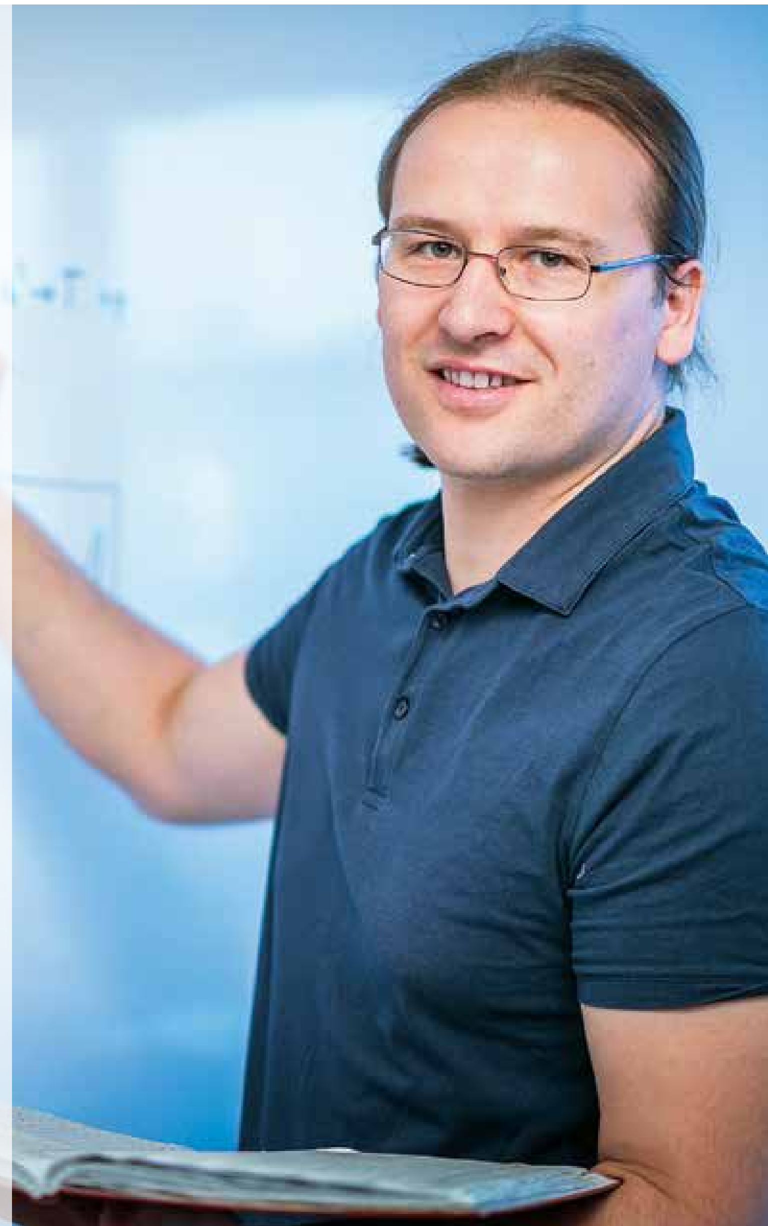
Of course, it is not only the brass discs in the nozzle that slow the neutrons down: Basically, anything in which the neutrons collide with its atomic nucleus can do the job even though they shoot through most objects as though they were not there. Benjamin Lutz has to factor all this into his calculations. Using computer simulations of the rooms at OncoRay, he tries to align the results of the measurement. To this end he needs to keep an eye on the most diverse parameters and, of course, the steel construction that can divert and decelerate the one or other free neutron during its flight. "It's like billiards," says Lutz.

Simple construction drawings do not deliver enough data for the simulation. "They're just sections of a room, but I have to reconstruct a three-dimensional image on the computer," the physicist explains. The form of the room, the material of the walls, the furniture, the suspended ceiling, the floor. In one way, even the actual measurements are simulated: researchers replace human bodies with water cubes and then call the whole thing a "phantom".

A comparison of the first spectra of the measurement and the simulation reveals that their model is pretty close to reality. The curves almost cover one another perfectly. "The results show that we're on the right path – and have apparently already covered a good deal of ground, but we haven't reached our destination yet," Lutz summarizes. He envisages another two years' work.

Stem cells in the tumor

While physicist Benjamin Lutz is conducting his experiments in the OncoRay basement, otherwise spending most of his time at the Helmholtz-Zentrum Dresden-Rossendorf, cancer researcher Anna Dubrovska and biologist Claudia Peitzsch are to be found on the second floor of the center. Even though OncoRay is widely known for driving proton therapy, classic radiobiology research is conducted here, too, and enjoys a considerable reputation in the community. Radiotherapy, which has been successfully employed for decades, is still ›



Tracking down neutrons: HZDR physicist Benjamin Lutz. Source: A. Wirsig

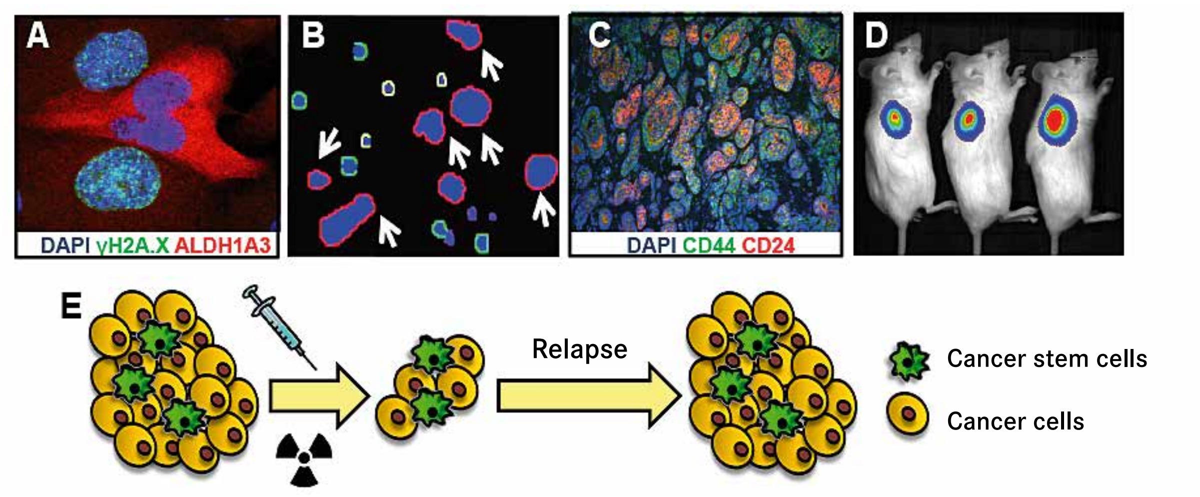


Illustration of the specific properties of cancer stem cells: (A) Cancer stem cells have specific biological properties and molecules (e.g. ALDH1A3). (B) One of the most essential cancer stem cell properties is their ability to renew themselves that can be analyzed e.g. by sphere forming assay. (C) Another essential property of cancer stem cells is their ability to differentiate into different cell types within the tumor (multipotency). (D) This is why it is assumed that they are responsible for tumor growth and metastasis (E) as well as why they fail to respond to radiotherapy.
Source: A. Dubrovska

being studied and can be improved. Sometimes scientists make less pleasing discoveries, such as those being investigated by Dubrovska and Peitzsch.

One of the important findings of cancer research in the last two decades has been that a tumor is not composed of homogenous cell tissue but, for all intents and purposes, is functionally differentiated and hierarchically organized. One group of cells plays a special role: cancer stem cells. And they can make a real nuisance of themselves during cancer treatment – including radiotherapy – as researchers discovered quite some time back.

First postulated in connection with leukemia more than two decades ago, the cancer stem cell hypothesis was contentious for many years. Nowadays, researchers agree that they do exist. They were given their name because they have the properties of stem cells: first of all, they keep on dividing indefinitely and can become the starting point for new tumors or renewed growth after successful therapy. Secondly, they can transform into different functional cell types within a tumor and some of them have the ability to exit it. They thus become the gateway for metastases.

Over time, medical researchers gradually realized that certain types of cancer could only be overcome by completely destroying all cancer stem cells. But that is easier said than done because they have proved to be particularly resistant to chemotherapy as well as radiotherapy. "Originally, it was assumed that tumor sensitivity to radiotherapy depends only on the number of cancer stem cells inside the tumor. And the more of them there are, the more likely it is that a few of them will survive the deadly attack," explains Anna Dubrovska who has headed the OncoRay research group "Biomarkers for the Individualized Radiotherapy" since 2011.

What triggers the transformation?

Nowadays, however, scientists believe that these cells also have special mechanisms that protect them better than other tumor cells. "These molecular processes are exciting in cell biology terms, but especially bad for treatment. The cells that are most important for tumor growth are the ones that are particularly well protected from radiotherapy," Dubrovska explains.

And that is not the worst of it because radiotherapy, which theoretically kills the tumor cells effectively, can actually awaken cancer stem cells: "Under certain circumstances, every population of tumor cells can transform," Claudia Peitzsch explains. It depends on the microenvironmental conditions in the surrounding tissue: in fast-growing tumors, for example, a lack of oxygen and nutrients can favor this transformation process. But, disastrously, reprogramming a tumor cell into a cancer stem cell can be triggered by energy-rich radiation, as demonstrated in 2012 by cancer and radiation researcher Frank Pajonk and his team for breast cancer. These radiation induced cancer stem cells are polyploid cells with a high chromosome content, which have induced expression of stem cell genes.

These results sparked the curiosity of Dubrovska's team and they decided to explore the as yet not elucidated mechanism of reprogramming. They selected prostate cancer to investigate the phenomenon – and confirmed Pajonk's results: after radiation, there were more cancer stem cells than before. But they also found an answer to the question as to what triggered this process and it turned out not only to be in certain stem cell-specific genes, as the Pajonk team had suspected.

"The DNA in the cell nucleus is tightly wound around special proteins known as histones," Peitzsch explains. Like a thread wrapped around an individual spool, the DNA runs around the histones and is thus packaged into a chromosome. The tighter the DNA is packed, the more difficult it is to transcribe the genes. Histones have protein ends that can be variously modified by attaching, for example, acetyl or methyl groups. Histone methylation is an epigenetic mark, substantially impacting activity of gene expression.

Anna Dubrovska (left) and Claudia Peitzsch study cancer stem cells at the OncoRay Center. Source: A. Wirsig

Sensitization for the diseased cells

Via changes in the methyl groups, environmental conditions can directly influence whether genes can be transcribed or not, "because methylation affects how tightly or loosely the DNA is packed in the chromosome," says Peitzsch. In 2016, the team demonstrated DNA methylation can be changed by the X-rays: a chromosome opens up and some genes can be transcribed, investing the cells with properties like the ability to form tumors, to repair DNA damage more efficiently or to migrate from their initial side.

Dubrovska, Peitzsch and their colleagues identified one of the genes that are transcribed: *ALDH1A1*, encodes the enzyme aldehyde dehydrogenase. It helps the cells to become more radioresistant by protecting against oxidative stress and DNA damage. This gave the researchers a foothold for interrupting the transformation of the tumor cell into a radioresistant cancer stem cell. When they prevented the transcription of this gene with a certain chemical drug, which affects histone methylation, the cells once again responded more sensitively to X-rays. The radiation damage to the DNA was greater and more tumor cells died. "Our results indicate that certain drugs, which can prevent changes in histone methylation after ionizing radiation, will potentially be able to increase the effectiveness of radiotherapy in future," explains Anna Dubrovska.

As promising as this initial evidence may be, the team still has a great deal of work ahead of it. Claudia Peitzsch is currently investigating other substances to find candidates that might potentially enhance the radiosensitivity of cancer stem cells in prostate carcinomas. One doctoral student is studying the same phenomenon in other types of cancer: "And it looks like different tumor types have a different potential for radiation-induced epigenetic reprogramming," says Anna Dubrovska. This fact makes the undertaking more difficult but that again is typical for science and completely in line with its mantra: new knowledge always generates new challenges, too.

Contact

_Institute of Radiooncology – OncoRay at HZDR
Prof. Anna Dubrosvka
a.dubrovska@hzdr.de

_National Center for Radiation Research in Oncology – OncoRay / National Center for Tumor Diseases – NCT Dresden
Dr. Claudia Peitzsch
claudia.peitzsch@oncoray.de

_Institute of Radiation Physics at HZDR
Dr. Benjamin Lutz
b.lutz@hzdr.de

Publications:

C. Peitzsch, M. Cojoc, L. Hein, I. Kurth, K. Mäbert, F. Trautmann, B. Klink, E. Schröck, M.P. Wirth, M. Krause, E.A. Stakhovsky, G.D. Telegeev, V. Novotny, M. Toma, M. Muders, G.B. Baretton, F.M. Frame, N.J. Maitland, M. Baumann, A. Dubrovska: An epigenetic reprogramming strategy to resensitize radioresistant prostate cancer cells, in Cancer Research, 2016 (DOI: 10.1158/0008-5472.CAN-15-2116)

M. Cojoc, C. Peitzsch, I. Kurth, F. Trautmann, L.A. Kunz-Schughart, G.D. Telegeev, E.A. Stakhovsky, J.R. Walker, K. Simin, S. Lyle, S. Fuessel, K. Erdmann, M.P. Wirth, M. Krause, M. Baumann, A. Dubrovska: Aldehyde dehydrogenase is regulated by β-catenin/TCF and promotes radioresistance in prostate cancer progenitor cells, Cancer Research, 2015 (DOI: 10.1158/0008-5472.CAN-14-1924)

NCT
NATIONAL CENTER
FOR TUMOR DISEASES
PARTNER SITE DRESDEN
UNIVERSITY CANCER CENTER UCC

Supported by:
German Cancer Research Center
University Hospital Carl Gustav Carus Dresden
Carl Gustav Carus Faculty of Medicine, TU Dresden
Helmholtz-Zentrum Dresden-Rossendorf

OncoRay
National Center for Radiation Research in Oncology Dresden

A building block for the individualized cancer therapy

The interaction between physicists and physicians has delivered the new insight: a parameter that facilitates more precise predictions for treating esophageal cancer. Collaboration between researchers at the University Hospital Dresden and HZDR made an important advance in improving the characterization of tumors in the esophagus. This could also drive personalized cancer therapy.

_Text . Inge Gerdes

Individualized cancer therapy presupposes we have the most detailed information about the tumor – not just size and location but also cancer cell metabolism. HZDR physicist Frank Hofheinz and physician Rebecca Bütof got together to investigate a new parameter which facilitates the characterization of metabolic activity in esophageal tumors. The value not only provides information on the biological properties of the tumor but also on whether the diseased cells will respond to treatment.

In order to quantify the tumor metabolism, until now, doctors have used a parameter called Standard Uptake Value (SUV). But it is generally known that SUV does not quantify the tumor metabolism very accurately. "That's why we developed a new parameter – Standard Uptake Ratio – in Jörg van den Hoff's HZDR research group," Frank Hofheinz explains. "It can be determined without much extra effort using PET images."

In positron emission tomography (PET) doctors utilize the tumor's sugar metabolism, which is usually elevated. Before taking measurements, a radioactive sugar solution, a so-called radiotracer, is injected into the patient's bloodstream. Special measuring devices detect the radioactive radiation on the basis of which three-dimensional images can be calculated. These images show the distribution of the radiotracer in the body and thus also the diseased cells. Several studies revealed that SUR could quantify the results significantly better than SUV – which raised the question as to whether this would be of advantage to patients.

It was quite by chance that Frank Hofheinz met Rebecca Bütof at the OncoRay Center that is operated jointly by HZDR, the University Hospital and the Medical Faculty at TU Dresden. The young doctor works in the Clinic and Outpatient Clinic for Radiotherapy and Radiooncology at Dresden University Hospital. During her training, she took the opportunity to focus on a research topic at OncoRay. Together, physicist and physician investigated the promising new parameter.

PET scan of a patient with an esophageal carcinoma: the diseased cells betray themselves by increased metabolic activity. Source: F. Hofheinz / R. Bütof

From lab to clinic

"The future aim is to predict the outcome of treatment more precisely and assess the risk of remote metastases or local recurrence," Bütof explains. "The latter means a new cancerous growth that can develop when a tumor has not been completely removed. If predictions like this can be made before therapy, we can adapt the treatment accordingly, with more intensive chemotherapy to prevent metastases, for example, or a higher dose of radiation to the tumor."

The two researchers evaluated the clinical data on 130 patients with esophageal cancer who had been treated in previous years at the University Cancer Center Dresden. "The patients were a homogenous collective, that means they all had a locally advanced tumor and had all received the same therapy, a primary radiochemotherapy," the doctor reports.

In their study, Hofheinz and Bütof correlated the PET parameters and other clinical properties of the tumor with the respective treatment process and discovered that SUR really did allow them to draw conclusions about the patient's chances of survival as well as the risk of remote metastases or local recurrence. "Admittedly, this is only a preliminary screening, but 130 patients are quite a significant number," Frank Hofheinz believes. "The study has shown that it's worth the extra effort of evaluating the PET data and could benefit patients in future. The good thing is that you have to do a PET scan anyway, so the patient is not subjected to any additional exposure."

The Dresden study is a prime example of translational research which seeks to benefit patients as quickly as possible. Rebecca Bütof does, however, point out that, so far, SUR has only been investigated retrospectively on cases that had already been closed: "The next step is to validate the new method on a larger number of patients. Then we'll be able to include the parameter from the word go and test how sound it is during therapy without changing the treatment method. But it'll be another ten years or so before it can be used in clinical practice."

Excellent collaboration

For the joint publication in the Journal of Nuclear Medicine, of which Rebecca Bütof is the lead author alongside Frank Hofheinz, the Society of Nuclear Medicine and Molecular Imaging granted her the 2016 Alavi-Mandell Publication Award. The prize, valued at 150 US dollars, is granted once a year to junior researchers who are still training at the time when the research is conducted.

Publication:

J. van den Hoff, L. Oehme, G. Schramm, J. Maus, A. Lougovski, J. Petr, B. Beuthien-Baumann, F. Hofheinz: The PET-derived tumor-to-blood standard uptake ratio (SUR) is superior to tumor SUV as a surrogate parameter of the metabolic rate of FDG, in EJNMMI Research, 2013 (DOI: 10.1186/2191-219X-3-77)

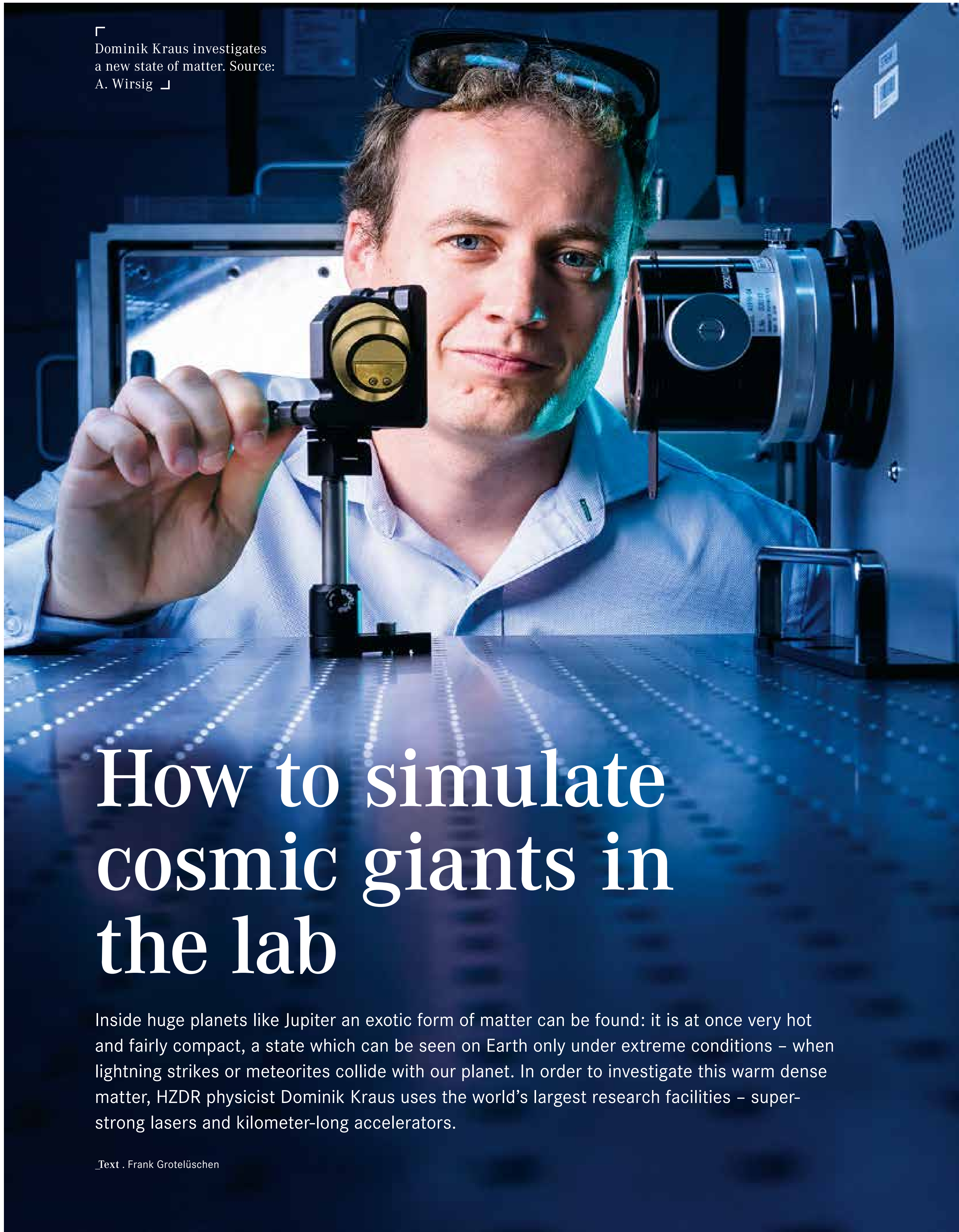
J. van den Hoff, A. Lougovski, G. Schramm, J. Maus, L. Oehme, J. Petr, B. Beuthien-Baumann, J. Kotzerke, F. Hofheinz: Correction of scan time dependence of standard uptake values in oncological PET, in EJNMMI Research, 2014 (DOI: 10.1186/2191-219X-4-18)

R. Bütof, F. Hofheinz, K. Zöphel, T. Stadelmann, J. Schmollack, C. Jentsch, S. Löck, J. Kotzerke, M. Baumann, J. van den Hoff: Prognostic value of pretherapeutic tumor-to-blood standardized uptake ratio in patients with esophageal carcinoma, in Journal of Nuclear Medicine, 2015 (DOI: 10.2967/jnumed.115.155309)

Contact

_National Center for Radiation Research in Oncology – OncoRay
Dr. Rebecca Bütof
rebecca.buetof@uniklinikum-dresden.de

_Institute of Radiopharmaceutical Cancer Research at HZDR
Dr. Frank Hofheinz
f.hofheinz@hzdr.de



Dominik Kraus investigates a new state of matter. Source: A. Wirsig

How to simulate cosmic giants in the lab

Inside huge planets like Jupiter an exotic form of matter can be found: it is at once very hot and fairly compact, a state which can be seen on Earth only under extreme conditions – when lightning strikes or meteorites collide with our planet. In order to investigate this warm dense matter, HZDR physicist Dominik Kraus uses the world's largest research facilities – super-strong lasers and kilometer-long accelerators.

_Text . Frank Grotelüschen

After the sun, Jupiter is the largest celestial body in our solar system with a mass greater than all the other planets put together. But with pressure of 50 million atmospheres and a temperature of 10,000 degrees, the interior of this giant is unusual as well. Such extreme conditions force the matter into a quite extraordinary form of existence: it is as dense as metal but also so hot that – just like a plasma – it is ionized.

"We call it warm dense matter," explains Dominik Kraus, head of a Helmholtz Young Investigator group at HZDR. "This is the transition regime between solid state and plasma." It is not exclusive to the interior of planets and certain dwarf stars but can also occur on Earth, if only briefly, when lightning strikes or a meteorite hits our planet.

So, how can you generate this unusual matter in the lab in order to scrutinize it in more detail? "You can do it with high-intensity laser flashes," Kraus answers. "We bombard a matter sample with strong laser flashes which heat up the surface extremely quickly." This then produces a veritable shock wave which storms through the sample. It compresses the matter and heats it up. At precisely this point, the desired state of warm dense matter is created – if only for a few nanoseconds.

Evidence suggests that the exotic carbon crystal Lonsdaleite occurs near meteorite impact craters. The colossal heat and massive pressure could turn graphite into the diamond-like matter. Dominik Kraus and his team are studying this process. Source: Lawrence Livermore National Laboratory

"Even so, that's long enough to measure this state," the Dresden physicist explains. "X-ray pulses are particularly useful because you can literally shine right through the warm dense matter with them." The problem is that standard X-ray tubes simply have too little power for the purpose. Dominik Kraus and his young investigator group – a postdoc and two Ph.D. candidates – therefore head for the strongest X-ray lasers in the world, such as the Linac Coherent Light Source in California.

Harder than diamonds

It was here that they conducted an interesting experiment a while ago: under laser bombardment, the researchers were able to observe the graphite samples changing into diamonds. Under certain conditions, they even seemed to form Lonsdaleite – an exotic carbon crystal which in its purest form must be harder than diamonds. "Evidence suggests that Lonsdaleite occurs near meteorite craters," Kraus explains. "It seems to be formed by the force of the impact." This summer, he headed back to California to substantiate his results with a follow-up experiment.

Spectacular results have also been achieved at the National Ignition Facility, one of the largest laser facilities worldwide, also located in California. Here, researchers subject their matter samples to 184 laser beams and thus create similar conditions to those in the interior of stars – the pressure of nearly a billion atmospheres. Initial experiments were very promising, further tests are planned for 2018.

In that year, work is due to start at another giant: the European XFEL is about to be launched in Hamburg. With a length of 3.4 kilometers, it is the largest X-ray laser in the world. Together with other Helmholtz partners, HZDR is constructing the Helmholtz International Beamline for Extreme Fields (HIBEF) there. It will house two new lasers which will allow matter samples to be highly effectively compressed and heated. "With flashes from the X-ray laser we'll be able to study warm dense matter with far greater precision than we had ever conceived of," Dominik Kraus enthuses. "We hope to discover much more detailed information about the interior of planets." The researchers want to elucidate, for example, how planetary magnetic fields are created by the flow behavior of warm dense matter – important fundamental knowledge for searching, amongst other things, for life-sustaining exoplanets.

Contact

_Institute of Radiation Physics at HZDR
Helmholtz Young Investigator Group:
Dynamic Warm Dense Matter Research with HIBEF
Dr. Dominik Kraus
d.kraus@hzdr.de

Mini-accelerators for research

Early this year, newly-honored Humboldt Research Award winner Michael Downer joined HZDR from the University of Texas at Austin. The expert for laser and plasma physics will be in Dresden until January of 2018, developing methods to better visualize the processes that occur during laser particle acceleration, the scientific basis for boosting the performance of a new type of accelerator. If successful, this new method could drastically reduce the dimension of our current, huge particle accelerators – a dream come true for many labs.

_Text . Simon Schmitt

One of his research focuses is an ultimate challenge for photographers, says Michael Downer. He is not exaggerating – because Downer wants to show what happens when a high-intensity laser pulse meets a gas at near-light speed. "This creates what is called plasma, a sizzling mix of charged particles," the US-researcher explains. "The pulse rips electrons out of the atoms, creating a sort of bubble in the plasma, which contains a strong electric field. This field, which the laser pulse drags behind it, traps the electrons, accelerating them tremendously." Due to the high speeds and short duration of this process, complex computer simulations used to be the only way to visualize the emerging structures and occurring processes.

Recently, however, Downer and his Texan team developed a method to record the emergence and spread of plasma bubbles, which they stimulated with a laser beam. "This gave us information about the optimum conditions for acceleration, which in turn enabled us to improve acceleration performance," Michael Downer summarizes. The scientist and another colleague together with two doctoral candidates from Texas now want to implement this technology, which is based on the capabilities of computer tomography, at HZDR, as well. The short-pulse laser DRACO in Dresden with its Petawatt-range power – that is one quadrillion watts – offers the perfect setting to push the technology forward.

Together with postdoc Rafal Zgadzaj (right) and doctoral candidate Maxwell Laberge (left), Michael Downer (middle) is working on a novel type of accelerator.

Dresden's excellent infrastructure is part of its appeal

"Compared to the laser we previously used to test the method, DRACO can generate larger plasma structures over longer distances," Downer explains. "And the facility also allows us to control the acceleration process with two laser pulses – the first one generates the structures, the second one controls the accelerated electrons. That allows us new insights into the physics of laser-plasma acceleration." Combined with expertise from Dresden and the HZDR simulation program PIConGPU, researchers from Texas and Saxony plan to generate four-dimensional images of the processes in order to improve the performance of laser-propelled accelerators. A few years ago, Michael Downer and his team were the first to accelerate electrons to energies of two gigaelectron-volts using this novel type of accelerator, which is small enough to fit on a table. Traditional linear accelerators would need a distance of several hundred meters to do the same.

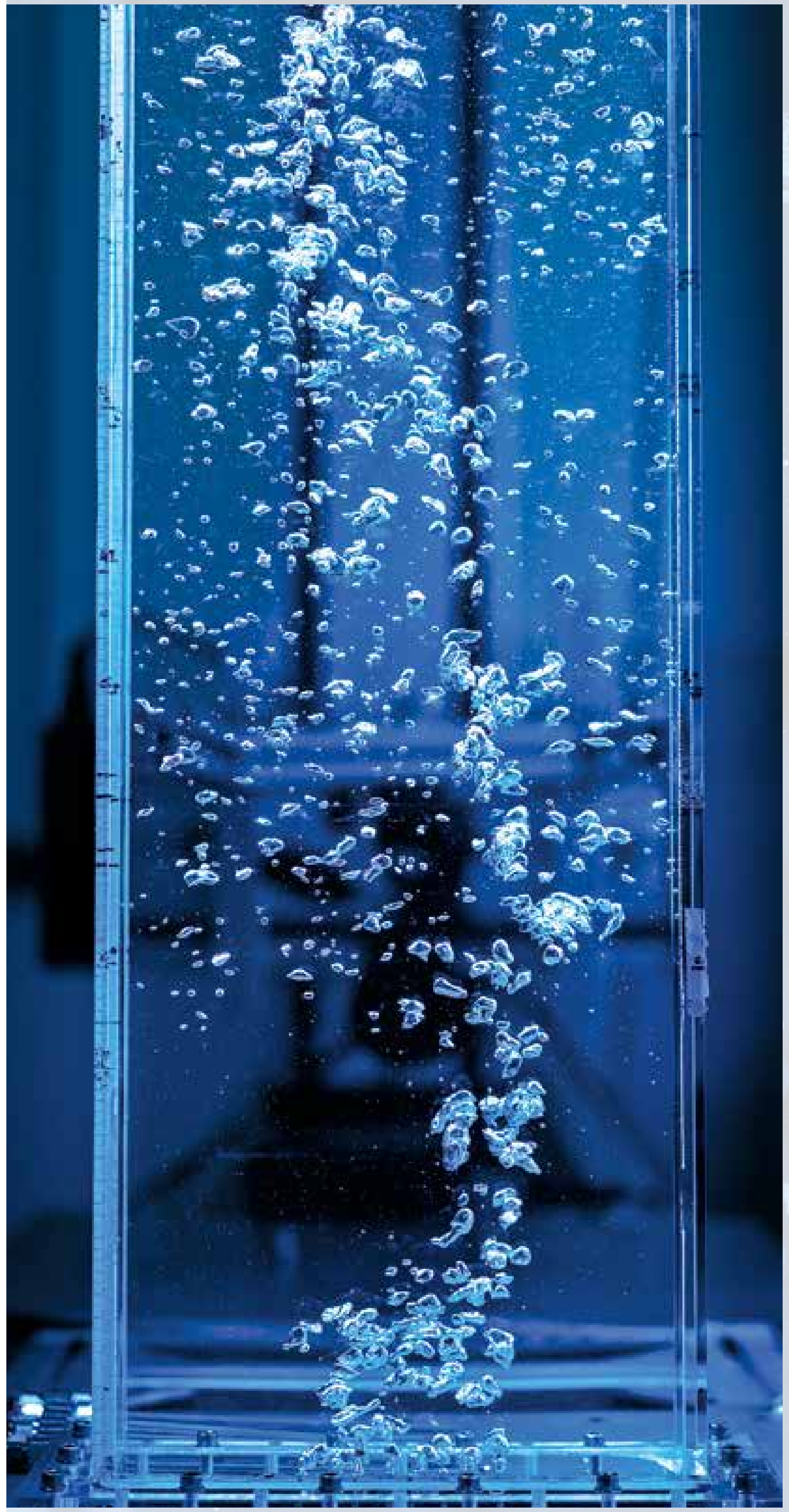
Laser-propelled acceleration could shrink these gigantic systems, enabling even smaller labs to obtain this previously prohibitively expensive infrastructure. "We can convert electrons into X-rays, which are just as bright as in the traditional facilities," Downer explains. "Chemists and biologists could, for example, use this radiation to study the molecular basis of matter in their own labs, without the need to travel to the large facilities."

Humboldt Research Award

Each year, the Alexander von Humboldt Foundation honors up to 100 internationally recognized scientists with a Humboldt Research Award, which is endowed with 60,000 Euros. The main selection criterion is whether the nominated researchers' discoveries and insights have had a profound and lasting impact on their own subject area and beyond.

Contact

_Institute of Radiation Physics at HZDR / University of Texas at Austin
Prof. Michael Downer
m.downer@hzdr.de



Unlike the reactors used in the chemical industry, the flow processes can be easily observed in transparent bubble columns. The similarity between the processes in both set-ups allows researchers to precisely investigate flow conditions. Source: A. Wirsig

A glimpse into the black box of flow

An encounter between liquids and gases often results in complex, turbulent flows, which even state-of-the-art computers cannot fully simulate. HZDR researchers are on a mission to change this with a modeling method that is also used in the construction of race cars and aircraft. The outcome could make nuclear plants safer and air conditioning systems more efficient.

_Text . Markus Fehrenbacher

When comparing a modern Formula 1 race car with a model from the 1950s, even those who are not particularly interested can see that they do not look very similar. The new models appear much more aerodynamic – because they are. The Bolide's vehicle body is the result of decades of research that was single-mindedly focused on reducing air resistance.

Twenty years ago, this required complex tests in a wind tunnel. Today, engineers and mechanics mostly rely on simulation programs to precisely model air flow on the computer. It works very well, even for the medium water, as evidenced by the design of modern ship hulls. Known in specialist circles as "Computational Fluid Dynamics" (CFD), this method has become the trusted tool of choice for experts to study the behavior of individual gases and liquids.

What happens, though, when the two substances meet, when bubbles form, or when the liquid even starts evaporating? Established models can no longer handle these far more complex scenarios. Yet this type of interaction is vital in many areas, "from the performance of an AC (air-conditioning) system to nuclear safety," says Dirk Lucas from the HZDR Institute of Fluid Dynamics. "At first sight, they seem to be two completely different systems. But when you take a closer look, you will see how similar they are."

More precise simulations mean greater safety ...

Whether a nuclear plant or an AC system: Liquids play a central role, both as cooling agents and for heat storage. The functionality of each system is very sensitive to the exact flow behavior of the fluid. "We want to understand precisely what is going on inside pipes and tubes," says Lucas, describing the goal of his research. "Computer simulations are usually the only way to gain detailed insights."

Insights, which in the case of nuclear plants help increase safety. To ensure incident-free operation, the fuel rods must be cooled at all times. In a pressurized water reactor, this is done with water, which the nuclear reaction heats up to about 300 degrees Celsius – a pretty 'hot cooling' – after all, the liquid also serves as a heat source to generate steam for the turbine. If there is a leak in the cooling cycle, emergency measures will kick in immediately: Fresh, much cooler water flows in to compensate for the loss. "This influx process is very complex," explains Eckhard Krepper, who works with Dirk Lucas to simulate such processes on the computer. "Water vaporizes, condenses again elsewhere, we get turbulent flows, air bubbles are being yanked along."

However, in order to avoid thermomechanical stress on the reactor wall, which in the worst case could lead to cracks and even a major incident, the water must mix as evenly as possible. Reliable simulations of the mixing process are needed to adjust the geometry of the emergency system to minimize such stresses on the material. This is the ambitious goal of the HZDR researchers, who benefit from TOPFLOW, an experimental facility that allows them to test their calculations under realistic conditions.

... and lower energy consumption

The interplay between gas and liquid is also crucial to the functioning of AC systems. The principle is simple: In the first half of the process, a cooling liquid is vaporized in a closed circuit by lowering pressure, in the second half, it is re-condensed with the help of a compressor, drawing heat from the area that is to be cooled and releasing it to the outside. The performance of the system largely depends on the geometry and set-up of the ducts, as they determine the complex flow behavior of the gas-liquid mix and thus the heat exchange with the environment. This is another area where simulations would be extremely useful to maximize efficiency. So far, engineers have no choice but to rely on empirical values.

But even small improvements can have a big impact on the environment, Krepper estimates: "In Germany, about 14 percent of our annual power consumption goes towards cooling technologies." Computer programs capable of calculating the complex flows of liquids and gases have been around only for a few years. "We still can’t conduct exact simulations that take account of all the details," Dirk Lucas concedes. "We have to develop approximate models." The boundary surfaces between liquids and gases are crucial. Not only larger air pockets, but even the tiniest bubbles impact chaotic flow behaviors. The problem is, there is no model that can equally and correctly describe both cases – large and small phase-boundary surfaces.

The scientists are therefore developing a novel concept that integrates various models and allows for a detailed description of different scales thanks to seamless transitions. The models’ validity range is another issue that occupies Lucas and his team. While a lot of research has been done on simulating flow on the computer, each study is only valid for a very narrow parameter range. "One should not attempt to apply the same model to a system with different geometries, temperatures or pressures," Lucas says, "simply because we do not yet have a full understanding of the individual phenomena. We can compensate for the resulting model errors in a specific case, but any deviation could lead to a wrong result."

This is why one of the researchers’ major goals is to design a model that is valid for any system, whether it is a nuclear reactor or an AC. "We have a long way to go." But so did the Formula 1 race car designers.

Contact

_Institute of Fluid Dynamics at HZDR
Dr. Dirk Lucas
d.lucas@hzdr.de

Dr. Eckhard Krepper
e.krepper@hzdr.de

Source: A. Wirsig

"The bubble does not care in which system it floats."

discovered: Computational fluid dynamics, or CFD, is known to many as a low-cost alternative to wind tunnel experiments. What does it have to do with energy-efficient processes in the chemical industry?

Dirk Lucas: Flow plays a vital role in many areas. Many chemical processes, for example, require the injection of gasses into liquids. That is a very energy-intensive process. System efficiency greatly depends on flow. And that is exactly the point of CFD: to reflect the flow conditions. The physics behind it is always the same.

What is the greatest challenge in this?

In contrast to wind tunnel experiments, we are dealing with multi-phase processes in chemical reactors. That means that at least two media will meet, such as gases and liquids. Many different combinations of substances are used in industrial applications. Also, each system has its own complex geometry. Many previous studies have been too narrowly focused on one individual scenario. That is not helpful in the long run because we want to be able to predict efficiency and potential improvements.

What does that mean for your research?

We have to take one step back towards the basics and develop more reliable simulations that work for a whole range of systems. That is why we are developing a baseline model that we apply to each problem first. If the results are not satisfying, we go back to the drawing board. Eventually, though, we will come up with a simulation model that allows for more precise predictions.

Interview by Simon Schmitt.

"We will be more dependent on resources"

Demand for steel, copper, cobalt, lithium, rare earths and other high-tech metals is on the rise, because they are needed for new wind, solar and energy storage facilities as well as electricity grids. Germany's dependence on metal imports will consequently increase, a risky trend which can, however, be addressed with a proactive raw materials policy. This is the recommendation of an expert panel of the German National Academy of Science and Engineering acatech, whose study aims to provide input for a fact-based debate about the challenges and opportunities of the *Energiewende*. "discovered" talked to one of the experts involved: Jens Gutzmer, Director of the Helmholtz Institute Freiberg for Resource Technology.

_Interview . Anja Weigl

discovered: Do we have sufficient resources for the *Energiewende* and other key technologies?
Jens Gutzmer: The *Energiewende* will decentralize our power supply. Large central power plants will be replaced by many scattered renewable energy facilities that must be interconnected. To build these facilities, we will need minerals and metals, such as rare earths and other high-tech metals, but also infrastructure metals and construction materials like copper, aluminum, steel, and concrete. Our energy system will be more complex and more resource-intensive. We could produce part of the required resources here in Germany by recycling, but we won't be able to cover the demand as it increases in future. That can only be done with natural resources – some of which we may even discover in our domestic realm.

Recycling can cover part of our resource demand, but it is not efficient enough yet. How can we do better?
Jens Gutzmer: Like any industrial product, wind turbines and solar panels have a certain life span. We have not yet figured out how to recycle them, which is why we need more research and development to boost energy and resource efficiency. We should also set standards for recycling to assure consumers that resources vested in products they purchase can really be recycled. Furthermore, we need the political actors to get involved, for example to prevent losing resources to illegal exports.

Jens Gutzmer, Director of the Helmholtz Institute Freiberg for Resource Technology. Source: D. Müller

How can we secure our natural resource supply?
Jens Gutzmer: We should pursue a more active raw materials policy. Mineral and metal resources should be taken just as seriously as the energy supply itself. Unfortunately, they don't get much attention in the current public and political debate. This might come back to haunt us, because when it comes to the supply of resources, German industry doesn't really seem to be able to take action on its own. This is why the study recommends to the German government stimulating the resource and recycling markets, for example by founding an exploration and mining company, even if this may constitute active interference with the market.

The resource alliance of German businesses failed and ended up being closed again ...
Jens Gutzmer: Yes, but a government-initiated start-up with the right experts could achieve a lot: It could get involved in promising exploration projects at an early stage, and thus secure access to resources that help our industry develop projects to secure our supply of critical resources. It could also promote recycling technologies and thus bring more resources onto the market when German industry needs them. From an economist's perspective, this recommendation in the study may be problematic. But the authors agree that the state needs to assume a more active role in our resource supply.

Are other countries more proactive when it comes to resource policies?
Jens Gutzmer: The US keeps strategic supplies of certain raw materials for their domestic industry. Japan and South Korea have state-owned, but commercially run companies tasked with surveying mining projects all over the world and buying stakes in them, with the intention of quickly passing them on to industry. These examples show that the state can indeed assume an active role in resource supply. This is the only way that Germany, as well as Europe, can influence its own fate.

Publication:
Resources for the energy revolution: pathways towards a secure and sustainable resource supply. acatech – German Academy of Science and Engineering, National Academy of Sciences Leopoldina, Union of the German Academies of Sciences and Humanities, Berlin 2017.

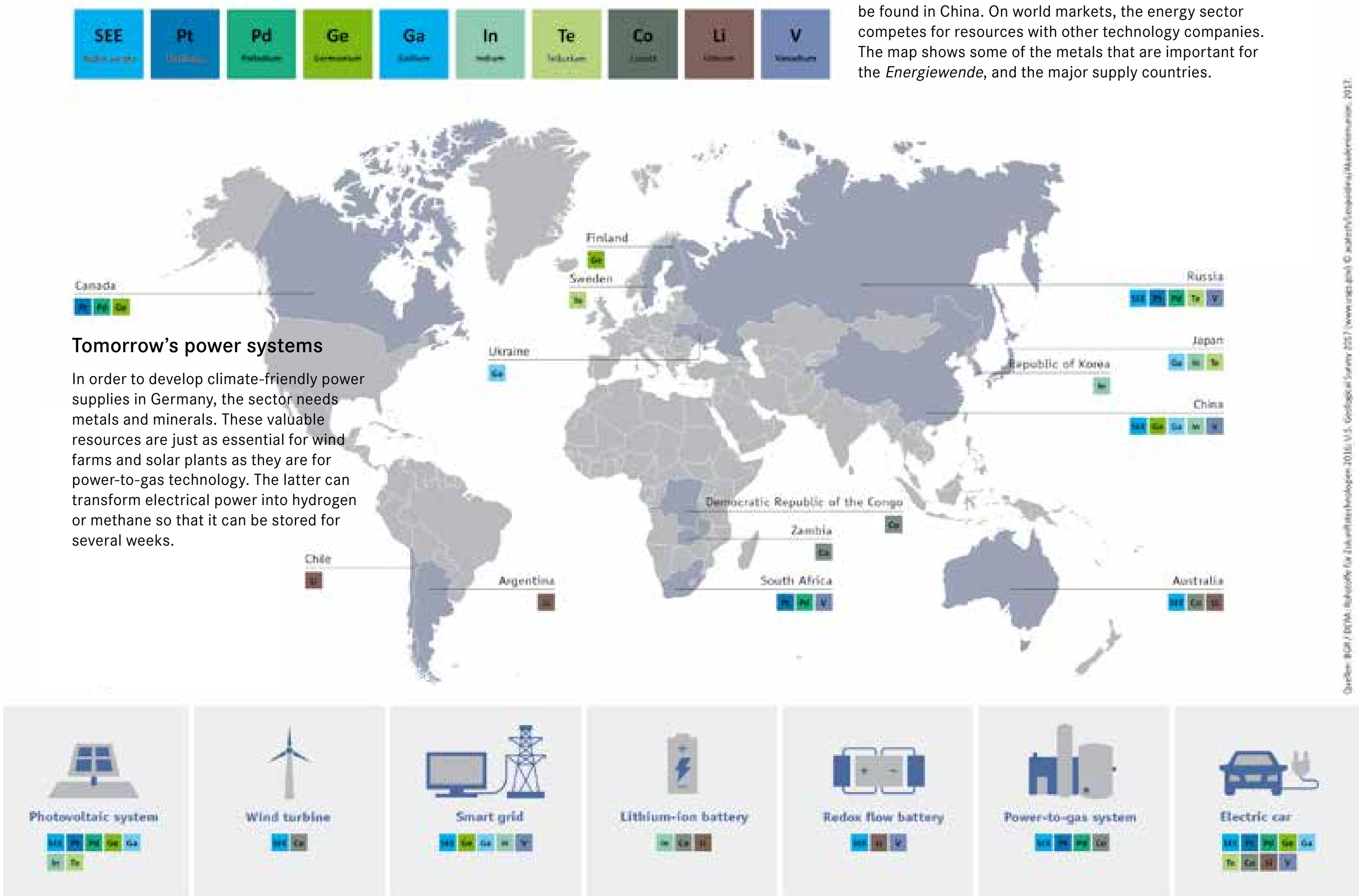
Contact

_Helmholtz Institute Freiberg for Resource Technology at HZDR
Prof. Jens Gutzmer
j.gutzmer@hzdr.de

No raw materials - no *Energiewende*

Resources from the entire world

Worldwide there are enough natural metal deposits for the *Energiewende*. However, they are very unevenly distributed. Four-fifths of rare earths, for example, are to be found in China. On world markets, the energy sector competes for resources with other technology companies. The map shows some of the metals that are important for the *Energiewende*, and the major supply countries.



AMAZED

A Rather Scientific Night

Undaunted by the poor weather, about 38,000 visitors turned out in mid-June for the Night of Science in Dresden, an adventurous journey through the world of modern research. HZDR was represented at no fewer than four different locations: at the lecture hall of TU Dresden, OncoRay and the National Center for Tumor Diseases Dresden as well as at the future particle lab in the ‘Felsenkeller’ rock cellar. About 7,400 science enthusiasts came to discover more about HZDR and its activities. The next day, HZDR resource experts at the Helmholtz Institute Freiberg for Resource Technology gave some insights into the microcosm of minerals during the Night of Science and Industry in Freiberg.

© J. Grebing

OPENED

Leipzig Modernism

After two and a half years of construction, the remodeled labs of the controlled area at HZDR’s research facility in Leipzig were reopened in mid-March. The Free State of Saxony had contributed 10 million euros to the renovation efforts. Leipzig-based scientists now enjoy modern work spaces on a total of almost 1.000 square meters. The focus will be mainly on cancer and radioactive waste repository research. Biologists and chemists in the Institute of Radiopharmaceutical Cancer Research, for example, are developing probes with radioactive markers to characterize brain tumors. Researchers from the Institute of Resource Ecology are also using positron emission tomography to study transport processes of radioactive substances inside rocks.

© O. Killig

FOUNDED

Shalom, Laser!

In late April, the Helmholtz-Zentrum Dresden-Rossendorf and the Weizmann Institute of Science laid the foundations for sharing their laser infrastructures by pooling their laser particle acceleration capabilities at WHELMI (Weizmann-Helmholtz Laboratory for Laser Matter Interaction). The focus will be on developing new targets – i.e. the objects the laser beam impacts. Over the next five years, the Helmholtz Association will provide 1.25 million euros from its Initiative and Networking Fund in support of the project. HZDR will match this contribution; another 2.5 million euros will come from the Weizmann Institute.

© O. Killig

ARRIVED

A Giant in the Basement

From England via Rossendorf into an underground rock tunnel: This has been the journey taken by the Pelletron accelerator which HZDR is currently setting up in the former ice depot of the ‘Felsenkeller’ brewery. The accelerator tank, which measures almost eight meters in length and weighs ten tonnes, arrived at its new home on the southwestern edge of Dresden in late April. Physicists plan to use the facility to simulate the processes that occur inside stars. The only other location in Europe where studies of this kind are possible is the LUNA Laboratory for Underground Nuclear Astrophysics inside the Italian Gran-Sasso mountain. Experiments are scheduled to start next year in Germany’s deepest particle lab, which HZDR is setting up in cooperation with TU Dresden. The two institutions will then boast Germany’s only subterranean particle accelerator. At the end of June, Physics Nobel laureate Arthur McDonald from Queen’s University in Kingston, Canada, gave the celebratory speech at the topping-out ceremony.

WHAT'S ON

26.10.2017 | 9:20 a.m. | TU Dresden
Lecture: Teilchenphysik in Bleistiftstaub:
Das Wundermaterial Graphen
Dr. Stephan Winnerl | Institute of Ion Beam Physics and Materials Research

06.11.2017 | 1 p.m. | TU Dresden
Lecture: Möglichkeiten der Kreislaufwirtschaft
Prof. Markus Reuter | Helmholtz Institute Freiberg for Resource Technology

07.11.2017
OptimOre Symposium
Helmholtz Institute Freiberg for Resource Technology

08.-09.11.2017
Conference: Aufbereitung und Recycling 2017
Helmholtz Institute Freiberg for Resource Technology

14.-17.11.2017
15th Multiphase Flow Short Course and Conference
Institute of Fluid Dynamics

09.01.2018 | 10 p.m.
Guided Tour: Ionen als Kunst-Detektive
Dr. Michael Mäder | Institute of Ion Beam Physics and Materials Research

UNDERWAY

Research and Treatment Under One Roof

The four institutions operating the National Center for Tumor Diseases (NCT) Dresden – the German Cancer Research Center, the University Hospital Carl Gustav Carus, the Faculty of Medicine at TU Dresden and HZDR – were joined by Saxony’s Minister President Stanislaw Tillich to lay the foundation stone for the NCT’s new building on the university campus. On more than 3.000 square meters cancer research and treatment will be closely interconnected. In addition to an innovative research platform, there will also be labs, study areas, and patient care facilities. The Free State of Saxony is providing 22 million euros for the construction project, which is scheduled to be completed in 2019.

↗ www.nct-dresden.de

LAUNCHED

Unlimited Access to Europe’s Light Sources

In early May, the European Union provided ten million euros to fund the CALIPSOplus project during the next four years. HZDR is coordinating the project, which involves all major synchrotron radiation sources and free electron lasers in Europe and the Middle East. In addition to a variety of training opportunities, the network provides free access to accelerator-based light sources, especially for scientists from Central and Eastern European countries, and even reimburses travel costs for outstanding researchers. The 19 partners will continue to expand their internet portal "wayforlight" as a central platform for information and research facility access:

↗ www.calipsoplus.eu/

IMPRINT

PUBLISHED BY
Professor Dr Dr h. c. Roland Sauerbrey and Professor Dr Dr h. c. Peter Joehnk,
Board of Directors of the Helmholtz-Zentrum Dresden-Rossendorf (HZDR)

DATE OF PUBLICATION
October 2017
ISSN: 2194-5705 // Issue 01.2017

EDITING
Simon Schmitt, Dr Christine Bohnet (editor-in-chief),
Dr Anna Kraft, Jana Grämer (images) | Communications and Media Relations at HZDR
Editorial Advisory Board:
Energy – Dr Harald Foerstendorf, Dr Frank Stefani
Health – Dr Fabian Lohaus, Dr Holger Stephan
Matter – Dr Stefan Facsko, Dr Andreas Wagner

AUTHORS
Marcus Anhäuser | Freelance science journalist, Dresden
Markus Fehrenbacher | Nürnberg
Inge Gerdes | Freelance science journalist, Dresden
Frank Grotelüschen | Freelance science journalist, Hamburg
Dr Anna Kraft | Press officer National Center for Tumor Diseases (NCT) Dresden and Institute of Radiooncology - OncoRay at HZDR
Nadine Querfurth | Journalistenbüro Schnittstelle
Anja Weigl | Press officer at Helmholtz Institute Freiberg for Resource Technology at HZDR

TRANSLATION
Dr Lynda Lich-Knight, ResearchComm Ltd

PICTURE CREDITS
HZDR staff, unless stated otherwise

LAYOUT
WERKSTATT X . Michael Voigt
www.werkstatt-x.de

PRINTING
Druckerei Mißbach
www.missbach.de

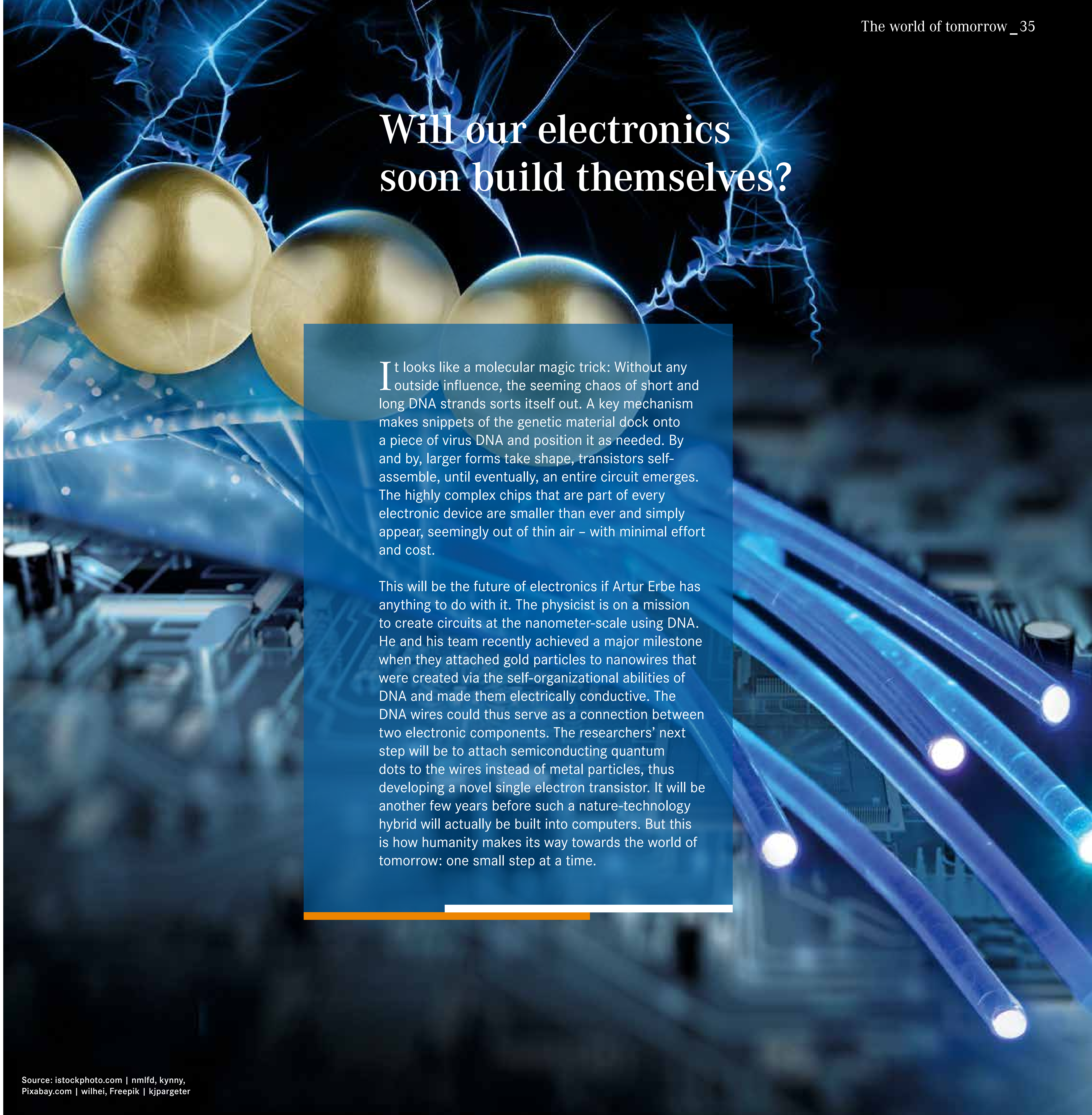
CIRCULATION
1,500 // Printed on Circlesilk (cover) and Circleoffset (content),
FSC certified and awarded with the EU Ecolabel

CONTACT/ORDER (free of charge)
Helmholtz-Zentrum Dresden-Rossendorf
Communications and Media Relations
Dr Christine Bohnet
Bautzner Landstraße 400, 01328 Dresden
Phone +49 (0)351 260 2450
Email c.bohnet@hzdr.de

The HZDR research magazine "discovered" appears twice a year,
also in German titled "entdeckt".
All print editions can be found in ePaper format on the HZDR website.

↗ **www.hzdr.de**

HZDR on Facebook and Twitter:
↗ **www.facebook.com/Helmholtz.Dresden**
↗ **www.twitter.com/hzdr_dresden**



Will our electronics soon build themselves?

It looks like a molecular magic trick: Without any outside influence, the seeming chaos of short and long DNA strands sorts itself out. A key mechanism makes snippets of the genetic material dock onto a piece of virus DNA and position it as needed. By and by, larger forms take shape, transistors self-assemble, until eventually, an entire circuit emerges. The highly complex chips that are part of every electronic device are smaller than ever and simply appear, seemingly out of thin air – with minimal effort and cost.

This will be the future of electronics if Artur Erbe has anything to do with it. The physicist is on a mission to create circuits at the nanometer-scale using DNA. He and his team recently achieved a major milestone when they attached gold particles to nanowires that were created via the self-organizational abilities of DNA and made them electrically conductive. The DNA wires could thus serve as a connection between two electronic components. The researchers' next step will be to attach semiconducting quantum dots to the wires instead of metal particles, thus developing a novel single electron transistor. It will be another few years before such a nature-technology hybrid will actually be built into computers. But this is how humanity makes its way towards the world of tomorrow: one small step at a time.

Source: istockphoto.com | nmlfd, kynny, Pixabay.com | wilhei, Freepik | kjpargeter

25 JAHRE

Forschungszentrum

25 Years Research Center