THE MAGAZINE OF THE **PRODUCTION TECHNOLOGY CENTER BERLIN**

futur

VISION | INNOVATION | REALIZATION

mRNA to the Rescue

mRNA-based vaccines against the novel coronavirus are one of the most important steps on the way out of the COVID-19 pandemic. Can their production be accelerated using new methods?

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High-tech Engineering for the Heart

The world's smallest heart pump comes from Germany. We spoke with Dirk Michels at its manufacturer Abiomed.

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Worked to the Bone

In the mobiLAB-4D project, the members of our expert panel are performing joint research into how the surfaces of implants can be improved to avoid clinical compli-cations.

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HEALTH AND MEDICINE

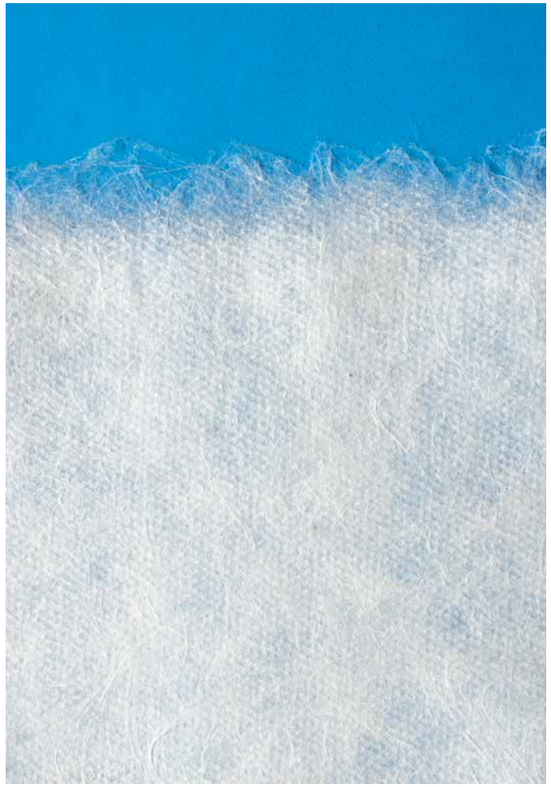
Fraunhofer
IPK

INSTITUTE
PRODUCTION SYSTEMS AND
DESIGN TECHNOLOGY

IWF

INSTITUTE MACHINE TOOLS
AND FACTORY MANAGEMENT
TECHNISCHE UNIVERSITÄT BERLIN

When Quality
Is a Matter of Survival



Can this inconspicuous piece of textile become a lifesaver? The quality decides.

↳ page **22**

Production Technology Center (PTZ) Berlin

PROFILE The Production Technology Center (PTZ) Berlin houses two research institutes: the Institute for Machine Tools and Factory Management IWF of the TU Berlin and the Fraunhofer Institute for Production Systems and Design Technology IPK. As production-related research and development partners with a distinctive IT competence, both institutes are in international demand. Their close cooperation in the PTZ puts them in the unique position of being able to completely cover the scientific innovation chain from fundamental research to application-oriented expertise and readiness for use.

We provide comprehensive support to companies along the entire process of value creation: Together with industrial customers and public-sector clients, we develop system solutions, individual technologies and services for the process chain of manufacturing companies – from product development, planning and control of machines and systems, including technologies for parts manufacturing, to comprehensive automation and management of factory operations. We also transfer production engineering solutions to areas of application outside industry, such as traffic and safety.

DEAR READERS,

the German medtech industry is a mirror of the national production landscape: SME-centered, highly innovative and strong in exports. According to the German Medical Technology Association BVMed, it employed 235,000 people in Germany and generated 34.4 billion euros in 2020. Two-thirds of the workforce were enlisted for medium-sized companies. The sector's innovative strength is particularly evident in its short product cycles: A third of all sales are made with products that are no more than three years old. This hardly comes as a surprise in an industry that invests nine percent of its revenue into research and development. The good reputation of German medical technology products precedes them. According to the German Federal Statistical Office, the export ratio of the medtech industry is around 66 percent.

At the Production Technology Center Berlin, we also play our part in this success. Our scientists work on a wide range of highly topical issues that are relevant to the manufacturing industry in terms of health and medicine. In this issue, we would like to give you an insight into our production technology research in these areas, as well as our biotechnology laboratories and cleanroom where it takes place.

Few topics are currently as relevant as the research to support vaccine production. We are presenting a project that aims to accelerate the production of mRNA-based vaccines. We are also playing a key role in driving forward the development of novel processes and technologies in the field of microfluidics. In this issue, we showcase the services we offer to our partners along the process chain of manufacturing. As an exemplary product, we are using a so-called lab-on-a-chip system.

Such microfluidic chips are also a central component in the mobiLAB-4D project, in which they are used to cultivate bone cells. The partners in this project are experts from industry, research, and clinical application. In our panel discussion, they reveal what makes their research particularly tricky and how they are hoping to make implants safer.

Health is also a major issue for traditional manufacturing work on the shopfloor. To prevent illnesses caused by poor posture during physically demanding work, our researchers have developed a unique textile exosuit that ensures more ergonomic movements. In this way, companies can be sure to preserve the well-being and working ability of their employees.

With best wishes, hoping that you are happy and healthy: Enjoy reading!

Yours

Eckart Uhlmann

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Microfluidics is one of the current industry trends in microproduction.
↪ more on page 10

How can mRNA molecules be made fit for vaccination and transport in the body?

↪ more on page 16

To ensure that FFP2 masks are as safe as they need to be, rigorous quality testing is necessary.
↪ more on page 22

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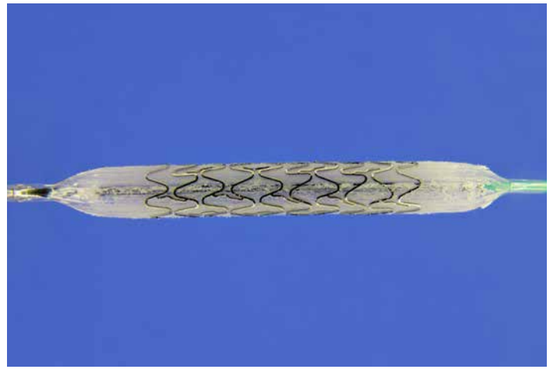

Will such stents on drug-coated balloon catheters still be necessary in the future?
↪ more on page 32

© OsiriX by Pixmeo, Geneva, Switzerland

Sensitive tissues such as gonads should be protected from harmful X-rays as much as possible.
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Not your average exoskeleton: the dual arm exosuit PowerGrasp

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Individual solutions for challenging research questions are developed in the laboratories of the Production Technology Center.
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SHORTCUTS | futur

NUMBER OF THE ISSUE

€ 33,400,000,000

That was the total turnover of the medical technology sector in Germany in 2019.
Read our article »Manufacturing for the Healthcare Sector«!

⮑ more on page 10

IN DETAIL

Find out **what kind of technology** is behind this image.

⮑ more on page 42

TAKE PART!

Fraunhofer IPK, in cooperation with EPIC (Centre of Excellence in Production Informatics and Control), is conducting an online survey to determine the direct impact of COVID-19 on industrial production. The focus is on the question »How can digitalization help to mitigate these impacts?«.

The survey is open until June 30, 2021.

Taking part is worth your time: As a thank you for your participation, you will be among the first to receive the digital edition of the study!

⮑ **Find out more at**
www.ipk.fraunhofer.de/epic-survey-corona

BIOLOGICAL TRANSFORMATION

⮑ **More information about the project and the event:**
http://www.ipk.fraunhofer.de/biofusion40-en

BioFusion 4.0
Industrie 4.0 plus biological principles equals BioFusion 4.0! The new research project explores the interdependencies between the principles of biological transformation and their interactions with production, services and work. It is not only the budget of over € 5.3 million (of which € 3.8 million are funded by BMBF) that makes this a major project. The consortium of two research partners, five application partners and six technology partners is also remarkable. Under the overall leadership of Fraunhofer IPK, participants in »BioFusion 4.0« include Mercedes-Benz, TU Berlin and the Werner-von-Siemens Centre for Industry and Science, as well as long-standing partners of Fraunhofer IPK such as budatec and Contact Software.

On June 10, 2021 the official kick-off event for BioFusion 4.0 will take place!

WELL SAID

»In an era of modern, agile and globally networked production and information systems and the increasing integration of 3D printing methods into production processes, it should be possible to realize individual solutions for every single patient.«

Dr. Philip Elsner, Berlin Heart GmbH, in his guest article for our alumni column on manufactory-based small-batch production of medical devices

⮑ more on page 46

Manufacturing for the Healthcare Sector

When manufacturing medical technology, biotechnology, and pharmaceutical products, a high level of engineering expertise is essential.

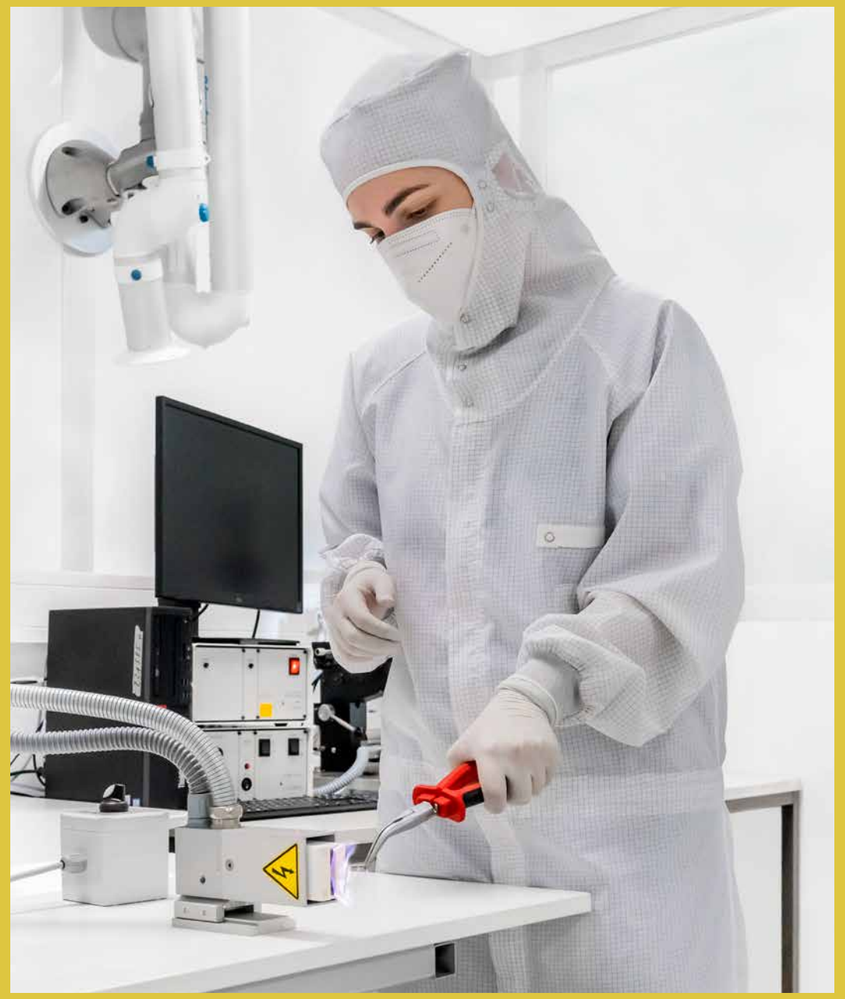

Image:
Researchers at PTZ are developing special manufacturing technologies for the production of microfluidic chips.

From the moment a patient commences medical treatment to the moment he or she can be declared cured, a number of things need to happen: From diagnostics to therapy up to the completion of rehabilitation – each of these steps requires biomedical or medical technology products and devices. Doctors, pharmacists, and nursing staff must be able to trust that the materials themselves and their finish are of the highest quality. Even tiny errors in the manufacturing of medical products can have life-threatening consequences.

It is precisely because of these exacting standards that medical engineering is among the most innovative industries. Whether it is less invasive operational procedures, more reliable implants, or more effective vaccines – new technologies and products increase our quality of life and help save lives. The current patent ranking of the European Patent Office highlights the innovative strength of the MedTech industry: It ranks first in terms of patent applications, ahead of digital communications and computer technologies. Equally remarkable is the dynamic momentum with which these innovations are taking place: According to BVMed, the German Medical Technology Association, German medical engineering manufacturers generate approximately one third of their sales from products that are less than three years old. Manufacturers also work extremely closely and transparently with users from the very beginning. In addition, in 52 percent of cases, it is doctors and nursing staff who provide the inspiration for the development of new products.

Rapidly putting new technologies into use in real-world applications without compromising on safety and effectiveness is a constant challenge for the industry.

Medical products must pass extensive technical checks before they are tested in clinical trials and approved for patients. This involves testing to determine whether the products' characteristics – e.g., density, strength, compatibility, sterility – meet the performance requirements that make their medical use possible in the first place.

Hence, without engineering research – no progress in medical technology. This applies in particular to the three major industry trends: miniaturization, microfluidics and digitalization.

MINIATURIZATION: MAXIMUM PRECISION FOR THE SMALLEST PRODUCTS

Medical disciplines such as cardiology, surgery, radiology and diagnostics currently rely on complex, miniaturized products. At the Production Technology Center (PTZ) Berlin, interdisciplinary teams consisting of mechanical engineers, biotechnologists and electrical engineers are conducting research on how they can be manufactured safely and efficiently. Using ultra- and high-precision processes alongside nano- and biotechnologies, they are for instance able to replicate structures for fluid mixing systems or cell separations.

Our researchers are also improving quality of life for people with prosthetic joints: They optimize materials and manufacturing processes in such a way that they obtain an improved stress state, thus enabling a longer service life for prostheses. In addition to conventional materials such as metals and plastics, scientists are also taking materials that are difficult to work with, such as

Without engineering research – no progress in medical technology.

THE MEDTECH INDUSTRY IN FIGURES

215,000
Employees in Germany

€ 33,4 Bn.
Total revenue in 2019

65 %
Export ratio

Source:
BVMed Branchenbericht Medizintechnologien 2020

metallic glass and refractory metals, and making them compatible for medical applications. They are, for example, developing ideal surfaces to prevent accumulation of microorganisms or rejection reactions.

MICROFLUIDICS: NEW SCALING POTENTIAL FOR PHARMACEUTICAL MANUFACTURERS

Fluid-conveying systems are widely used in real-world medical applications, such as in lab-on-a-chip systems for point-of-care diagnostics. Researchers at the PTZ are developing special manufacturing technologies for producing such microfluidic chips. In their own research, they are using chips to optimize the enveloping of mRNA molecules in lipid nanoparticles – an important step in scaling up the production of vaccines against the corona virus.

Another aspect of vaccine production: Currently, vaccines based on cell and gene therapy are still being produced laboriously in manual batch-based production processes. However, fully automated and integrated end-to-end processes could soon revolutionize not just vaccine production, but pharmaceutical production as a whole. The Fraunhofer »Pharmaceutical Production 4.0« initiative is therefore developing innovative concepts for the automation, digitalization, and modularization of pharmaceutical production and quality assurance of drugs. Application scenarios include not only vaccines, but also cell therapeutics and stem cells for oncology and regenerative medicine, as well as for the treatment of immune and infectious diseases. The team of researchers at Fraunhofer IPK, with its expertise in production and material technologies, as well as actuators and sensors, is working primarily on the parallelization of manufacturing processes and on facilitating high-throughput processes. This could drastically reduce development and production cycles in the future.

DIGITALIZATION: BETTER DIAGNOSES AND THERAPIES

Nearly every aspect of today's world requires digitalization to function – and medicine is no exception. Whether it is biosensors for blood glucose measurements, camera chips for retinal implants, or AI-supported imaging processes for surgery – digital technologies have become indispensable in healthcare. They allow medical professionals to detect diseases earlier and administer treatments more efficiently – i.e. more individually tailored to the patient – as well as to optimize follow-up treatments, including rehabilitation and care.

However, digital solutions in medicine have even greater potential applications. Since 2016 and embedded in the German federal government's High-tech Strategy 2025 and Digital Agenda, the German Federal Ministry of Education and Research has been funding new developments in the field of medical engineering, above all in the areas of medical informatics, big data, as well as digital diagnosis and therapy methods. eHealth, telemedicine, and telemonitoring play a key role in this regard, both for healthcare and for medical technology companies. While surgeons in future could be performing minimally invasive surgery with Augmented Reality (AR), or patients with spastic movement disorders treated with the aid of Virtual Reality (VR), context-sensitive assistance may support manufacturers with their highly specialized production processes. Here, AR and VR solutions could help ensure the zero-error strategy required in medical technology production, as well as guide specialists through individual process steps in a targeted manner that is tailored to their respective level of training.

Image:
Today, such miniaturized sensors are used for blood pressure measurement.
© *BVMed*

The prerequisite for this is effective process monitoring. Scientists at PTZ Berlin are therefore applying long-established condition monitoring strategies from mechanical and plant engineering to medical engineering. But this transfer of strategies is not a one-way street – conversely, they are also utilizing technologies originally developed for medical applications in the production halls of injection molding manufacturers and automotive suppliers. One such example involves imaging processes such as computer tomography. In high-throughput processes for manufacturing electric vehicle components, an inline CT now provides seamless documentation of all processing steps, thereby ensuring reliable and stable process and component monitoring. ◆

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Smallest Components – Greatest Performance

At the Production Technology Center, we offer R&D services along the entire process chain. Let us demonstrate our services for tool and mold making using the example of a microfluidic chip.

Demand

A biopharma company wants to have a lab-on-a-chip system developed for a point-of-care application. The basics are already in place at full lab-scale.

Our services:
- Preparation of market studies
- Biotechnological evaluation and technology optimization

Production planning

Our team plans a manufacturing process chain according to specific batch size, materials, and precision requirements.

Our services:
- Planning of manufacturing technologies and manufacturing process chain in preparation for market launch
- Determination of direct structuring or replicative manufacturing technologies
- Design, manufacture, and sampling of high-precision injection molds

Component design

Our researchers design and manufacture a chip to transfer laboratory methods into the lab-on-a-chip system and hand over functional samples to the client for evaluation.

Our services:
- Design and simulation of microfluidic systems
- Direct manufacturing of evaluation samples with cutting or additive manufacturing processes
- Fluid mechanical analysis and functional optimization
- Development of surface functionalizations

Production

To manufacture the microfluidic systems, the production technologies researched at Fraunhofer IPK are applied and used for the production of a first pilot series.

Our services:
- Injection molding or direct manufacturing of the microfluidic components
- Cleaning, sealing, and functionalization of the manufactured systems
- Planning and implementation of an application-adapted quality control system
- Short-term adjustments to the system design
- Parallel biotechnological evaluation at Fraunhofer IPK

Technology transfer

Manufacturing technologies are transferred to the final manufacturer and serial production can begin.

Our services:
- Transfer of the manufacturing technologies to the environment of a production partner
- Technology optimization in the fields of cutting, electrical discharge machining, and replicative manufacturing technologies
- Design and implementation of quality control methods and procedures

Pictograms: Flaticon.com

mRNA to the Rescue

mRNA-based vaccines against the novel coronavirus are one of the most important steps on the way out of the COVID-19 pandemic. Can the production of mRNA-based vaccines be accelerated using new methods?

The mRNA is processed in the ISO Class 7 clean room of the Application Center for Microproduction Technology – AMP to avoid contamination of the sensitive samples with foreign particles or harmful enzymes.

After passing through the microfluidic setup, the mRNA is checked for its integrity using the method of agarose gel electrophoresis to detect any shear defects in the molecule.

The mRNA is coated with a lipid layer within the microfluidic setup. The process is evaluated among other things by microscopic observation.

The best way out of the pandemic has already been much discussed. Only one thing seems certain: Without a vaccine, it will be difficult. A successful, rapid vaccination campaign is essential. Some vaccines have already been approved and administered by the millions. Many others are still in various stages of development, and the World Health Organization (WHO) is aware of nearly 300 vaccine projects. All over the world, people are striving for the rapid production, distribution, and administration of an unprecedented number of vaccine doses. The novel mRNA vaccines are in especially high demand on a global scale. Not only do they show high efficacy and very low side effects, but they are also relatively easy to adjust. In principle, they could be engineered to generate a robust immune response even to mutated variants of Sars-CoV-2. The German enterprise CureVac is one of the companies researching such a vaccine and has attracted global interest. The German government, among others, supports their research. Tesla CEO Elon Musk has been working on a »vaccine printer« with CureVac since earlier this year. Fraunhofer IPK is cooperating with the Tübingen-based company to advance the development and production of the vaccine.

HOW DO MRNA VACCINATIONS WORK?

Even though companies such as CureVac have been researching mRNA technologies for two decades (more about this on page 21), until recently there had not been any approved vaccines based on these technologies. The urgency of a global pandemic with the prospect of paralyzing entire economies for years to come has now helped this technology make a breakthrough. Because unlike known viruses such as measles, diphtheria, or influenza, there was no »traditional« vaccine for the coronavirus. To date, most vaccines have been based on the idea of supplying the body with what are called antigens. These are either attenuated or dead versions of the virus against which the vaccine is administered, or what are called vectors: harmless vaccine viruses that are »disguised« with fragments of the harmful virus' genetic information, thus feigning an infection. Although these antigens cannot cause disease, they can stimulate the body to react as if they did. The body can »remember« this defensive reaction for a certain period of time and add it to its immune defense arsenal. It can then be called up immediately, if the real virus is ever detected. In contrast, mRNA vaccines do not contain any components of the virus against which the vaccine is administered. With single-stranded mRNA, short for messenger RNA, it is merely a genetic construction manual that is introduced into the body of the vaccinated person. It is able to stimulate the body's own cells to produce viral protein building blocks that are recognized as components of the virus and trigger a corresponding immune defense reaction. In other words: Based on the mRNA information, the body produces the antigens itself and then reacts to them. As reported in the Deutsches Ärzteblatt, this type of vaccination offers »a significantly better safety profile and fewer side effects.«

Images:
1
High-precision channel geometries within the microfluidic chip ensure the controlled generation of lipid nanoparticles.
2
The gel electrophoresis chamber separates the mRNA molecules according to their size by applying an electrical voltage, allowing their integrity to be assessed via the number of molecule fragments.

1

2

»Development using mRNA as a vaccine was initially halting. This was mainly due to the fact that RNA molecules are degraded very quickly enzymatically.«

Image:
By binding a fluorescent dye to the mRNA and subsequently measuring the samples spectrometrically, the quantification of the encapsulated nucleic acids is conducted on a sterile workbench in the AMP's biomedical laboratory.

More information:
www.ipk.fraunhofer.de/helimol-en

So why did it take so long for mRNA vaccines to break through? The journal writes: »Development using mRNA as a vaccine was initially halting. This was mainly due to the fact that RNA molecules are degraded very quickly enzymatically.« This means that without special protection, the mRNA molecules cannot remain in the body long enough to bring about their intended effect in the right place.

MOLECULAR PROTECTION

So how can the mRNA molecules be made suitable for vaccination and transport in the body? The German Federal Institute for Vaccines and Biomedicines, the Paul-Ehrlich-Institut, summarizes the principle as follows: »mRNA/DNA vaccines do not require a vector for vaccination, i.e. no carrier virus, but rather liquid nanoparticles (droplets of fat) so that they can enter certain body cells.« The mRNA molecules must therefore be encapsulated in a protective lipid envelope. However, currently available technologies for generating such lipid nanoparticles and encapsulating the molecules are not yet very advanced. The SARS-CoV-2 vaccine candidates currently in development can therefore only be replicated and tested slowly. In particular, with the current state of the art, these difficulties also affect vaccine production once development is completed. This is how the collaborative project HeLiMol to produce lipid nanoformulations for the encapsulation of mRNA molecules with Fraunhofer IPK came about. In this project, which is supported by CureVac in the form of equipment, material, and expertise and funded by the Fraunhofer-Gesellschaft within the »Fraunhofer vs. Corona« campaign, two possible approaches are being researched almost in parallel. The two approaches differ in the method of mixing the mRNA molecules and the lipid phase for fast and uniform encapsulation. This will allow microfluidic encapsulation technologies to be developed that allow for GMP-compliant encapsulation and scaling of production capacities at the same time. In addition, an entirely new approach to macroscopic high-throughput encapsulation of mRNA molecules is being researched, which will allow the required production capacities to be achieved even without the complex parallelization of microfluidic structures. ◆

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© picture alliance / dpa

CureVac – Developed from the Building Blocks of Life

The Tübingen-based company conducts research on mRNA-based agents. It became world-famous almost overnight – thanks to a promising vaccine candidate against the novel coronavirus SARS-CoV-2.

Founded in 2000, CureVac pioneered the discovery of the potential of messenger RNA (also known as mRNA) to treat diseases and produce vaccines. It was the first company worldwide to successfully use mRNA for medical purposes. The single-stranded messenger molecules of ribonucleic acid (mRNA) contain genetic information for the structure of certain proteins in a cell. These are transcribed as a code in the sequence of the nucleobases of the molecules. The research and optimization of this genetic »construction manual« hold great potential for biopharmaceutical research. For example, it can be used to stimulate cells of the human immune system to initiate important reactions to fight or prevent diseases. However, the mRNA biomolecules are very unstable on their own, making them unable to withstand being transported to their destination within the human body. As a doctoral student, CureVac's founder, Dr. Ingmar Hoerr, discovered how to optimize mRNA for use as a therapeutic vaccine or active ingredient when administered directly into the tissue. The company uses its proprietary technologies to develop prophylactic vaccines, cancer therapies, antibody therapies, and protein therapies.

Today, more than 600 people work at CureVac. The most important and best-known project at present is an mRNA vaccine against the novel coronavirus SARS-CoV-2. Read more about the research on this vaccine candidate and how Fraunhofer IPK is helping to equip the mRNA molecules with their own protective shield in the previous article. ◆

Contact
www.curevac.com

The sight of such FFP2 masks has become almost as common as that of glasses or hats. To ensure the safety of face coverings, rigorous quality testing is necessary.

When Quality Is a Matter of Survival

Protective medical masks are an essential component for combating the pandemic. Their quality ought to be verified automatically and reliably.

There is no doubt that the German economy is experiencing a recession as a result of the COVID-19 pandemic. Compared to the previous year, the gross domestic product shrank by almost five percent in 2020. Some sectors were certainly hit harder than others. But it also opened up new markets: Disinfectant shortages prompted resourceful manufacturers of spirits to convert their production lines. In no time at all, existing facilities were adapted to produce the germicides which were in high demand.

But it was not possible to respond quite as quickly to another sudden increase in demand: namely medical mouth and nose coverings, i.e., surgical masks and FFP masks. As everyone will recall: These masks were particularly scarce at the beginning of the pandemic and were mainly used to protect hospital and clinic staff who came into contact with patients on a daily basis. Imports from the Far East provided a short-term remedy, but often at the expense of quality.

In this case as well, companies in Germany reconfigured their manufacturing operations. Before the pandemic, some were producing seat covers for automobile manufacturers, but now began to produce protective masks. A clever strategy, because there is still no end in sight to the demand for medical masks. In many areas, they are now mandatory when shopping and using public transport and have replaced the everyday masks that were previously commonplace.

HOLISTIC APPROACH TO PROTECTIVE TEXTILES

Particularly in the field of life-saving protective textiles, quality naturally plays a crucial role. A scientific team at

1

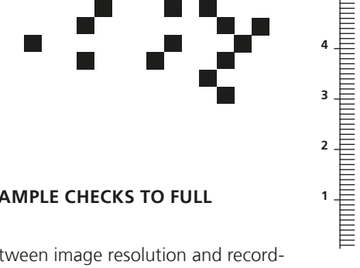
Fraunhofer IPK is therefore developing an inspection system that will visually examine both the input materials and finished mask textiles. This endeavor is part of the »Next Generation Protection Textiles« project, which is funded as part of the »Fraunhofer vs. Corona« campaign. The consortium comprises ten Fraunhofer institutes.

Together, they are pursuing a new, holistic approach to the development of protective textiles. Apart from an improved filtering effect against viruses, new methods for manufacturing the input materials will also be tested. Utilizing two demonstrators, the researchers also intend to investigate practical aspects such as wearing comfort and improved speech intelligibility.

QUALITY IS KEY

For intelligent quality assurance in the form of 100% inspections, the highly precise requirements which textiles need to fulfill in the micro- and nanometer range pose a particular challenge. Sensors capable of generating images in these resolution ranges are extremely expensive to purchase. They are too expensive for the SMEs that produce the masks in Germany. Moreover, with such systems, the process of data collection is slowed down due to the fact that many steps are performed manually. Conventional image processing systems available on the market, on the other hand, are able to perform fully automated 100% inspections even with high processing speeds – but only at the expense of resolution accuracy.

Images:
1
Optical examination is used to support the 100% inspection.
2
Perfect balance between fast image acquisition and highly accurate resolution is required.
3
The microscopic image shows high-quality material.
© Fraunhofer IMWS
4
Using the transmitted light method, critical areas in low-quality textiles become visible.
© Fraunhofer IMWS



FROM MANUAL SAMPLE CHECKS TO FULL AUTOMATION

The compromise between image resolution and recording speed is not the sole issue experienced with existing technical solutions. This is because even if an image processing system is able to capture a defect pattern in a manner satisfying the necessary specifications, it must also subsequently be recognized as a defect in the image material. The vast volume of image data captured during the inspection process cannot be evaluated by humans. To do so, companies would either need an impossibly large team in their quality control division, or processing speeds would need to be greatly reduced to be able to inspect all the image data. Both these scenarios are far outside the realm of what is economically sensible.

To enable fully automated, live optical inspection of the manufacturing process despite these challenging conditions, a good trade-off between rapid image acquisition and highly precise resolution is needed. It is precisely this perfect balance which the Fraunhofer IPK team is aiming for. Conventional industrial cameras combined with special optics serve as hardware. Similarly, on the software side, a wide variety of image processing algorithms – ranging from traditional image processing algorithms to the latest machine learning methods – are being tested in order to identify all defect patterns in the images with a high degree of precision.

By the time the project is concluded in October 2021, the researchers expect to have made a breakthrough in this area. It would be a major success for quality assurance – and ultimately also for protection against this and future pandemics. ◆

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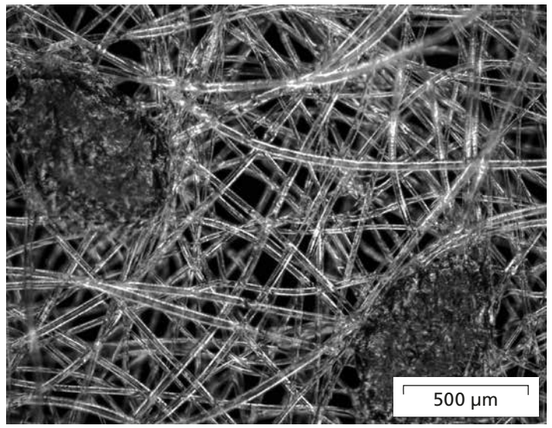

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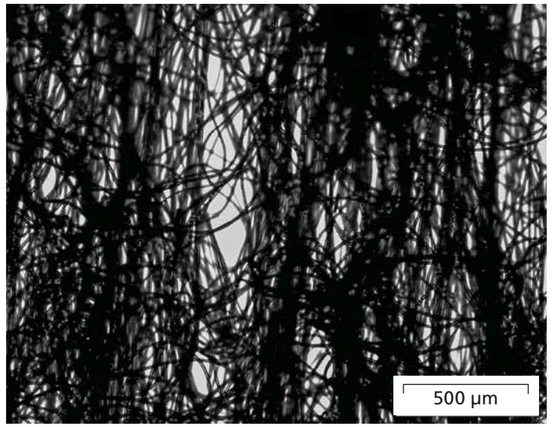

4

Virus vs. Open Source

Documentation is the mantra for open-source hardware communities. This was found by the OPEN.Effect study, which evaluated ventilator manufacturing projects.

About a year ago, ventilators were in short supply. The COVID-19 pandemic had caused demand to skyrocket, leading to global supply shortages. In Germany alone, the number of intensive care beds with ventilator capability was increased from about 22,000 before the pandemic, to more than 28,000 today, not including reserves, according to the German Hospital Association (DKG). At the same time, numerous open-source projects for the production of ventilators by decentralized manufacturers emerged worldwide. In May 2020, a scientific team from Fraunhofer IPK, in collaboration with the non-profit organization Public Invention, set out to collect, analyze and evaluate these projects with the OPEN.Effect study.

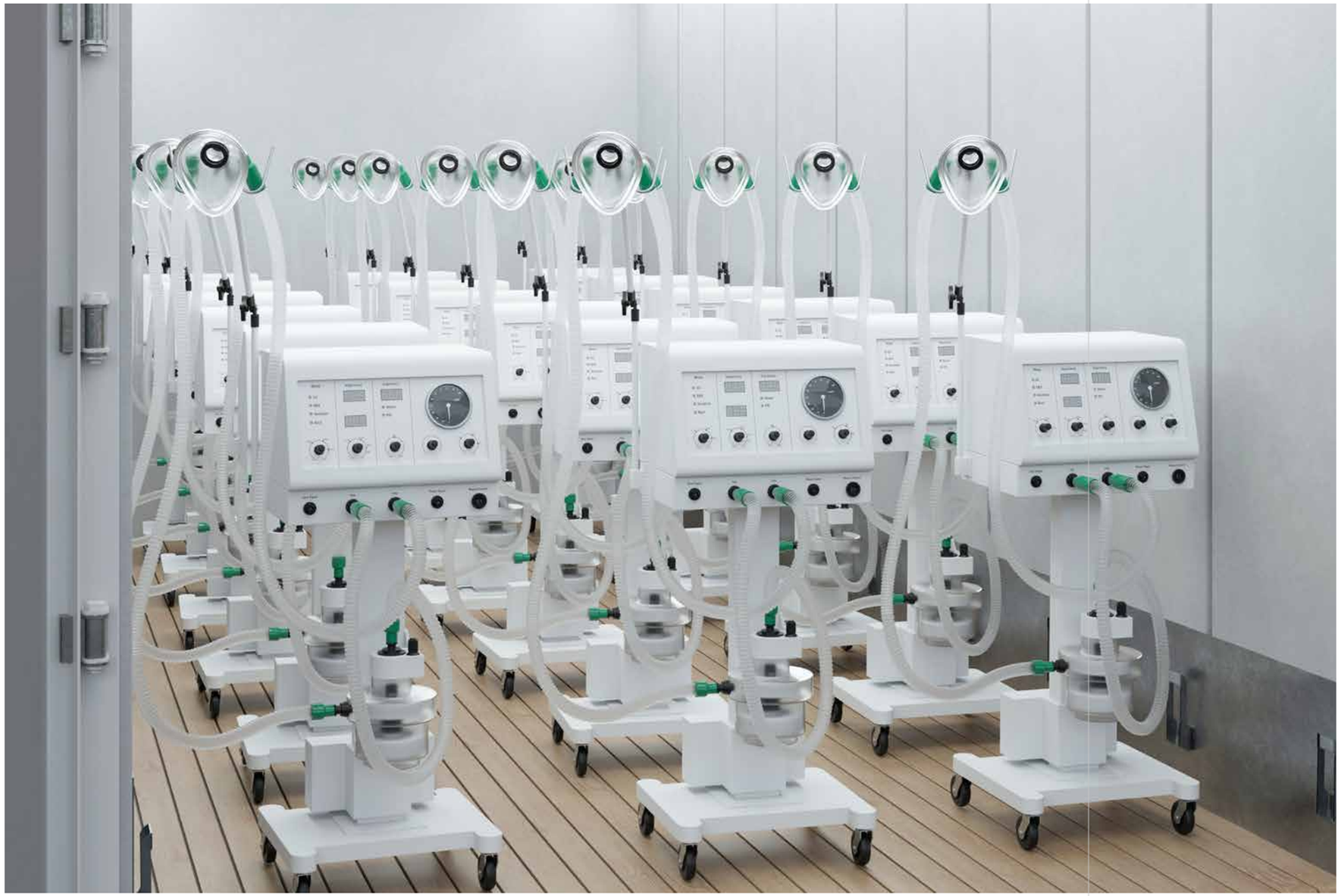

Image:
Such ventilators are valuable lifesavers. Well-planned and executed open-source hardware projects can help to produce them quickly and safely.

OPEN METHOD, OPEN FEEDBACK

For the study, 27 contributors to 14 representative projects in the open-source hardware (OSH) community were interviewed about their experiences. Interviewees came from a variety of disciplines, including project management, software and hardware development, and design. A variety of organizational forms were also represented, from open communities to non-profit organizations and research institutes to companies. The interviews were based on 13 criteria for OSH projects, developed on the basis of the preliminary research, including for example openness, buildability or functional and reliability testing.

The results of the interviews provide an overall picture of the status of the projects, as well as which procedures have proven to be optimal and which challenges have arisen. On the basis of this information, the authors of the study have derived some suggestions that could be helpful for other OSH projects in the future.

FROM IDEA TO DEPLOYMENT

How can the OSH community and its projects be further developed in concrete terms? A ventilator goes through a number of phases, from design to deployment on ill patients. Along these phases, the authors of the OPEN.Effect study make specific suggestions for improving processes.

Some examples are:

1. **Medical personnel** or other end users should be involved in the development process from the very beginning, in order to align the technology with common device models and provide tutorials.
2. Due to difficulties in the **supply chain**, regionally available and standardized components should be used to enable modularity and interchangeability.
3. The **development process** of the device should be fully and continuously documented for future projects.
4. The finished device must meet the high **quality standards** of the medical industry. Centralized testing facilities can greatly reduce the burden on (decentralized) manufacturers to procure test equipment. Standardized testing procedures and protocols offer an advantage here.
5. The final and decisive hurdle after the test phase is the **application for approval** for the finished ventilator by national authorities. The laborious bureaucratic process should be fully documented, which will facilitate future projects.

More information:
http://www.ipk.fraunhofer.de/open-effect-en

Overall, the study shows that it is possible for open communities to provide fast and safe solutions to a critical problem during the pandemic. The complete English-language study can be downloaded for free at www.ipk.fraunhofer.de/open-effect. OPEN.Effect was funded as part of the »Fraunhofer vs. Corona« campaign by the Fraunhofer-Gesellschaft. ◆

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High-tech Engineering for the Heart

Interview with Dirk Michels, Abiomed Europe GmbH

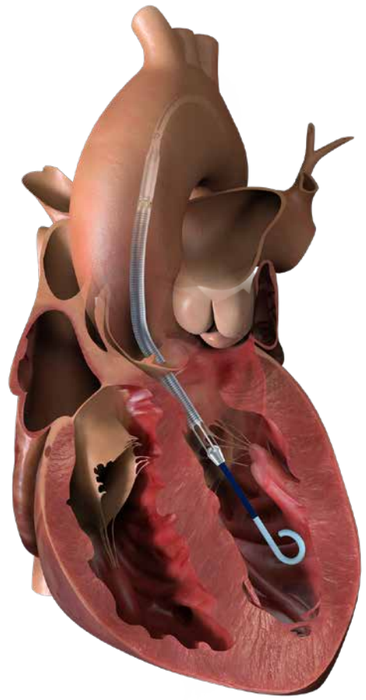

Image:
Impella CP with
SmartAssist heart pump
© *Abiomed*

The smallest heart pump in the world comes from Germany. The Impella heart pump is used in emergency medicine and for treating coronary heart diseases and heart failure. The purpose of Impella heart pumps, which can be used minimally invasively or surgically, is to support and relieve strain on the heart, regenerate cardiac function, and allow patients to enjoy an improved quality of life.

We spoke with Dirk Michels, Vice President Global Manufacturing & Supply Chain and Managing Director Abiomed Europe Operations at the manufacturer Abiomed, about the importance of modern medical technology solutions and how findings from research and development can be rapidly and safely used in applications for real-world care.

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DIRK MICHELS
VICE PRESIDENT GLOBAL MANUFACTURING & SUPPLY CHAIN AND MANAGING DIRECTOR ABIOMED EUROPE OPERATIONS

Dirk Michels obtained his Master of Science in Mechanical Engineering from the University of Aachen and MIT in Cambridge, Massachusetts, USA. Dirk Michels has been with Abiomed since 2005. In his current position, he heads all purchasing and supply chain activities as well as global supplier management. He is also responsible for global production and in particular for the expansion of production facilities in Europe.

| futur | Heart failure and coronary artery disease are the leading causes of death in both men and women. How do your products and technologies aid in the treatment of heart disease?
/ Michels / Our heart pumps are used during complex coronary interventions and in emergency medicine. Around the world, more than 170,000 patients have been treated with our small Impella heart pumps.

The Impella heart pump restores heart function by being inserted minimally invasively into the human heart via the femoral or shoulder artery and, depending on the pump type, temporarily taking over all or part of the heart's pumping function, such as during a percutaneous coronary intervention. Hence, our heart pumps make the intervention safer and more effective in high-risk patients.

In emergency medicine, in the event of a heart attack, for example, the Impella heart pump enables cardiac recovery in shock patients. Our heart pumps aid with blood circulation, stabilize hemodynamics in patients, and improve the blood supply to end organs. As a result, they are able to promote regeneration of the heart muscle and thus improve quality of life for patients.

| futur | Ever smaller, smarter and digitally networked – this is what Impella technology claims to be. What challenges does this pose for manufacturing and production?
/ Michels / High-tech engineering is where we are at home. Manufacturing of the Impella heart pump requires compliance with the highest standards – from the supply chains and the materials used to the actual production and the final inspection. This requires maximum performance from our employees each day and can only succeed thanks to long-standing experience, technical expertise, and quality management. The latest technology in our product portfolio is the world's smallest heart pump with a diameter of 3 mm – the Impella ECP heart pump, which, by the way, is »Made in Berlin«.

| futur | Apart from your SmartAssist and Impella Connect product lines you also provide service platforms. What is the motivation behind this and how have patients and physicians responded to these offerings?
/ Michels / SmartAssist, our most recent platform-based innovation, provides concrete advantages for treatment: For example, SmartAssist sensor technology can be used to make a necessary correction in the position of the Impella heart pump even without imaging and relieve stress on the heart more effectively during treatment.

Our new Impella Connect technology, which is currently being introduced in German hospitals, is a cloud-based platform that enables physicians to provide patients using our Impella heart pumps with even better care. With Impella Connect technology, patients' treatment and recovery progress can be monitored and controlled online, 24 hours a day, 7 days a week, from any internet-enabled mobile device.

| futur | Medical devices are required to undergo extensive technical testing and clinical trials before they can be used on patients. How do you ensure that your latest developments are brought to market quickly and safely?
/ Michels / We have decades of experience in translating innovative technologies into safe, market-ready products. Apart from our own R&D department, we also invest in clinical research in order to achieve the best possible results for our patients. We have now completed seven U.S. Food and Drug Administration (FDA) studies and five post-market approval studies which demonstrate the benefits of Impella heart pumps.

| futur | What does the future of cardiac medicine look like? Which products and technologies will become necessary?
/ Michels / We see a great deal of opportunity for users and patients where telemedicine and digitalization are concerned, because with the targeted use of these technologies, we will be able to continuously improve treatment outcomes for patients.

| futur | The Corona pandemic has shown us all how important medical technology products and processes are for our health, life, and quality of life. To what extent do you notice this increased appreciation in your company, as well as the effects of the crisis?
/ Michels / Our focus has always been on the patient. That is exactly why we at Abiomed have dedicated ourselves entirely to the patients' well-being in everything we do and all the initiatives we launch. Our solutions are specifically designed to further improve individually tailored patient treatments, which has become necessary as a result of the Corona pandemic. Because that is ultimately our goal – focusing on patients and helping them in the best possible manner. ◆

»We see a great deal of opportunity in telemedicine and digitalization, because they can continuously improve treatment outcomes for patients.«

Dirk Michels

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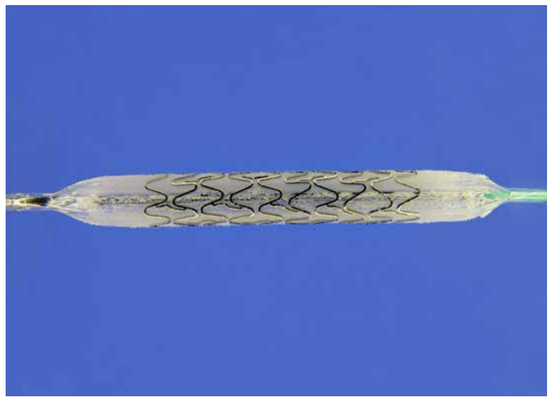

2

Using Balloons to Combat Heart Attacks

A new research project aims to demonstrate how automatically coated balloon catheters can be used to dilate arteries and keep them dilated – so that the heart can keep on pumping.

A stabbing feeling in the chest, a pain in the arm, breathing difficulties – the common symptoms of a heart attack are burned deep into our collective consciousness. In many cases, heart attacks are a result of coronary heart disease (CHD), a widespread disease that affects about seven out of every 100 women and ten out of every 100 men in Germany over the course of their lifetime.

The leading cause of CHD is a narrowing of the coronary arteries due to calcium deposits on the inner walls of the arteries, which is known as arteriosclerosis. Even if it does not result in a heart attack, those affected often suffer from chronic problems such as shortness of breath or pain. This is because the calcification causes a narrowing (stenosis) of the vessels, which means the heart can no longer be supplied with sufficient oxygen.

Images:
1
Optical inspection of a balloon catheter
© BVMed.de
2
A stent on a drug-coated balloon catheter
© InnoRa

Once such a narrowing has occurred, it needs to be removed mechanically. Until now, this has usually been done via a minimally invasive procedure in which a balloon catheter is inserted into the narrowed artery. On top of the balloon catheter is a plastic support called a stent. The stent expands as the balloon is inflated, and remains in the vessel in its expanded state. In this manner, it provides support for the artery walls and restores an uninterrupted flow of blood.

Like any foreign body, stents that remain in the artery carry risks. Tissue irritated by the dilatation may form a layer around the stent as it attempts to regenerate. In doing so, it may grow into the blood vessel after a few months. The resulting re-narrowing of the vessel segment, called restenosis, occurs in approximately one-third of all treatments involving a stent, and requires costly follow-up surgery. In order to reduce this risk to

about ten percent, the stents can be coated with immunosuppressive drugs that diminish cell growth. However, one potential long-term consequence of this procedure is a thrombosis.

Image:
A balloon catheter is inserted in a minimally invasive procedure.
© *BVMed.de*

ALTERNATIVE TO STENTS

Medical research is therefore focused on a lower-risk alternative: Instead of the stents, the balloon catheter used to widen the blood vessel is coated with immunosuppressants. The active substance is introduced directly into the cells of the arterial walls via the balloon's surface. This prevents cell growth – and thus the blood vessel from narrowing again – without leaving behind an object in the body.

To ensure that the oxygen supply is not completely interrupted for too long, the dilatation cannot take longer than 60 seconds. Unlike coated stents, which release an active substance over a longer period of time, balloon catheters therefore need to transfer it to the artery wall immediately. For good penetration through the cell wall, the coating has to be designed such that the microscopic crystals of the drug all point outward in the same direction.

Until now, however, these highly specialized crystalline coatings could only be applied to the catheters manually by experienced personnel – an extremely laborious and inefficient process that also resulted in a great deal of wastage. This technique quickly reaches its limits when it comes to the mass production of these high-quality medical devices.

LIFE-SAVING AUTOMATION

A team at Fraunhofer IPK is researching how the laborious process of coating balloon catheters can be automated. As part of the joint »Heliko – Automated and process-safe coating of balloon catheters with active substances« project funded by the German Federal Ministry of Education and Research (BMBF), an automated coating machine prototype is currently being developed. With this technology demonstrator, researchers intend to show how the process can be performed in a reliable and scalable fashion. By doing so, they aim to ensure a consistent level of quality and a higher overall effectiveness of the coated balloon catheters. Through the automation of production steps which are currently performed manually, the crystal structures of the drugs can be developed more reliably on the balloon's surface. At the same time, the costs of manufacturing will be significantly reduced.

As is generally the case at Fraunhofer, the scientists are collaborating closely with companies that are pioneers in this field. The company InnoRa is lending its expertise on the coating of the balloons and validating the results obtained in its own experiments. Organical CAD/CAM is using the coating system developed to build a machine tool so that the balloons can be manufactured on an industrial scale.

The automated coating machine is expected to be completed by the end of 2022, after which it will be swiftly launched onto the market. Dr. Thomas Speck, managing director at InnoRa, is optimistic: »As a result of the project, we expect an increase in the market share of drug-coated balloon catheters and in the acceptance of this specific form of therapy over conventional stent treatment.« Future patients could thus be spared the occurrence of late thrombosis. ◆

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»As a result of the project, we expect an increase in the market share of drug-coated balloon catheters and in the acceptance of this specific form of therapy over conventional stent treatment.«

Dr. Thomas Speck, managing director at InnoRa

All Accounted For?

Complaints regarding missing instruments in the operating room are a daily occurrence in hospitals. An AI-based system for automated completeness checks aims to avoid this.

1

2

Images:
1
Medical instruments, here in non-sterile condition
2
The AI main system (left) is used for the initial creation of training data and training of neuronal networks. The client workstation (right) sends recognition requests during the packing process to the AI main system.

Each day, approximately 3,500 medical devices are prepared for surgical procedures in accordance with the strictest hygiene and quality standards and delivered to be used by medical personnel in university hospitals. Up to 160 pairs of scissors, forceps, clamps, and other instruments fit on a tray the size of a sheet of A3 paper. Before use, they need to be cleaned, disinfected, packaged, and sterilized in reprocessing units for medical devices. A demanding task, because complaints from the operating room due to missing instruments are a daily affair.

NEEDLE IN A HAYSTACK

But is the clamp they are looking for really missing, or is the surgical team unable to find it among the many, very similar-looking instruments? Is the complaint justified? Service companies such as Charité CFM Facility Management GmbH are only able to investigate issues after the fact, when employees manually restack the trays using the packing list to verify whether all the required instruments are present. The trays are then packed, sealed, sterilized, and returned to the users. By scanning unique barcodes at defined scan points, CFM is able to locate surgical trays even after they have left the reprocessing unit. CFM contacted Fraunhofer IPK with the aim of jointly employing the latest AI-based image processing technologies to ensure that the trays are correctly packaged before being sent on their way.

AUTOMATED ASSISTANTS

For this purpose, researchers at Fraunhofer IPK are developing a Decision Support System which uses algorithms to automatically recognize surgical instruments. This consists of a detection system equipped with up to three cameras, a core AI system, and a packing station as a client unit. The core AI system is the processing unit and the heart of the technology. It allows surgical instrument image data to be collected and stored and enables neural networks to be trained based on this image data. This is accomplished by a holistic image processing and decision making approach using Convolutional Neural Networks (CNN). Compared to classical image processing methods, these have the advantage that the AI automatically configures complex parameters and continuously adapts all weights and parameters more precisely to the existing data as part of an automated training process. The overall system is implemented in accordance with the two-man rule as a supplementary testing instance for employees in the packing process and aims to help document the work steps on the packing trays as well as ensure their quality. This aims to reduce the number of complaints regarding incorrectly packed trays.

GET IT RIGHT FROM THE START

In a feasibility study, Fraunhofer experts have successfully demonstrated that their technologies are suitable for the automated recognition of surgical instruments. The sample comprised 156 different surgical instruments, which were automatically recognized with a Top 1 accuracy of 99.9 percent and a Top 5 accuracy of 100 percent, based on a data set containing a total of 9,672 images. The prototype, which is currently being developed, is expected to be available as a Decision Support System in the reprocessing unit for medical devices at the Charité Campus Benjamin Franklin from the fall of 2021. ◆

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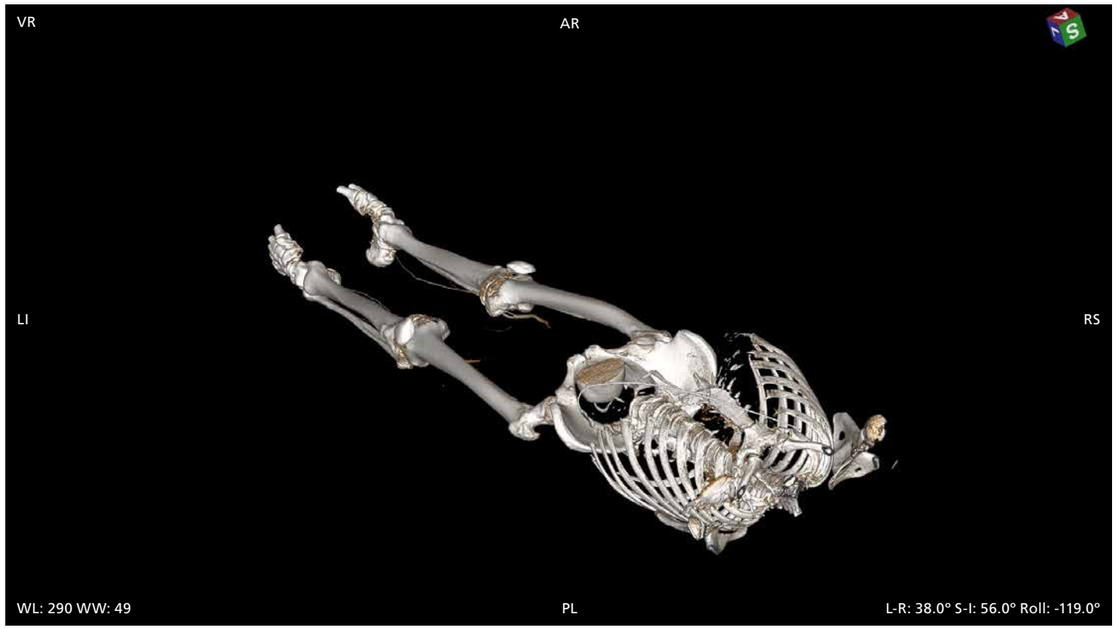

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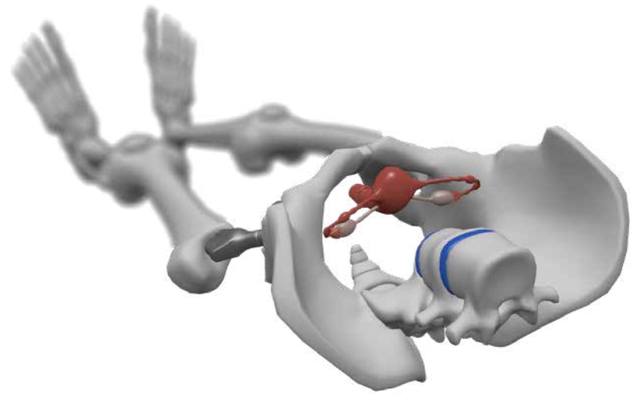


2

Minimal Radiation Exposure, Maximum Image Details

3D X-ray procedures are invaluable as diagnostic aids, but radiation-intensive. Novel simulation methods can help reduce radiation exposure.

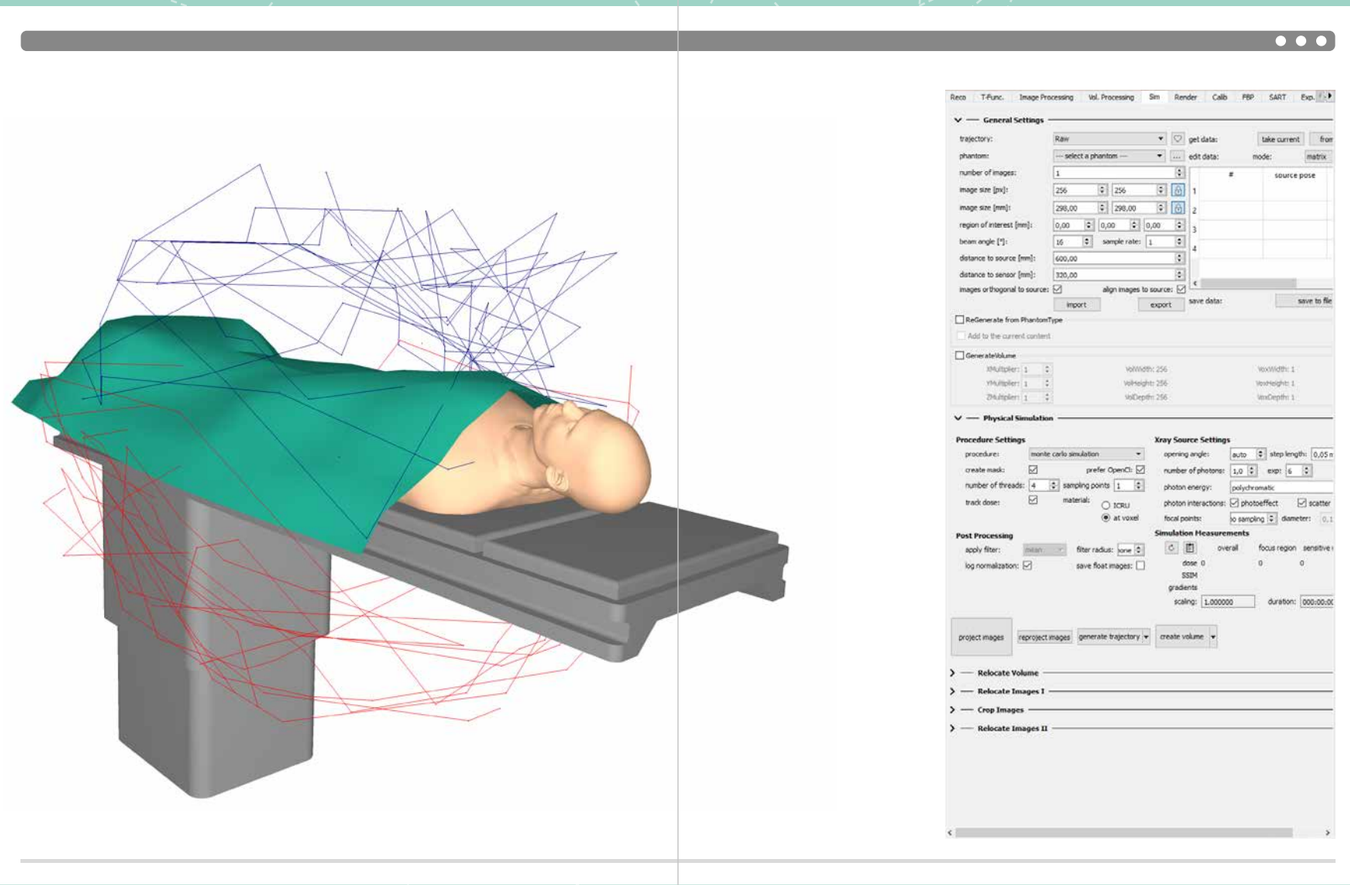
Images:
1
3D X-ray image
© OsiriX by Pixmeo, Geneva, Switzerland
2
Model of a pelvis with X-ray sensitive reproductive organs

Since Wilhelm Conrad Röntgen immortalized his wife's hand in the first image obtained using X-rays, a great deal of progress has been made. The technology now not only takes into account two, but three dimensions: Today, 3D X-ray imaging has established itself as an indispensable tool for answering complex clinical questions. These three-dimensional images of the body regions to be examined are created by exposing them to radiation using an X-ray system. To date, the entire region of the body has to be uniformly exposed to radiation – even though in most cases, only a small part of the image volume obtained is relevant for answering the clinical question. Is it technically and economically possible to design the imaging components' guidance systems in such a manner that only the required regions are exposed to radiation?

EACH TYPE OF TISSUE IS DIFFERENT

Different tissue types in the body react to X-radiation with varying degrees of sensitivity. Particularly critical, for example, are the lenses of the eye, glandular tissue such as the breast and thyroid glands, reproductive organs, and the intestines. Radiologists generally avoid X-raying these anatomical structures, as radiation-induced genetic alterations in these structures may have particularly severe repercussions. Accordingly, an equal dose with weighted distribution throughout the tissue dose is aimed for. The total dose of radiation administered remains the same, but the more sensitive tissue types are significantly less irradiated. 3D X-ray imaging systems available on the market today are unable to meet these complex medical requirements.

The imaging components of a 3D X-ray system – the X-ray source and X-ray detector – are guided mainly along standardized, circular trajectories. If it were possible to better adapt the motion paths of these components to each individual case, the reduction of radiation exposure of sensitive structures such as reproductive organs could be achieved, while at the



same time maintaining most of the image quality. As part of his dissertation at Fraunhofer IPK, medical engineer Felix Fehlhaber is therefore investigating how such specialized motion paths can be implemented in practice.

THE PROOF IS IN THE SIMULATION

For this purpose, he has developed simulation software that simulates medical X-ray processes in a physically precise manner. »The method is based on the Monte Carlo principle: A large number of small experiments are used to approximate the actual result,« explains Fehlhaber. The experiment simulated in this case: A photon, which is a light particle operating in the X-ray spectrum, is followed virtually on its path through realistically modeled tissue. At the same time, all medically relevant physical interaction effects are taken into account. Fehlhaber explains: »This provides a highly precise overview of where photons release the most energy in the body – i.e., potentially causing damage due to radiation – and how photons propagate in the body.« Utilizing special quality assessment procedures, he is also able to objectively evaluate how much a modified arrangement of imaging components in the simulation would affect the quality of the actual image. Based on findings from the simulation experiments, Fehlhaber expanded the software to include an optimization algorithm. This algorithm identifies the optimal trajectories for specific clinical issues. It automatically determines which path the imaging components will need to follow to achieve an optimal balance between the lowest possible radiation exposure and adequate image quality for the anatomical structures being examined. Fehlhaber was able to prove that this method can reduce exposure to radiation. Above all, highly sensitive structures such as the uterus and ovaries are exposed to significantly less radiation. »However, the exact simulation of all fluoroscopies required to optimize the trajectory necessitates a great deal of computing power. For complex tissues, this currently takes several days,« explains Fehlhaber. He will be publishing the results of his experiments as part of his doctorate in the fall of 2021.

Image:
Simulated trajectory of X-ray source (red) and detector (blue) with significantly reduced effective dose during scan of the pelvis

BACK TO THE FUTURE

Considering the current state of the art and the hardware developments over the past decade, it can be assumed that such optimizations will only become established in the field of radiology in a few years. Only then will the original goal of reducing the effective radiation dose become ready for mass implementation. Until such time, researchers at Fraunhofer IPK will continue to develop and optimize the speed of the algorithm. Fehlhaber envisions a great deal of potential for future research questions: »The medical models which are indispensable for realistic simulations are constantly being refined. And we are also using the simulation software to investigate procedures that improve the image quality of 3D X-ray imaging.« ◆

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New Ergonomics

Illnesses caused by poor posture at the workplace are a major challenge of our time. They can be prevented by PowerGrasp, a textile exosuit, which provides ergonomic and strength support.

Our society is aging. Demographic change is no longer a future scenario, but already fully underway. This is particularly evident when it comes to physical activity: The number of musculoskeletal system disorders is constantly increasing. These disorders lead to temporary and permanent absences from work, the inability to plan reliably, as well as a lack of resources. Wear and tear and injuries to the musculoskeletal system are therefore fundamental challenges faced by our society.

Persons who spend 30 years working on an assembly line have a right to ergonomically optimal working conditions. A safe working environment and ergonomics training are half the battle in this regard. The rest could be provided by automation solutions, for example. But even the increasing integration of robotics into work processes cannot provide one hundred percent relief from injurious activities, because not everything can be automated. Humans remain far superior to any robot in terms of cognitive and sensorimotor abilities, and thus flexibility as well. Therefore, if a large number of work processes cannot be performed by robots, ergonomic work must be supported by automation that is as flexible and inventive as humans themselves.

MAN AND MACHINE

This is where body-mounted support systems come in. A distinction is made between purely ergonomic support and systems that provide additional strength support. Ergonomic support is provided by the ErgoJack® orthosis developed at Fraunhofer IPK, which uses sensors to detect movement in order to inform wearers when they are moving in a manner that is ergonomically unfavorable. However, such systems reach their limits when ergonomic posture is not possible during a particular activity. This includes, for example, handling objects in an overhead position.

Passive and active exoskeletons address this problem by providing strength support. A passive exoskeleton does so via mechanical components such as spring elements. These redirect the force applied by the worker from overworked areas to more robust regions of the body. However, this type of force redistribution also has disadvantages, as movements that do not require stress relief receive equal support, such that the wearer must apply a great amount of force to overcome the weight relief.

Image:
1
PowerGrasp provides ergonomic and strength support.

1

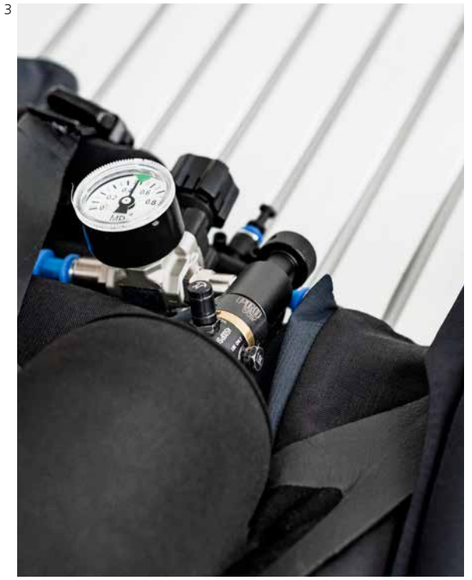
2

Images:
2
The back module contains valves and control technology for strength assistance.
3
The compressed air bottle is quickly changed: Refilling takes about one minute.

Active exoskeletons, on the other hand, are supplemented with electrical or pneumatic components. Motion steps are operated via a control console or even sensors which measure muscle tension directly. The downside of these systems, some of which are extremely heavy, rigid and expensive, is the potential risk of injuries when malfunctions occur. As a result, both types of exoskeleton have a limited range of applications. Because of their disadvantages, they are often ruled out as an option. This is exactly where PowerGrasp comes in.

The exosuit contains almost no rigid elements. Instead, force relief is provided via precisely applied compressed air.

3



NOTHING BUT HOT (COMPRESSED) AIR

Anyone who has ever worn a more traditional exoskeleton will understand what it is like to be a character in a science fiction movie. When it comes to PowerGrasp, these complex constructions are nowhere to be found, as the dual arm exosuit offers maximum wearing comfort: It is worn like a textile vest. It contains almost no rigid elements. Instead, force relief is provided via precisely applied compressed air. The process is conceivably easy. The wearer's movements are detected via sensors and analyzed by a control unit. Air pressure is then built up in a targeted fashion in the shoulder joint actuators to provide upper arm strength support.

The system requires no adjustment or calibration in advance, so wearers can start working immediately after switching it on. PowerGrasp is designed for 50 to 150 overhead work cycles. After this, the empty compressed air cylinder can be replaced in a few simple

1

2

Images:
1
The single arm exosuit supports overhead work.
2
Back view of the dual arm exosuit

steps and refilled in about a minute, after which it is once again ready for use.

The risk of injury associated with more traditional exoskeletons is eliminated, as users can counteract and override the force of the actuator even in the event of malfunctions. The total weight of the system is 6.5 kilograms – an enormous contrast to active exoskeletons which weigh 15 to 20 kilograms. Instead of a bulky frame, the back module only contains the mobile compressed air supply and control system, a rechargeable battery, and an embedded control unit. The concept can be applied to almost all areas of the body and has been implemented at Fraunhofer IPK to showcase an application for arm and wrist joints.

CREATIVE HELPER

PowerGrasp manages to satisfy the human requirement for flexibility and creativity with its ergonomic and strength support: The closely fitting exosuit works not only by means of traditional force compensation, but also uses novel neuronal networks that offer situation-dependent process control for relieving the load. In future, this will enable the system to respond to the user's fatigue by increasing assistance. PowerGrasp is thus currently being further developed into a system that significantly improves work ergonomics whilst providing maximum wearing comfort and a minimal risk of injury. ◆

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Medical Devices in Manufactory-based Small-batch Production
Challenge or dilemma?

In light of increasingly stringent requirements for medical devices, in particular as a result of the implementation of the EU Medical Device Regulation (MDR), the situation for manufacturers and distributors of medical devices in Germany and Europe is growing increasingly complex and cost-intensive.

A guest article by Dr. Philip Elsner, Berlin Heart GmbH

© Berlin Heart

Medical devices have become such an essential and well-integrated part of our everyday lives that it is practically impossible to imagine adequate healthcare without them. From a simple band aid to artificial tissue substitutes, from Covid-19 rapid tests to sophisticated diagnostic procedures, and from dental fillings to artificial organs, there is almost no part of the human body for which there is not some kind of medical product. These apparently simple products belie what are usually complex functions, hidden in a multi-layered interaction between the technical system itself and the human biological system. This results in what are sometimes highly elaborate development processes, as well as increasingly complex approval processes. Comparable to the approval of pharmaceuticals, such processes can sometimes take years, if not a decade. This therefore raises the question of whether further innovations are at all possible or even financially viable once a lengthy approval has been obtained.

The other aspect when considering a medical device is the human being as an individual. A person is characterized in particular by his or her diverse set of abilities and skills – each in his or her own individual way. Which begs the question: Are standardized therapies at all applicable, when customized, individualized medical devices and therapies actually have a better chance of success? Of course, many established procedures can be applied when the corresponding symptoms present themselves, but it would be fatal to regard the human body as conforming to a set standard.

In an era of modern, agile and globally networked production and information systems and the increasing integration of 3D printing methods into production processes, it should be possible to realize individual solutions for every single patient. In the bigger picture, the technical challenges and the medical proof-of-concept are currently the smaller hurdles to overcome. The primary challenge is to address patient individuality and its demands in the context of an increasingly regulated and, in some cases, over-regulated approval environment. The revised EU Medical Device Regulation (MDR) currently provides little to no leeway for considering or even implementing individual patient solutions as the norm. This is precisely where the challenge for the coming years lies. It should be possible to create custom solutions for patients, far removed from modular systems containing standardized components. The basis for this is not only valid manufacturing processes or, alternatively, purely manufactory-based small-batch productions, which in turn possess a maximum degree of freedom, but also all peripheral process chains for information processing, approval, clinical documentation and, ultimately, data security as well. Such an interdisciplinary approach not only holds the opportunity for large-scale production of mass products, but also for the best possible and tailored individual patient care. ◆

Dr.-Ing. Philip Elsner

studied mechanical engineering at the Technical University of Berlin and received his doctorate at Fraunhofer IPK in 2009. His thesis was on the 3D printing of graded material properties. To this day, his professional career continues to be characterized by looking beyond the boundaries of the conventional and constantly seeking new ways to make production in Germany innovative and attractive.

Dr. Elsner has been with Berlin Heart GmbH since 2007, where he initially headed the Process Engineering department. The company develops, produces, and markets innovative systems for mechanical circulatory support. Since 2017, he has also been responsible for the overall production of sterile products and drive units as the division director. »The particular challenges in our day-to-day production lie in meeting the constantly increasing requirements for medical products in manufactory-based small-batch productions,« says Elsner. »True to our motto: Innovative medical products, by people for people.«

Pharmaceutical Production Made Efficient

Fraunhofer IPK supported a globally active pharmaceutical company in establishing a learning factory in Berlin. It is helping to implement Lean methods and train employees in their application.

Safe and affordable medication is essential to the healthcare system. And, bearing in mind the need for rapid distribution of COVID-19 vaccines: Shortest possible delivery times are at least of equal importance. Pharmaceutical production must face these and other challenges, and at the same time not only supply patients, but also convince regulatory authorities. How can this be achieved?

According to a Fraunhofer IPK partner from the pharmaceutical sector, the foundation for stable and efficient production is operational excellence through consistent Lean management. Lean management follows the aim of optimally coordinating all activities in the value chain and avoiding superfluous tasks. However, the approach only works, if employees actively apply it. Hence, the minds in a company are the most important resource for achieving operational excellence.

Fraunhofer IPK's research-based pharmaceutical partner employs an in-house Lean production system tailored to its specific needs. In order to support the engagement of employees, the company has joined forces with Fraunhofer IPK, TU Berlin and ITCL GmbH to set up its own learning factory in Berlin, the LEAN Factory. It is designed to do more than just impart knowledge. The training courses in the learning factory are to enable employees to contribute actively to operational excellence.

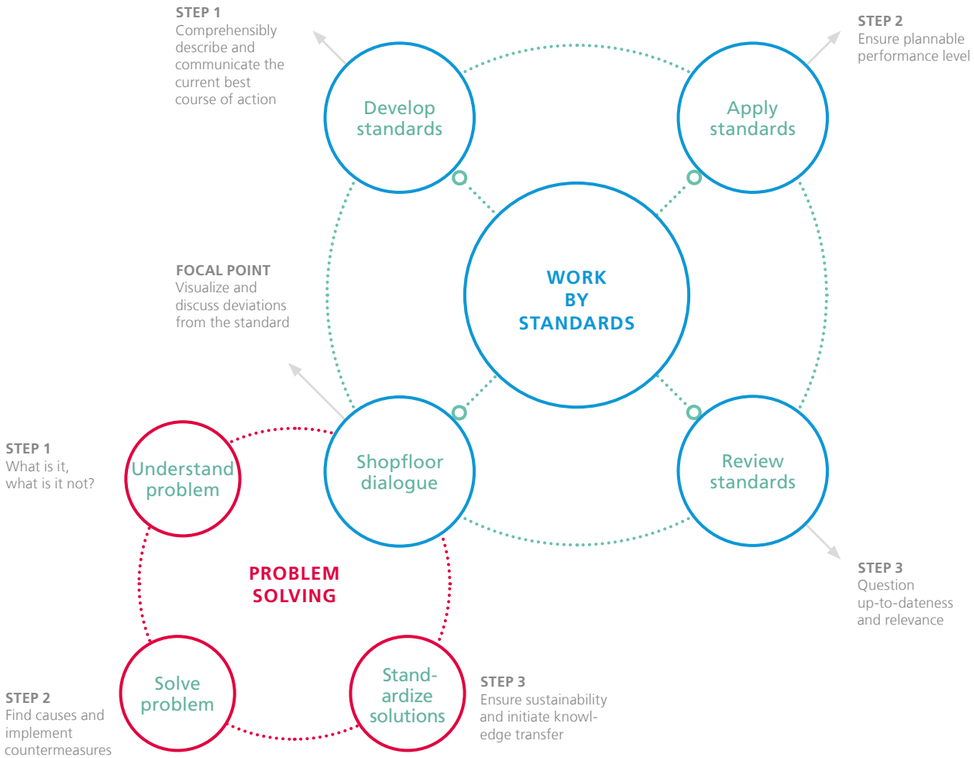
Image:
Learning factory with recreated tablet production in Berlin

HANDS-ON EXPERIMENTATION

In essence, the LEAN Factory is a simulated tablet production facility where learning takes place in a practical fashion. Employees experiment actively and learn through first-hand experience – in an environment which closely mimics the actual company, but without affecting the ongoing pharmaceutical production. This way, the courses in the learning factory demonstrate how Lean management can work in the pharmaceutical industry. After all, not all approaches can simply be copied from the automotive industry. Dividing up chemical processes into equal process segments lasting an arbitrary period of time accurate to the second – seems rather impossible. Synchronizing laboratory samples and batches in production such that products can be released more quickly, is however perfectly feasible. Case examples, plenty of time for discussion and constantly switching between the seminar room and production help reinforce what has been learned.

The training courses have been designed so that they can be adapted to participants from a broad mix of company divisions, as the circumstances in the different plants and work areas vary. Factors that may be commonplace in production may be new in administrative processes. Instead of giving participants a »one-fits-all« toolbox, it is made clear how the individual elements of

STANDARDS AND PROBLEM SOLVING IN DAILY SHOPFLOOR MANAGEMENT



the production system are interrelated so that the appropriate solutions can be developed on site – in a manner that is independent yet based on global standards.

HELPING TO SHAPE THE PRODUCTION SYSTEM

Shopfloor dialogues, in which the current performance is examined, form the core of the production system. They are based on standards for daily work that are defined, applied, and continuously reviewed. Shopfloor dialogues allow for the rapid identification of deviations, both positive and negative. Such deviations are discussed in the shopfloor dialogues in order to identify suitable measures. Positive deviations can be utilized to immediately improve standards, while negative ones trigger problem solving. In turn, a problem that has been solved results in a new or improved standard.

To correctly learn how standardization works, participants in the learning factory are sent directly to the tablet press and granulator. They learn to describe the relevant changeover processes as visually and clearly as possible. Subsequently, participants review each other's results in a small competition for completeness and clarity and discuss best practices. As an introduction to the real-world aspects of shopfloor dialogs, participants role-play possible scenarios at the end of a shift, with increasing levels of difficulty ranging from

In the LEAN Factory, employees actively experiment and learn from their own experience – close to the reality of the company, but without influencing the ongoing production.

packaging material delays to teamwork problems. Problem-solving skills, on the other hand, are trained using specific issues faced by the participants. In many cases the teams come up with ideas that they can immediately implement back at the workplace.

TRAINING TO INSPIRE

Upon completing the training, it is not just about key learnings of Lean management. Employees should, more importantly, want to apply what they have learned to their own area of work. In order for this to succeed, the courses begin with the managers. For them, the focus is not on how a changeover can be performed as efficiently as possible, but how to motivate their own team and support them with the necessary resources. Hence, courses at the learning factory also include role plays where the technician is permitted to fold his arms and defiantly reply: »I really have more important things to do now than sorting and rearranging.« To prepare management for such situations on the shopfloor, the learning factory is visited by groups ranging from future foremen to the entire management team of a facility.

After more than seven years of collaboration and 2000 colleagues receiving training, the conclusion is: Practical exposure generates enthusiasm. Whether it is re-organizing a chaotic production setup, personally setting up the tablet press, or role-playing – the theory section needs to be brief and the exercises highly varied. What is important is exchanging different points of view. The company's internal trainer presents the situation within the company. The Fraunhofer IPK trainer provides an unadulterated, external perspective. But participants also learn a great deal from each other. When employees from different sites and divisions discuss their experiences, they also share their own difficulties and the solutions they have successfully implemented. Alternatively, a team may come together to get in sync and establish a common understanding of the implementation. Since this is important across the globe and it is not possible for employees from all locations to fly to Berlin (even without COVID-19) e-learning is already being used for a number of topics. But the practical examples from the LEAN Factory remain. And the reverse approach is also being practiced: Particularly when it comes to workshops or operational implementation, trainers come directly to the employees on the line. ◆

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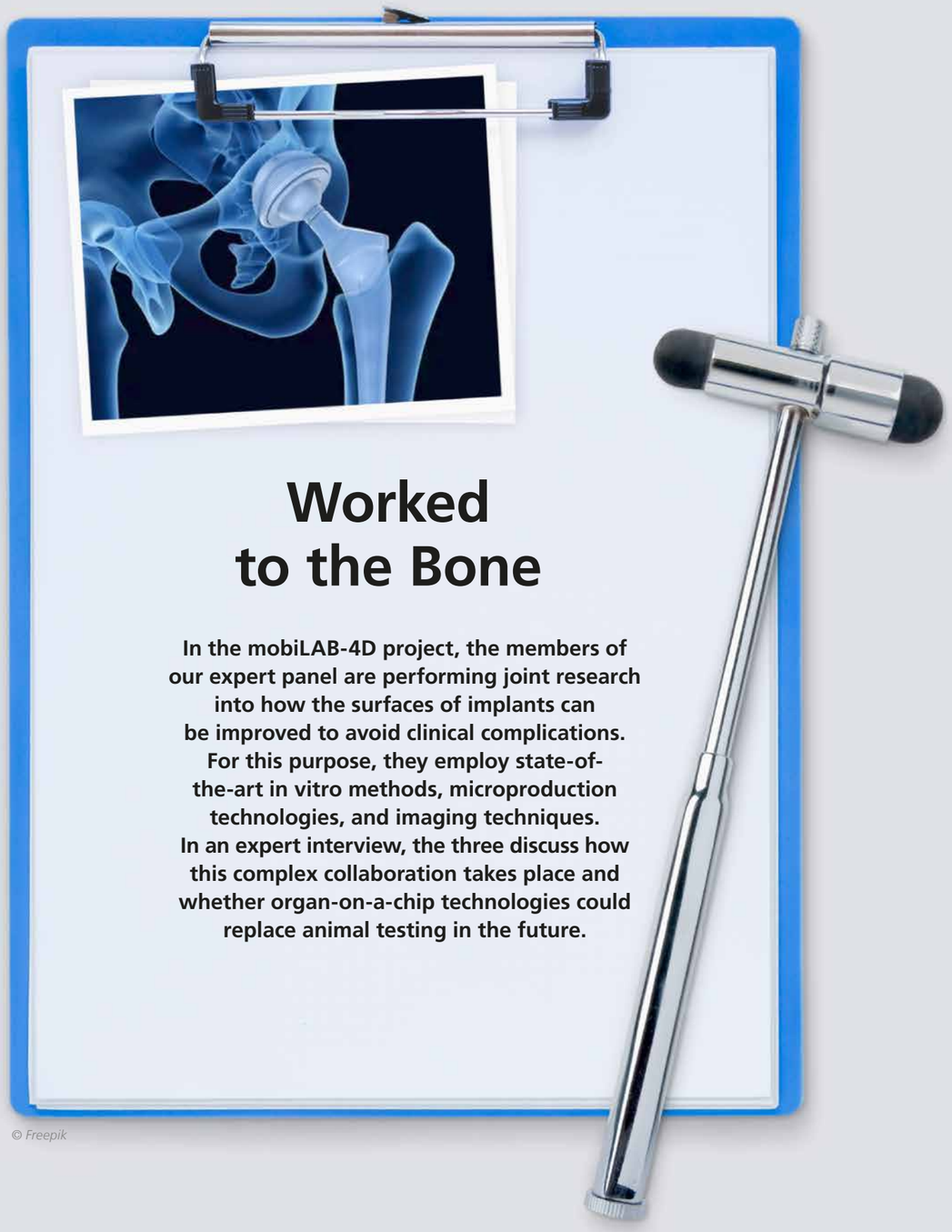

Worked to the Bone

In the mobiLAB-4D project, the members of our expert panel are performing joint research into how the surfaces of implants can be improved to avoid clinical complications. For this purpose, they employ state-of-the-art in vitro methods, microproduction technologies, and imaging techniques. In an expert interview, the three discuss how this complex collaboration takes place and whether organ-on-a-chip technologies could replace animal testing in the future.

© Freepik

| futur | **Dr. Schoon, how has research on orthopedic materials evolved as a result of recent breakthroughs in microfluidics?**

/ SCHOON / We are currently witnessing major changes in the preclinical testing of implant materials. Our goal is to be able to make better predictions in the future, with respect to reactions such as bone ingrowth of implant materials, in human in vitro models compared to animal models. This way, we hope to further improve patient safety.

| futur | **Mr. Schweitzer, from the perspective of a production engineer: What makes working with patient samples and the microfluidic chips you obtained from them so challenging?**

/ SCHWEITZER / The challenge is to ensure reliable transport. We need to be able to culture the cells on site for the 4D measurement in a synchrotron facility in a non-trivial environment just as well as in the lab. In order to do this, we need to keep all parameters that are important for cell growth stable at all times, such as the temperatures and CO_2 saturation. We also need to be able to constantly guarantee the sterility of the chip systems, even during transport.

| futur | **This means that a lot of effort goes into making the samples suitable for measuring them in the synchrotron. Dr. Hesse, what are the advantages of 4D microtomography in a synchrotron as compared to other imaging methods?**

INTRODUCING MOBILAB-4D

Complications following the insertion of dental, hip, or knee implants are extremely stressful for affected patients and can lead to additional surgeries. The mobiLAB-4D project aims to reduce such complications:

–
Release of nanoparticles: The metallic implant should release as little material as possible into the surrounding tissue.
–
Toxic effects: The particles released must not be toxic.
–
Problems with osseointegration: The implant should integrate itself into the existing bone as well as possible.
–
Peri-implantitis: Inflammation of the surrounding tissue due to the ingress of germs needs to be prevented.

These problems are to be avoided through optimization of the surface structure and material of the implants. The project partners are therefore looking into implant surfaces and materials that are particularly suited for use in the human body.

/ HESSE / In the synchrotron, up to one hundred billion times more radiation is generated than in the laboratory. This extremely high X-ray intensity allows for better imaging. Synchrotron radiation is also coherent radiation. This equates to higher contrast for various material phases. Bone is a dynamic material, and we need to be able to identify extremely minute differences in its mineralization in 3D. Almost nothing else can compete with the synchrotron CT to comply with these requirements. With constantly improving hardware, the imaging can also be performed in such short and stable sequences that we can examine samples in a time-resolved manner, i.e., at several different points in time. The difficulty faced by our approach are the particularly long time sequences. The remodeling kinetics of bone are in the range of days, weeks, and sometimes even months. We need a system that will remain stable over such a long period of time.

/ SCHOON / The method developed can also be used with other long-term applications, for example the bio-degradation of materials or even corrosion processes.

| futur | **Do the samples remain in the synchrotron for the duration, or do you remove them and then return them later?**

/ HESSE / The X-radiation procedure only requires a few minutes in each case. Subsequently, samples are further cultivated on site for a few days in the laboratories. This is why the mobile measurement and transport unit being developed at Fraun-

Division of Labor between the Project Partners

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1

Dr. Janosch Schoon

RESEARCHER AT THE ORTHOPEDICS DEPARTMENT OF THE UNIVERSITY HOSPITAL OF GREIFSWALD IN THE RESEARCH DEPARTMENT HUMAN CELLS AND ORTHOPEDIC MATERIALS

cultivates human bone cells from patient samples. They are transferred onto microfluidic chips to study the interaction of the tissue with implants featuring different laser-textured surface structures and materials.

2

Luiz G. De Souza Schweitzer

RESEARCHER AND KEY ACCOUNT MANAGER FOR MEDICAL ENGINEERING AT THE APPLICATION CENTER FOR MICROPRODUCTION TECHNOLOGY AT FRAUNHOFER IPK

is developing a measurement and transport unit which allows cell samples to be transferred reliably and in a sterile environment for measurement at the synchrotron facility and further cultivated on site over a period of several weeks.

3

Dr. Bernhard Hesse

CEO AT XPLORAYTION GMBH

performs the time-resolved µCT measurements at the synchrotron facility and evaluates the measurement results.

hofer IPK is so important. It allows us to transport the chip systems that are currently at the Charité or in Greifswald, such that we can continue to culture them for weeks at the synchrotron in Grenoble or Paris, where we perform most of our work.

/ SCHWEITZER / After each measurement, samples need to be returned to the organ-on-a-chip via a double door system for further culturing. If a problem occurs during this process, e.g. due to contamination (e.g. bacterial), we have to stop the tests. That is why we need to ensure that everything remains sterile at all times, both the measurement chamber as well as the chips.

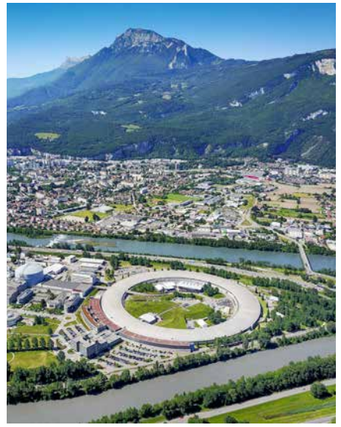
| futur | **The consortium for your joint research project is an interdisciplinary one, with specialists from fields as diverse as medical research, radiation physics and production engineering. How does this influence your work?**

/ SCHOON / By working with experts from other fields, you stand to learn something yourself. I was at the synchrotron facility in Grenoble for the first time in 2018 with Dr. Hesse. We would not have been able to gain direct access without an expert, our physicist. However, this technology is quintessential for answering our questions in any relevant fashion. That is why this relationship is so very important.

/ HESSE / The collaboration on mobiLAB-4D was initiated by Luiz Schweitzer, who recognized relatively early on what we can achieve together. For our research,

»In the synchrotron, up to one hundred billion times more radiation is generated than in the laboratory.«

Dr. Bernhard Hesse



»We need to be able to culture the cells on site for the 4D measurement in a synchrotron facility in a non-trivial environment just as well as in the lab.«

Luiz G. De Souza Schweitzer

Image:
The European Synchrotron Radiation Facility (ESRF) in Grenoble
© *ESRF / J. CHAVY.*

it is key to make existing lab-on-a-chip systems synchrotron-compatible. Equally important is an understanding of and the evaluation of synchrotron CTs and the handling of cell samples. This interdisciplinarity is crucial.

/ SCHWEITZER / Thanks to this project, we have also come up with many ideas on how to continue collaborating on other clinical aspects, such as degradable implant materials. With clinical input from the University Hospital of Greifswald, we can focus on the issues that are truly important for application in medicine.

| futur | **You mentioned the practical application of your research findings in clinical healthcare – that is the central idea of translational medicine. How do you ensure that these findings will actually be helping people?**

/ SCHOON / We intend to turn the findings we obtain into a product through patent applications, for example an implant component. Working with medical device manufacturers, we can then launch this optimized product on the market in order to minimize infection rates or improve the ingrowth behavior of implants. This allows patients to benefit from our research in the long term. One other translational aspect is the preclinical method: For example, if we modify the implant surface in five different ways and observe in our experiments that a large quantity of aluminum is released by the implant in four of them, our analyses prevent us from proceeding to the preclinical phase or even to a clinical trial.

GLOSSAR

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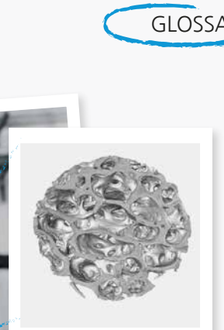

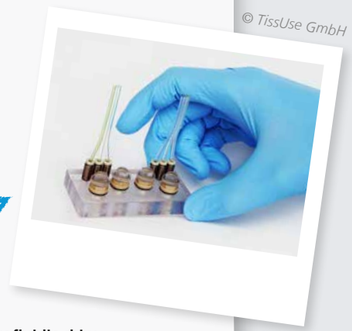

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Microfluidic chip:
A system in which chemical, biochemical and biological processes can be performed and investigated in a very small space. Liquids and gases are transported along microscopic channels with the aid of capillary forces. Also known as lab-on-a-chip when the chip fulfills the functions of a laboratory, such as for point-of-care diagnostics, and organ-on-a-chip when cell cultures are used to replicate an organ or, as in our case, a bone.

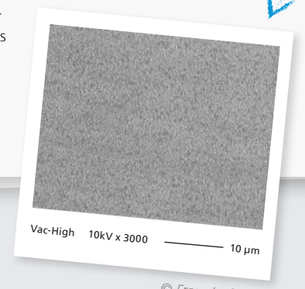
Computed tomography (CT):
A computer-aided process in which an object is irradiated with strong X-rays in order to obtain a three-dimensional image. Time-resolved CT or 4D CT is when the same object is imaged at multiple points in time. A µCT or micro-CT provides particularly high resolutions with details accurate down to the micrometer range.

In vitro:
Organic processes that take place outside a living organism, for example in a test tube or on an organ-on-a-chip. In contrast, in vivo processes take place in a living organism, for example in a laboratory animal.

Laser-textured surfaces:
Treatment of the implant surface with ultra-short pulse laser beams

Synchrotron:
A particle accelerator in which charged elementary particles (ions) can be made to travel at high speeds and used for high-resolution X-ray processes.

Translational medicine:
The transfer of research findings into practical applications for healthcare.



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| futur | **Without the organ-on-a-chip systems, you would have to conduct your trials on animals. In your example, several mice would have been used to evaluate each of these different implant surfaces. Will we soon be able to discontinue such animal testing entirely?**

/ SCHOON / It is my belief that we will not be able to abandon animal testing entirely. However, we will be able to perform more screening before proceeding on to animal studies. Animal testing will then only take place, if the product or drug being developed shows great potential for continuing on to the clinical phase. The greatest advantage with such 3D cultures and chip models is that we are working in a human context. An example: The chip system we are using within the consortium contains immune cells from bone marrow. The immune systems of a mouse that is kept sterile and a human are very different. We are dealing with cells from patients with an immunological history. If we use multiple chip systems with samples from multiple donors, we may also be including some that have already been sensitized to specific metals used in orthopedics. This is the only way that we can model a realistic setting for immune responses. For example, there are no mouse strains that exhibit specific immune responses to cobalt. Cells from different donors present the reality of patient variability, and it is precisely these patient-specific differences that are crucial.

»The immune systems of a mouse that is kept sterile and a human are very different. We are dealing with cells from patients with an immunological history.«

Dr. Janosch Schoon

More information:
www.ipk.fraunhofer.de/mobilab4D

»It is more affordable for pharmaceutical or implant manufacturers to carry out such preliminary tests on chips.«

Dr. Bernhard Hesse

/ SCHWEITZER / The in vitro method is what makes the time-resolved measurement of the exact same sample possible in the first place. In the in vivo model, it would be necessary to kill the animals in order to examine the samples. On the organ-on-a-chip, on the other hand, we are able to continue culturing cells between the individual measurements in the CT. This is a unique aspect of this project, and one which could significantly expand the future relevance of the in vitro method.

/ HESSE / With the help of organ-on-a-chip systems, we are also able to involve researchers from other disciplines. Many experts simply do not possess the infrastructure to work on animal models. I myself am not trained to perform experiments on mice. Finally, there is also a financial argument: It is more affordable for pharmaceutical or implant manufacturers to carry out such preliminary tests on chips. This means that they only conduct very expensive preclinical experiments on candidates that show real promise. ◆

This project is supported by Investitionsbank Berlin and co-financed by the European Regional Development Fund (EFRE).

EUROPEAN UNION
European Regional Development Fund
Investitionsbank Berlin

Bio Meets Micro Meets Tech

Custom solutions for challenging research questions: Biotechnology and production engineering are brought together in the laboratories of the Application Center for Microproduction Technology.

1

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Whether it is biomedical engineering manufacturers, pharmaceutical companies, or specialized production facilities – many industries and users today have research questions that require highly specialized laboratory environments and equipment. Factors such as sterility, atmospheric conditions, temperature, and spatial vibrations need to be precisely controlled for this purpose.

The laboratories of the Application Center for Microproduction Technology – AMP are designed precisely with this in mind. The biomedical laboratory and clean room enable the conceptualization, manufacturing, and functionalization of medical technology products. Effective sterilization strategies can be developed here and validated from a molecular and microbiological perspective for specific applications. Researchers have a wide range of methods and equipment at their disposal which allow customer orders to be mapped and processed along the entire micro production process chain. All of this is performed in-house and along short decision-making paths, thereby allowing individual solutions to be realized rapidly.

OUR RESEARCH AND DEVELOPMENT

- Development of antimicrobial strategies based on alternative active ingredients (image 1; p. 60, image 2)
- Microbiological analysis and management of technical fluids, particularly cooling lubricants (p. 60, image 1)
- Antimicrobial functionalization of medical technology products
- Development and optimization of microfluidic systems (image 2)
- Microbiological production of biopolymers

BIOMEDICAL LABORATORY

In the **biomedical laboratory** corresponding to safety level 1 according to GenTSV (Genetic Technology Safety Regulations) as well as safety level 2 according to BioStoffV (Biological Agent Ordinance), partners are offered a microbial contamination testing for their applications. Once this contamination has been identified and characterized, researchers design suitable disinfection strategies and develop and test individually tailored technologies. Also available are sustainable process solutions, both in the form of innovative alternatives to conventional biocides as well as for the production and processing of bioplastics.


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EQUIPMENT AND METHODS:

Microbiology:
- Safety cabinet / sterile bench
- Cultivation of microorganisms
- Fluorescence microscope (image 4)
- Autoclave
- Strain maintenance
- Enzyme conservation
- Precision balances

Molecular genetics – analysis of DNA, RNA and proteins:
- Traditional PCR and real-time PCR (image 5)
- DNA analyses (electrophoresis, imager), DNA isolation
- Expression analyses (gel electrophoresis, blotting methods)
- Photometer, microtiter plate reader (FilterMax F5)

Bioprocess engineering:
- »Biostat B Single MO 2L« fermenter (image 3)
- Avanti® J30I (110,000 x g) high-speed centrifuge
- High pressure homogenizer, sample volume 2 to 15 ml


5

CLEANROOM


6

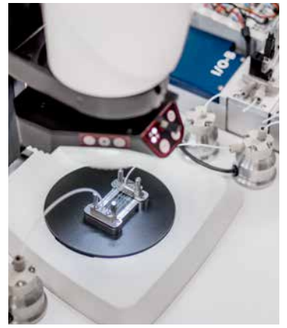

7

In the ISO Class 7 **cleanroom** which complies with DIN EN ISO 14644-1 (image 8), research teams develop coating strategies and production technology-based scaling methods for micro- and macrofluidic systems in a controlled atmosphere. Prototypes and small series are also manufactured here at the request of customers.

EQUIPMENT:
- Thermobonder FINEPLACER® pico (image 6)
- Low- and high-pressure pump system
- Plasma station (image 9)
- Microscope M205C (image 10)
- Magnetron sputtering system
- Coating station for medical devices
- Particle sizer (image 7)


8


9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Pesquisa e Desenvolvimento
Research and Development

Since 2012, Fraunhofer IPK has been assisting the Brazilian industry training service SENAI with establishing innovation institutes based on the Fraunhofer model.

COOPERATION SENAI – FRAUNHOFER IN FIGURES

8
years passed until

25
SENAI institutes were up and running, employing more than

700
researchers.

44%
have a doctorate or master's degree. They are backed by a further

100
project management and back-office specialists.

1100
research and development projects have been completed to date, supporting

609
companies and generating

1,046
billion reais (just under 200 million euros) in revenue, which includes the economic counterparts of industry partners and the institutes.

At the beginning of the millennium, the only way for the Brazilian economy to go was up. Between 2002 and 2011, its gross domestic product (GDP) grew fivefold, from US$ 508 billion to US$ 2600 billion. Since then, the world's ninth-largest economy has suffered major setbacks: Due in part to several political crises and the corona pandemic, GDP shrank by almost one third to what is currently approx. US$ 1800 billion.

One area with considerable potential for improvement is the country's capacity for innovation. The Brazilian economy is very reliant on raw material exports, primarily of soy, coffee, meat, and similar products. These products certainly generate a huge turnover. In the first decade of the new millennium, they allowed the Brazilian economy to achieve impressive growth rates. However, since the figures were also underpinned by high oil prices and social programs, representatives from leading Brazilian industrial companies were already pushing for a restructuring of the Brazilian economy at the time. Their intention was to transition toward greater value creation, particularly in the technological sectors of the economy, which appeared essential for sustainable economic growth.

HIGH R&D DEMAND

This initiative was overdue: Industrial sectors which manufacture technical products are weakly positioned in Brazil. Where high technology and electronic products are concerned, Brazil is dependent on imports. Furthermore, with the exception of a few global players such as the cosmetics group Natura & Co and the aircraft manufacturer Embraer S.A., the Brazilian industry is not very innovative. Quite to the contrary, research and development are viewed more as a cost than an investment, because returns appear uncertain. As a result, there is virtually no culture of innovation in industry.

To make matters worse, application-oriented research outside of industry is not well developed. Brazil certainly features robust basic research, and academic indicators have also improved over the last two decades. But with just a few exceptions, universities are not equipped for industry-oriented research. There are hardly any non-university research institutions that conduct research with or for industry. Essentially, it is only international corporations which perform research and development – and usually entirely internally, coordinated from headquarters outside of the country and with a focus on »tropicalization« – the adaptation of products to local conditions.

INNOVATION CULTURE FROM THE DRAWING BOARD

These shortcomings prompted CEOs of the country's largest industrial companies to call for a national initiative aimed at introducing technology and innovation in Brazilian industry. The goal was to strengthen the competitiveness of Brazilian companies in a globalized economy. With the Brazilian Ministry of Science, Technology, Innovation and Communications (MCTIC) and the Ministry of Development, Industry and Foreign Trade (MDIC), the initiative was able to gain important political supporters as well as a strong financial partner, the Brazilian Development Bank BNDES.

Thanks to this network, the Brazilian National Confederation of Industry (CNI) was subsequently able to commission its subordinate National Service for Industrial Training (SENAI) with establishing a network of 25 innovation institutes (in Portuguese Instituto SENAI de Inovação, abbreviated ISI) that would bring R&D initiatives to local industries. The institutes were to face a number of challenges. On the one hand, they would need to gain an understanding of the entrepreneurial requirements of industry and translate these into technological solutions. At the same time, they would have to communicate with industry in a language it understood, act in an agile manner, and adhere to project schedules and delivery deadlines in order to build industry confidence in R&D providers.

For SENAI, establishing such facilities for applied research was a new task. The organization had provided technological services in the past, such as metrological support and technical advice. But the organization with around 28,000 employees at various locations throughout Brazil had little experience in technological development and innovation.

SENAI's headquarters in Brasília therefore searched for international partners who would be able to support its ambitious strategy. After benchmarking organizations for applied research worldwide, SENAI decided to seek a strategic partnership with the Massachusetts Institute of Technology (MIT) and the Fraunhofer-Gesellschaft. While MIT was charged with accompanying research, SENAI chose Fraunhofer IPK as its

1

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Images:
1
Interactive competence building workshop with representatives of all ISI
© Fraunhofer IPK / Fabian Hecklau
2
Technology audit at the ISI for Laser Processing by employees of Fraunhofer ILT and Fraunhofer IPK
© Fraunhofer IPK / Fabian Hecklau

Images:
3
Institute building of the ISI Laser in Joinville, Santa Catarina, Brazil
© Instituto SENAI de Inovação em Processamento a Laser
4
The additive manufacturing of complex structures is the subject of the FERA project.
© Instituto SENAI de Inovação em Processamento a Laser

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4

SENAI INNOVATION INSTITUTE FOR LASER PROCESSING

One example of a SENAI institute that was created as part of the project is the ISI for Laser Processing. It is the first institute concerned with laser processing in Latin America and addresses additive laser manufacturing, laser surface treatment, and laser welding and cutting. The institute maintains close cooperation with Fraunhofer IPK, for example through joint research projects.

FERA project

The FERA consortia project is developing additive manufacturing technologies to improve the competitiveness of Brazilian tool manufacturers in this sector. Its topics are based on needs of the local automotive and tooling industry: semi-automated additive repair of stamping tools and additive manufacturing of tools with complex geometries, of fixtures and spare parts. »Our contribution includes automated laser metal deposition processes to repair tools for car bodies and structural components, as well as a market analysis and trainings on additive technologies,« reports Dr. David Domingos from Fraunhofer IPK, who is driving the R&D cooperation between SENAI and Fraunhofer.

partner for the planning and practical implementation of the envisioned national R&D network. Two arguments spoke in favor of the Berlin-based institute: Apart from its own long-standing experience in applied research, its tried and tested methods and references from the field of corporate management for the strategic planning of innovation systems were particularly compelling.

STRUCTURED ESTABLISHMENT OF 25 INSTITUTES

In the summer of 2012, work on establishing the 25 institutes commenced, in some cases entirely from the ground up. The initial focus was on creating business plans for each institute. Researchers from Fraunhofer IPK chose a participatory approach, in which the strategies were developed in a series of on-site workshops alongside the institute managers. This approach proved highly compatible with Brazilian work culture. It resulted not only in professional business plans for the main investor BNDES, but also an initial transfer of knowledge, and the parties involved developed a common understanding of their own business strategy.

In this initial collaboration phase with SENAI, Fraunhofer IPK succeeded in proving itself to be a reliable cooperation partner. In mid-2013, the consulting contract was expanded, and an initial five-year framework agreement entered into effect, which was extended until 2020. This marked the beginning of a second project phase in which scientists from Fraunhofer IPK assisted with the actual implementation of the 25 institutes by designing suitable management and support processes. On the one hand, the aim was to retain the agile start-up character of the institutes at the beginning of the initiative, while simultaneously underpinning the constant growth and necessary elaboration of organizational structures as well as the continuous professionalization of the institutes and network as a whole.

MATURITY LEVEL AUDITING

The first two project phases culminated in the development of a comprehensive evaluation system in the third phase. For this purpose, two sets of methods were developed at Fraunhofer IPK. The »Management Audit« evaluates performance and maturity where the strategy and management of the SENAI innovation institutes are concerned in order to continuously derive measures for their further strategic development and coordinate them with SENAI management at the regional and national levels.

Complementing this, the second set of methods deals with the assessment of the SENAI institutes' technological performance. »We developed a ›Technology Assessment‹ and a subsequent ›Technology Dialogue‹ to pursue the goal of strengthening professional contacts between the various SENAI institutes and the respective ›sister institute‹ on the Fraunhofer side. The aim is to initiate collaborative projects in the future«, explains Fraunhofer IPK's Fabian Hecklau. As deputy project manager, he is responsible for developing the Technology Assessment.

In the meantime, the project team has handed over the management maturity auditing of the innovation institutes to SENAI headquarters and equipped the responsible experts there with methodological guidelines, tools, and templates, as well as a series of training courses. Fraunhofer IPK continues to be responsible for evaluating the technological maturity of the institutes. In this role, the Berlin institute acts as a supplier of methodologies and a hub within the Fraunhofer-Gesellschaft for integrating the respective technological counterpart and suitable technology experts within the Fraunhofer network for each SENAI institute. Following in the footsteps of the Fraunhofer institutes, each SENAI innovation institute also focuses on

LOCATIONS OF THE SENAI INSTITUTES

a clearly defined technological and research field – across industries and with a mandate for the national market.

OUTLOOK: ESCALATE SENAI ON FOUR LEVELS

The strategic partnership between Fraunhofer IPK and SENAI is in the meantime entering its ninth year. During this time, it has created an active research network in Brazil. Moreover, the 26th innovation institute was implemented by SENAI itself. Fraunhofer and SENAI are currently taking their collaboration to a whole new level.

A new framework agreement signed in 2020 carrying the promising name »ESCalate SENAI – Excellence, Sustainability, Cooperation« will run until the end of 2025.

This follow-up project connects Fraunhofer IPK to the SENAI institutes on four levels: At the level of the individual innovation institute, the evaluation of technological maturity will be continuously pursued. At the level of the overall ISI network, Fraunhofer IPK experts will be providing targeted training and coaching units on strategy, organization and management methods for the innovation institutes, the regional departments in the federal states, as well as the SENAI headquarters, if they have identified a corresponding need for these measures in their regular management evaluations. In this manner, management competency is developed throughout the network as required in order to further support its professionalization and growth.

»At the national level, work is being done to strategically position SENAI within the Brazilian innovation system,« project member Florian Kidschun states. He develops impact analyses that underscore the new research network's value for Brazilian industry and society. Lastly, R&D collaborations are being driven forward at the international level – not exclusively, but also in conjunction with the partner institutes on the Fraunhofer end. A wide range of corresponding joint market development measures have already been implemented, for example to provide holistic support for German automotive manufacturers with production sites in Brazil, i.e. »from both sides of the Atlantic«, where digitally networked production is concerned. ◆

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HEALTH RESEARCH AT SENAI

Medical and pharmaceutical topics are the focus of research at the SENAI Innovation Institute for Advanced Health Systems and the Institute for Green Chemistry. The ISI for Advanced Health Systems in Salvador, Bahia, addresses a wide range of topics from the development of vaccines, adjuvants, biological medicines, cell and gene therapy products, diagnostic kits and medical devices to bioprospecting studies, biological and diagnostic tests, clinical studies and regulatory processes.

ISI for Green Chemistry in Rio de Janeiro creates industrial solutions using alternative techniques and renewable raw materials. The research aim is to generate more efficient and lower-cost products and processes that reduce or eliminate the use and generation of substances that are harmful to health and environment.

SENAI Molecular Biology Network

The two institutes are collaborating in the SENAI Molecular Biology Network, which was established to combat the COVID-19 pandemic in Brazil. The network is taking emergency action to provide molecular diagnostic services for SARS-CoV-2. In the medium and long term, it also aims to help industry establish new methods, products and processes related to applied biotechnology with different industrial sectors.

Currently, in addition to performing a high number of PCR tests, the Molecular Biology Network is working on topics such as designing new SARS-CoV-2 signaling molecules, detecting viruses in drinking water and wastewater, and new approaches to using sample pools in COVID-19 diagnostics.

Images:
1
Life science laboratory at the ISI for Advanced Health Systems
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2
Improving SARS-COV-2 diagnostics is the central goal of the SENAI network for Molecular Biology.
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Maintenance: a Holistic Approach

Image:
Machine monitoring by means of mobile terminals

At the first digital Hannover Messe 2021, Fraunhofer IPK presented a concept for smart monitoring and maintenance of machine tools. A ball screw drive, which is used to move workpiece carriers or tools with extreme precision, served as an example.

Wear endangers the operation of machine tools. Modern production systems work so precisely that even the smallest deviations from »good condition« can turn a workpiece into scrap. Using inexpensive sensor technology and machine learning, our solution identifies even the smallest irregularities before they become serious problems.

Fraunhofer IPK's solution addresses three task areas:
- machine monitoring,
- damage detection on machine components, and
- damage repair.

From intelligent condition monitoring to failure predictions and support for service technicians during maintenance – Smart Maintenance for machine tools by Fraunhofer IPK does it all. At the virtual Hannover Messe, the concept was presented with the help of videos and a 3D model. The digital edition of the fair was very well received: According to information from Deutsche Messe AG, around 90,000 participants generated more than 3.5 million page views and 700,000 search queries on the exhibition platform over five days of the fair. ◆

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www.ipk.fraunhofer.de/hm21-en

Sustainability Benchmarking for SME at the »Woche der Umwelt«

Federal President Frank-Walter Steinmeier and the Deutsche Bundesstiftung Umwelt (DBU) are hosting the digital »Woche der Umwelt« (Week of the Environment) – and Fraunhofer IPK will be there! Expect exciting discussions and an attractive specialized program on important future issues on June 10 and 11, 2021.

Fraunhofer IPK will present the results of the two-year project »Sustainability benchmarking for medium-sized companies«. The researchers had worked closely with the Bundesverband mittelständische Wirtschaft – Unternehmerverband Deutschland e. V. and a total of 60 medium-sized companies from various industries to test the sustainability benchmarking system. The results include thematic highlights such as resource substitution and efficiency, environmental protection and product stewardship, as well as equity and social responsibility. The case studies portray concrete options for action for sustainable management, which are compiled in a method and measures guide. The project was funded by the Deutsche Bundesstiftung Umwelt. ◆

More information:
www.ipk.fraunhofer.de/woche-der-umwelt-21

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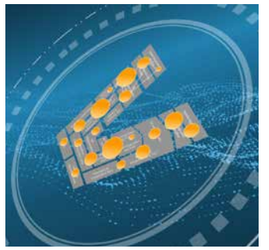

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