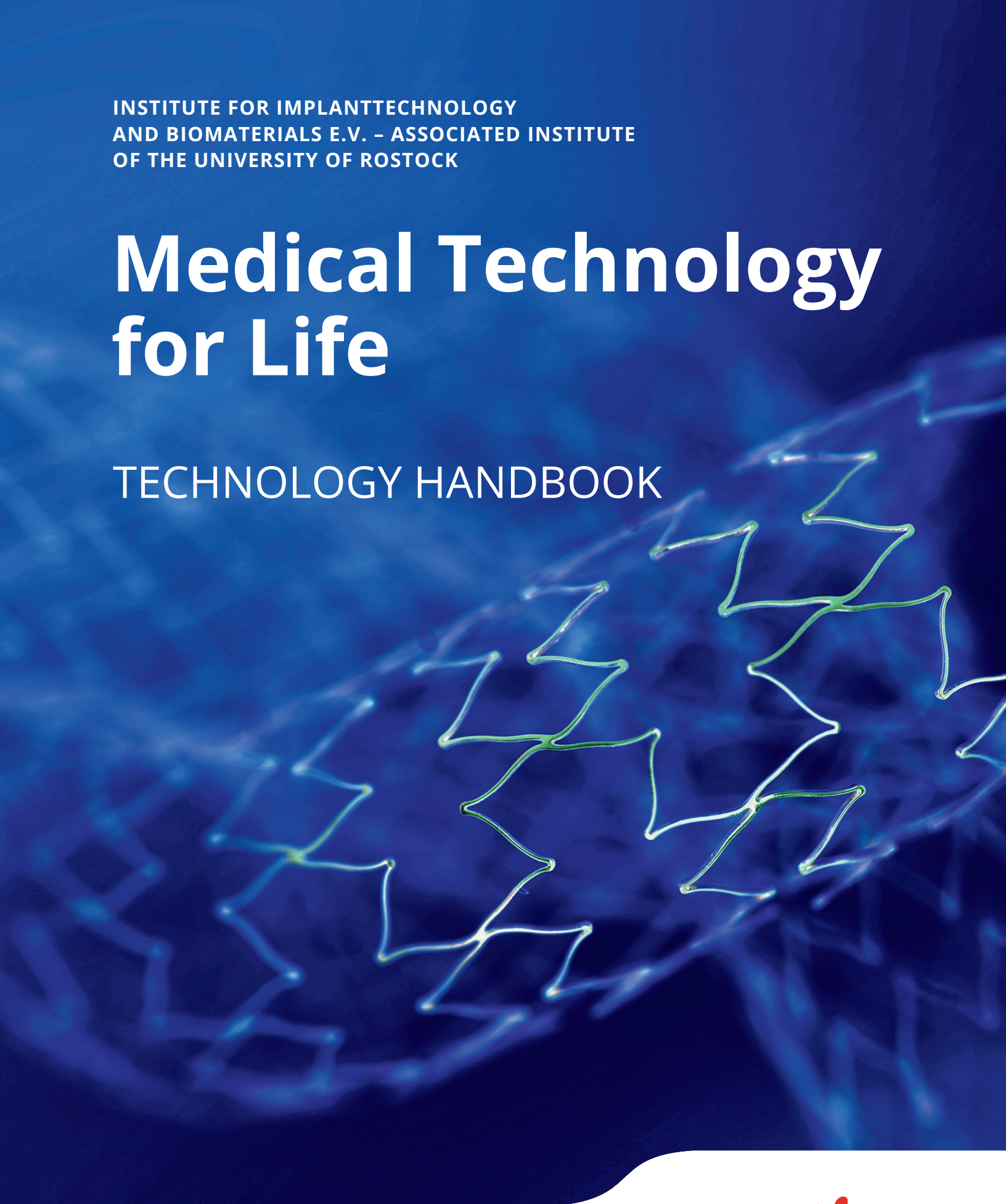
INSTITUTE FOR IMPLANTTECHNOLOGY
AND BIOMATERIALS E.V. – ASSOCIATED INSTITUTE
OF THE UNIVERSITY OF ROSTOCK

# Medical Technology for Life

## TECHNOLOGY HANDBOOK



IIB-ev.de

# “Medical Technology Belongs in the Clinic.”

Medical technology has always placed the highest demands on both people and technology. Today more than ever, it is essential to develop innovative ideas and to combine expertise in order to realize visionary solutions for the benefit of patients. Scientific knowledge forms the foundation of technological progress and is a key driver of prosperity in our society.

The successful transformation of knowledge into competitive products depends decisively on the commitment and expertise of the people working in science and industry.

Since 1996, the Institute for ImplantTechnology and Biomaterials e.V. (IIB e.V.) has been established as a research and development partner as well as a service provider for the medical technology industry and for companies and research institutions in related high-tech fields. Thanks to our modern equipment infrastructure, we are able to support medical technology companies - particularly in Mecklenburg-Western Pomerania and throughout Germany - through our research activities.

The goal of all our efforts must be - and we are firmly convinced of this - that ideas and concepts do not remain theoretical. “Medical technology belongs in the clinic” is a guiding principle that continuously drives us at IIB e.V. Innovation and creativity must ultimately prove themselves in the form of market-ready products and services in everyday practice.

We need more innovative value creation within our own country and more knowledge-based jobs. These are the convictions we stand for at IIB e.V.

Through close collaboration with regional industry as well as with universities, we make an important contribution to the sustainable development of Mecklenburg-Western Pomerania as a technology hub. Medical technology is one of the key industrial fields of the future in our state and represents a particular area of strength with international visibility.

The designation of IIB e.V. as the Competence Center for Medical Technology Mecklenburg-Western Pomerania by the Ministry of Economic Affairs underscores the importance of joint efforts to sustainably expand a high-performance research and development infrastructure in support of a future-oriented technology location within the state.

***Prof. Dr.-Ing. Klaus-Peter Schmitz***
*Director of the Institute and Chairman of the executive Board, IIB e.V.*

***Andrea Bock***
*Managing Director IIB e.V.*

# Contents

# IIB e.V. at a Glance

The Institute for ImplantTechnology and Biomaterials e.V. (IIB e.V.) was founded in 1996 in Rostock-Warnemünde and is a non-profit, non-university research institute as well as an affiliated institute of the University of Rostock. As the Competence Center for Medical Technology of Mecklenburg-Western Pomerania, IIB e.V. supports companies, research institutions, and clinics across the full innovation chain of medical technology products, ranging from fundamental research through development, prototyping, testing, regulatory approval, and industrial implementation.
With the support of regional industry and close cooperation with universities, IIB e.V. actively contributes to the sustainable development of Mecklenburg-Western Pomerania as a leading technology location in Germany with international visibility and recognition.

## Over 30 years of IIB e.V.

As a strong research and development partner for science and industry in Mecklenburg-Western Pomerania and throughout Germany.

The goal: Shaping structural change through innovation and technology transfer from medical technology to the clinic.

# “Focus on Science and Industry”

**Competence Center for Medical Technology Mecklenburg-Western Pomerania at IIB e.V.**

Since 2014, IIB e.V. has served as the Competence Center for Medical Technology Mecklenburg-Western Pomerania, supporting companies in the research, development, and approval of medical products. The approximately 800 m² of laboratory and office space, equipped with state-of-the-art facilities funded by EU, federal, and state programs, enable hands-on research and technology transfer throughout the entire innovation process.

Close cooperation with the University and University Medical Center Rostock, particularly with the Institute of Biomedical Engineering, provides the foundation for interdisciplinary work at the interface of medicine, engineering, and the natural sciences. This collaboration creates synergies in research, teaching, and technology transfer while fostering the next generation of scientists in the Rostock area.

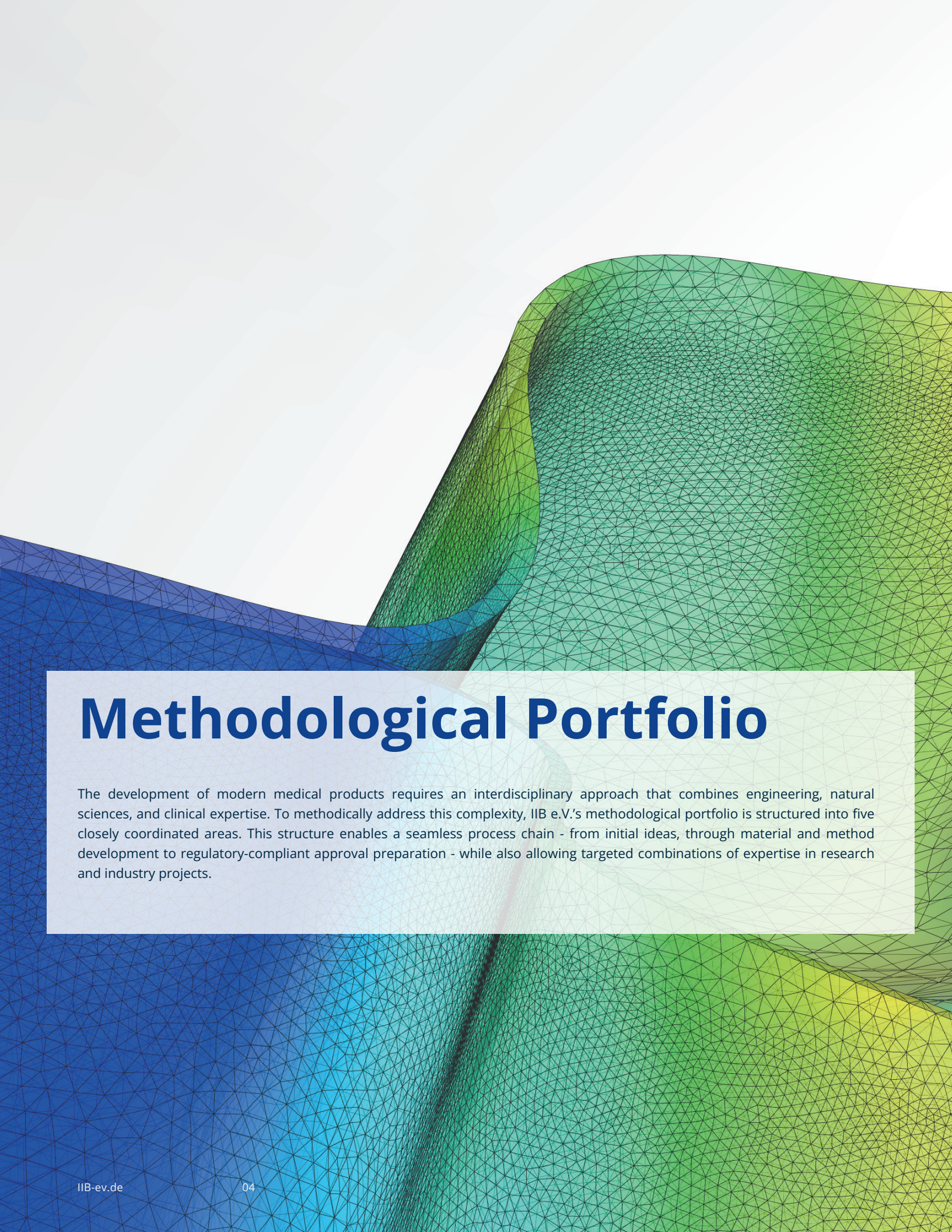
Furthermore, IIB e.V. contributes its expertise to regional innovation networks and cluster structures to actively promote the transfer of knowledge between academic research and industrial application. Joint courses, theses, and internships also strengthen direct interaction between students, researchers, and industry.

**Research Network and Regional Impact**

IIB e.V. is part of a national and international research network with partners from science and industry across Germany. In numerous publicly funded projects - supported by the Federal Ministry for Research, Technology, and Space, the Federal Ministry for Economic Affairs and Energy, the EU, and the State of Mecklenburg-Western Pomerania - the institute works on the development of novel implants, materials, and testing technologies.

By combining scientific excellence, industry-oriented focus, and international networking, IIB e.V. strengthens the innovation capacity, competitiveness, and visibility of the medical technology sector in Mecklenburg-Western Pomerania and makes a sustainable contribution to the positioning of Rostock as a technology location.

As an active partner in regional networks and industrial collaborations, the institute promotes the creation of new value chains and strengthens cooperation between research institutions, small and medium-sized enterprises, and clinics. Through participation in international consortia, IIB e.V. also contributes to the global positioning of northern Germany’s medical technology sector.



# Methodological Portfolio

The development of modern medical products requires an interdisciplinary approach that combines engineering, natural sciences, and clinical expertise. To methodically address this complexity, IIB e.V.'s methodological portfolio is structured into five closely coordinated areas. This structure enables a seamless process chain - from initial ideas, through material and method development to regulatory-compliant approval preparation - while also allowing targeted combinations of expertise in research and industry projects.

In **product development and prototyping**, clinical, functional, and regulatory requirements are systematically translated into technical solutions. The scope ranges from requirements analysis and virtual product development to prototype manufacturing. Digital models, simulations, and modern manufacturing technologies enable patient-oriented development and testing of fully functional implants.

Since standardized testing methods often do not exist for innovative medical products, the methodological portfolio also includes the **development of measurement procedures and specialized equipment**. At IIB e.V., tailored measurement concepts, test rigs, and specialized devices are designed to account for physiological boundary conditions, precise sensors, and validated measurement methods. These solutions serve both product development and quality assurance, while supporting compliance with relevant quality management standards.

In the field of **biomaterials and polymer chemistry**, the focus is on the development, modification, and characterization of polymer-based biomaterials. The aim is to tailor material properties and surface functionalities to improve biocompatibility, promote tissue integration, and, if applicable, enable controlled drug release.

Building on this, the field of **biological testing of materials and implants** focuses on establishing *in vitro* methods to investigate cellular and tissue responses to new materials. The methodological portfolio includes cytotoxicity, microscopic, and molecular biological analyses according to international standards (e.g., DIN EN ISO 10993-5), as well as feasibility studies using animal tissue and 3D cell culture models. This enables the targeted assessment of the biological safety of new materials.

Finally, the methodological portfolio includes **regulatory requirements and approval preparation**, through which IIB e.V. supports companies and research institutions in the compliant implementation of regulatory processes. This includes the preparation of technical documentation, risk management, preclinical and clinical evaluation, as well as strategic preparation for product approval under the European Medical Device Regulation (MDR 2017/745).

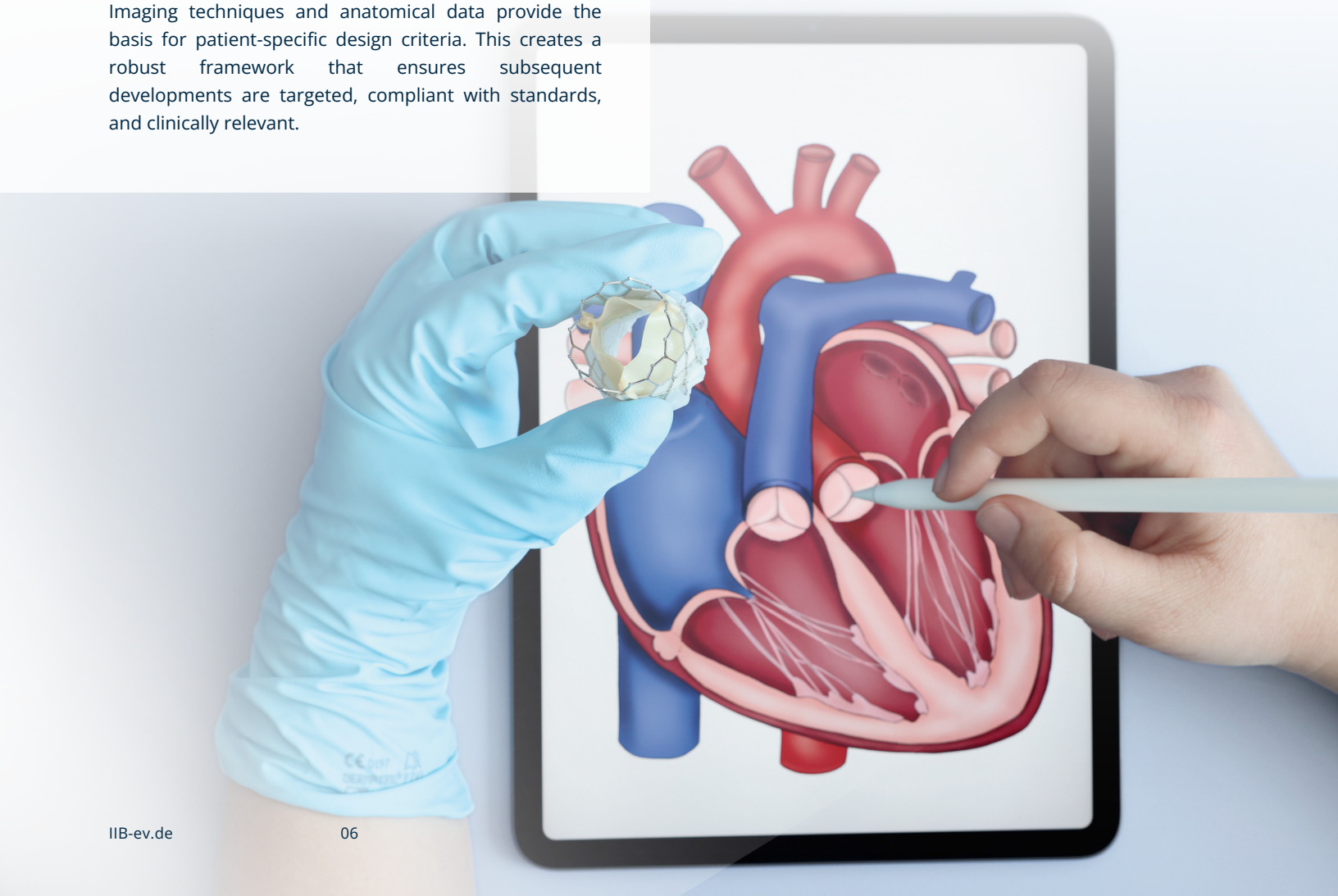
# Product Development and Prototyping

The development of innovative medical products requires a structured, interdisciplinary approach that integrates medical requirements, technical feasibility, and regulatory safety.

At IIB e.V., three interlocking methodological pillars are combined in product development and prototyping: **requirements analysis for product development, virtual product development, and prototype manufacturing of medical products**. This approach covers the entire process chain - from the initial idea to a fully functional implant.

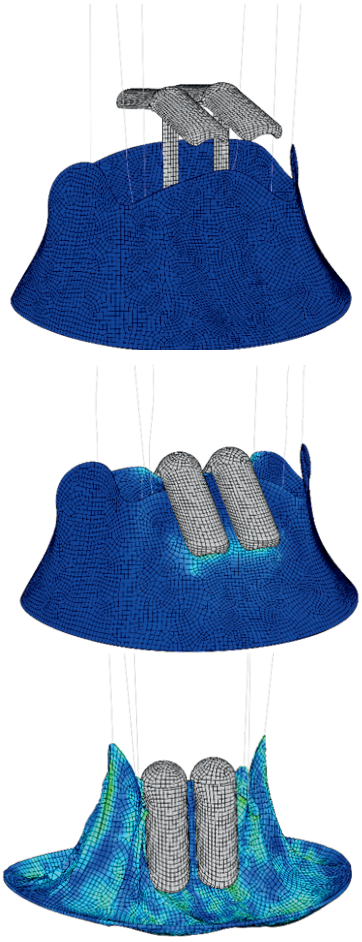
**Product Development Requirements Analysis**

As a foundation for development, clinical, functional, and regulatory requirements are systematically collected, prioritized, and translated into technical specifications. Imaging techniques and anatomical data provide the basis for patient-specific design criteria. This creates a robust framework that ensures subsequent developments are targeted, compliant with standards, and clinically relevant.



## Virtual Product Development

Building on the requirements analysis, digital models of the anatomical target structure and the implant are created, which can be flexibly adapted through parametric design. Numerical simulations - from structural mechanics to fluid dynamics - enable efficient evaluation and optimization of implant design variants. Patient-specific virtual models of anatomical target structures allow implants to be tested in a clinical context even before a physical prototype is produced. Validation steps ensure the transferability of the simulation results.



## Prototyping of Medical Devices

Designs developed in the virtual environment are then translated into physical prototypes. Using state-of-the-art manufacturing processes - from laser cutting and thermal forming to 3D printing - fully functional implant prototypes are produced. Surface modifications, coatings, and assembly processes provide the means to selectively influence product properties. Final verification in the accredited testing laboratory ensures that the prototypes meet the previously defined requirements.

The development of innovative medical products at IIB e.V. is not a linear process. At defined milestones, systematic and interdisciplinary evaluations of process progress are conducted in feedback loops with development partners from clinics and the medical technology industry. The results of the requirements analysis form the basis for virtual product development by defining concrete design and testing criteria. The virtual models, in turn, provide crucial insights into implant behavior under realistic conditions, enabling targeted optimization before physical prototypes are produced. In prototype manufacturing, the digital concepts are translated into real implants and validated through comprehensive testing. The resulting data feeds back into risk assessment and the further refinement of requirements, creating a continuous improvement process. In this way, the three methodological pillars interlock to ensure an efficient, evidence-based, and clinically relevant product development process.

# Product Development Requirements Analysis

Systematic requirements analysis provides a central foundation for the development of safe and effective medical products - particularly in the sensitive field of cardiovascular medical technology. At IIB e.V., this process is carried out based on international standards, specifically ISO 13485 “Medical Devices – Quality Management Systems” and ISO 14971 “Medical Devices – Risk Management.” The goal is to capture requirements in a structured manner at an early stage, ensure regulatory compliance, and translate them into technical specifications.

## Methods of Requirements Analysis at IIB e.V.


### 1 Collection of Medical Requirements

At IIB e.V., clinical use scenarios are analyzed in close cooperation with university hospitals, and **key system requirements** are derived from these analyses. The focus is particularly on biocompatibility, hemocompatibility, and interaction with surrounding tissue. In addition, systematic literature reviews are conducted to verify established requirements and to identify new evidence-based criteria. Anatomical requirements are derived both from studies on human specimens, e.g., in collaboration with the University Medical Center Rostock, and from analyses of animal specimens, e.g., in cooperation with the Research Institute for Farm Animal Biology (FBN), Dummerstorf, and are consolidated into the design and development process.

## 2 Market Analysis and Reverse Engineering

As part of the requirements analysis for implant development, IIB e.V. conducts comprehensive **market analyses** to systematically capture and evaluate existing products, technological trends, and regulatory requirements. These analyses form the basis for deriving technical, functional, and safety-related requirements. In addition, reverse engineering methods are employed. The institute has access to state-of-the-art technical resources for this purpose, such as a µCT scanner for high-resolution imaging and precise measurement technology for geometric and functional characterization. The combination of market analysis and detailed technical investigation provides the foundation for innovative and regulatory-compliant product development. At the same time, market opportunities are strategically enhanced by addressing demand, competition, and unique selling points at an early stage.

## 3 Patent Search

A key component of the requirements analysis is the **patent search**, which examines which technical solutions are already protected and therefore cannot be used in the development of new medical products. By evaluating national and international patent databases, IIB e.V. identifies existing intellectual property and potential freedom-to-operate for its own developments. The results of this search are directly incorporated into the requirements catalog and serve as the basis for assessing the level of innovation and patentability of new concepts.

## 4 Technical Specifications

Subsequently, **technical specifications** and functional requirements for the developed concepts are defined. All clinical, anatomical, and regulatory insights are translated into concrete, verifiable design inputs. The functional requirements are documented in a structured manner according to ISO 13485, translated into technical parameters, and then prioritized. On this basis, a requirements catalog - or specification sheet - is created, forming the foundation for further development of new medical product ideas and providing guidance for design, material selection, and subsequent testing.

## 5 Regulatory Compliance

A central component of the requirements analysis is ensuring **regulatory compliance** of the planned developments. At IIB e.V., relevant legal requirements, standards, and guidelines are taken into account to identify potential regulatory risks at an early stage. These include, among others, the EU Medical Device Regulation (MDR), international standards such as ISO 13485 for quality management systems, and product-specific standards (e.g., ISO 25539 for vascular implants). Based on these requirements, a requirements catalog is developed to ensure that the product concept is testable, documentable, and approvable from the outset. Furthermore, the regulatory assessment is incorporated into the development's risk structure and serves as the basis for subsequent approval strategies.

## 6 Early Risk Analysis

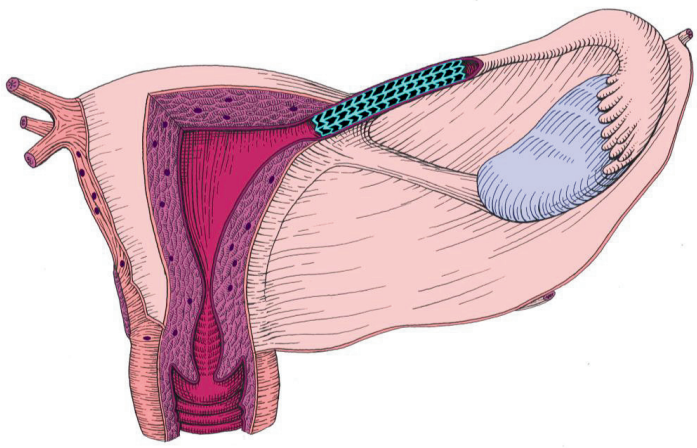
IIB e.V. supports ISO 14971-compliant **risk analysis of medical products** already in the early development phase. Together with companies, potential hazards are identified based on literature, bench tests, and clinical feedback. These risks are assessed in terms of severity and probability of occurrence and prioritized in a risk matrix. This forms the basis for discussing appropriate risk control measures, such as optimizing geometry, surface properties, or material and assembly concepts. An important aspect is the definition of verifiable acceptance criteria and their linkage to verification and validation activities.

# Requirements Analysis for the Development of a Biodegradable Microstent for the Treatment of Fallopian Tube Obstructions

The development of a biodegradable microstent for the treatment of Fallopian Tube obstructions is being carried out in cooperation between the Clinic and Polyclinic for Gynecology and Obstetrics at the University Medical Center Greifswald and IIB e.V. Close collaboration between clinical and technical research is essential to directly translate medical requirements into the implant's technical specifications.
Since no comparable product currently exists, fundamental requirements regarding function, material behavior, and implantation conditions must first be determined experimentally. The goal is to develop a safe, functional, and biodegradable implant based on anatomical and mechanical data.
This **case study** illustrates the individual steps of the requirements analysis - from anatomical characterization through market and patent research to early-stage risk analysis.

### Analysis of Medical Requirements for the Implant

In order to precisely define medical and functional requirements, IIB e.V. systematically records the anatomical, physiological, and biomechanical boundary conditions of the implantation site and derives robust specifications for the implant design from this information.

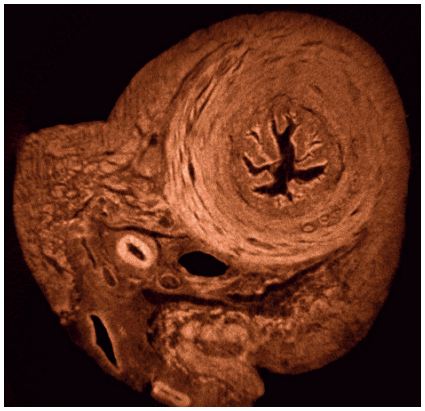


*Concept of a polymeric microstent for the minimally invasive treatment of Fallopian Tube obstructions*

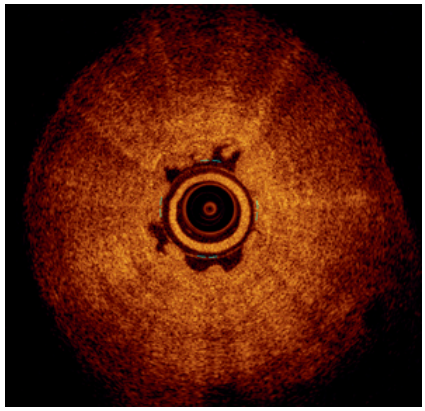
### Technical Specifications and Functional Requirements

- Low surface coverage for optimal ovum transport
- High biocompatibility, particularly with different cell types of the fallopian tube epithelium, at various stages of the oocyte, and with sperm cells
- Sufficient radial force to restore the lumen
- High flexibility, i.e., low bending stiffness
- Good visibility under ultrasound imaging

µCT scans are used to determine geometric parameters, as well as the fold structure, lumen path, wall thickness of the Fallopian Tube. Mechanical target values required for implant design are derived based on OCT measurements.



*µCT Scan of a Fallopian Tube for characterization of the lumen structure*



*OCT Scan of a Fallopian Tube for determination of mechanical properties*

In addition to technical specifications and functional requirements, a **market analysis** is conducted to systematically capture and evaluate existing medical products and therapeutic procedures relevant to the application. The goal is to identify technological references and established solutions, providing additional insights for the requirements catalog and assessing the market potential.

In the case of the biodegradable microstent for the treatment of Fallopian Tube obstructions, the development represents a novelty - no comparable medical product is currently available on the market. Nevertheless, the market analysis examines alternative treatment methods, such as microsurgical reconstructions or catheter-based procedures. Analysis of these alternatives provides valuable information on functional requirements, material properties, and potential risks, which feed into further product development.

In addition to analyzing commercially available products, a comprehensive **patent search** is performed. This serves to identify existing technological approaches and intellectual property, and to verify whether certain design principles or functional concepts are already patented and therefore not available for the new development. In the field of microstents, patents already exist covering various stent geometries and mechanisms for different body regions, including the fallopian tube.

### Regulatory Compliance

In addition to its specific properties, a microstent for the treatment of Fallopian Tube obstructions must meet the general requirements for a stent. According to the international testing standard DIN EN ISO 25539-2, these include the following aspects: (i) uniform, precise, and safe deployment, (ii) maintenance of position and apposition at the implantation site, (iii) preservation of sufficient structural integrity, (iv) compatibility of the stent size with the diameter of the implantation site, (v) unobstructed flow, and (vi) visibility in imaging.

### Early Risk Analysis

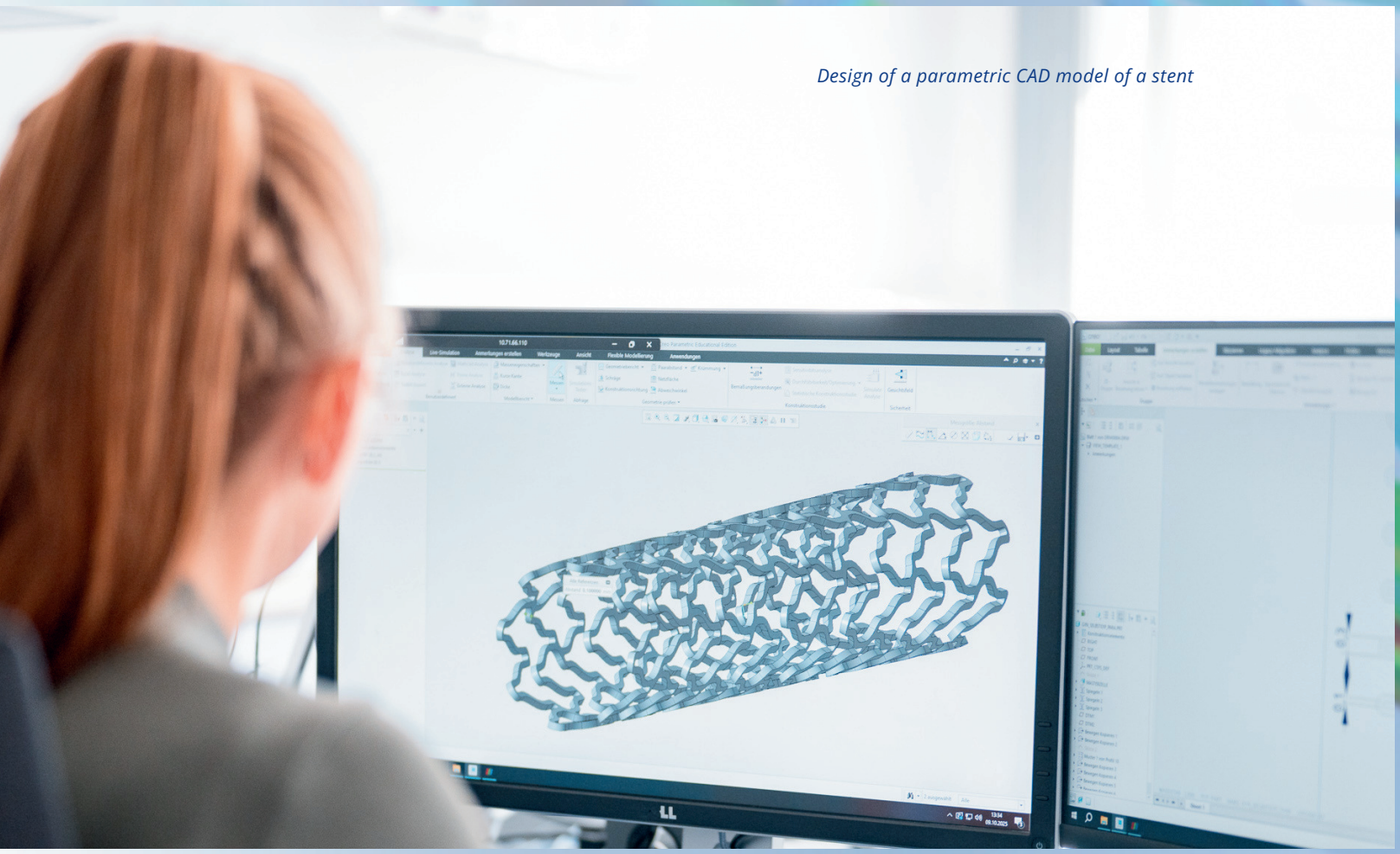
Already in the early development phase, IIB e.V. conducts an ISO 14971-compliant risk analysis to identify potential hazards and derive appropriate risk mitigation measures. For the biodegradable microstent, the focus is particularly on imaging visibility, controlled degradation, and biocompatibility.
Key risks include the reliable localization of the stent under ultrasound or MRI, potential tissue reactions to degradation products, as well as mechanical stability and anchoring within the Fallopian Tube lumen. Based on this analysis, optimizations of geometry, surface structure, and material selection are derived to ensure the safety and functionality of the microstent in clinical use at an early stage.

# Virtual Product Development

**Virtual product development is a central component of modern medical technology and enables efficient, safe, and targeted development of innovative implants. At IIB e.V., the methodological portfolio encompasses the entire digital process chain - from parametric CAD design, structural and fluid mechanical simulations, to virtual clinical studies and experimental validation.**

The starting point of every development process is a detailed requirements analysis, in which the anatomical, mechanical, and functional conditions of the intended implantation site are defined. Based on this, a suitable material - such as cobalt-chromium, Nitinol, or bioresorbable PLLA is selected. Each of these materials exhibits specific properties regarding strength, strain behavior, shape memory, or time-dependent degradation, which are carefully considered during the development phase.

**Parametric CAD models** enable the creation of rule-based design variants, allowing consistent adjustment of geometric parameters. These CAD models serve as the basis for simulation-driven optimizations, facilitating rapid design modifications to achieve the best possible implant solution for the specific requirements.



*Design of a parametric CAD model of a stent*

**Structural mechanical simulations (FEA)** are used to evaluate radial strength, expansion behavior, as well as stress distributions under physiological and pathological loads. Both idealized and patient-specific models are employed. Complex processes, such as the implantation of self-expanding devices or the design of catheter systems are also modeled virtually to identify critical loading scenarios and failure mechanisms at an early stage.

In addition, **computational fluid dynamics (CFD) analyses** are employed to evaluate the impact of implants on hemodynamic processes. The Biofluid Mechanics group at IIB e.V. specifically investigates how design parameters affect local flow, shear stress distributions, and associated complications such as restenosis or thrombogenicity. Suitable blood models, physiological boundary conditions, and quantitative evaluation criteria are developed for this purpose.

For particularly complex questions - such as in transcatheter aortic valve prostheses - **fluid-structure interaction (FSI) simulations** are performed, mathematically coupling implant deformation with flow characteristics. This allows, for example, the virtual analysis of the opening and closing behavior of a heart valve prosthesis and the optimization of the implant. For these complex simulations, IIB e.V. has access to several high-performance workstations (see p. 53) and can additionally utilize the computing cluster of the University of Rostock.

A central element of virtual product development at IIB e.V. is the **experimental validation** of simulations. The institute provides a comprehensive measurement infrastructure to experimentally verify the mechanical and functional properties of implants. This includes systems for measuring radial force, static testing machines for tensile, compression, bending, or torsion tests, and fatigue testers (see p. 52), as well as pulse duplicator systems (see p. 51) to replicate physiological boundary conditions. High-speed cameras are used to capture dynamic deformations with high precision (see p. 43) and compare them with simulated deformations. Additionally, a particle image velocimetry (PIV) system allows the measurement of local velocity fields (see p. 50), enabling detailed validation of fluid dynamics simulations. The direct comparison of simulations and experiments under various loading scenarios significantly enhances the reliability and predictive power of the numerical models.

To systematically classify the significance, limitations, and potential of simulations, modeling is performed according to the concepts of Context of Use (CoU) and Question of Interest (QoI), as defined, among others, by the U.S. Food and Drug Administration (FDA) and the American Society of Mechanical Engineers (ASME).

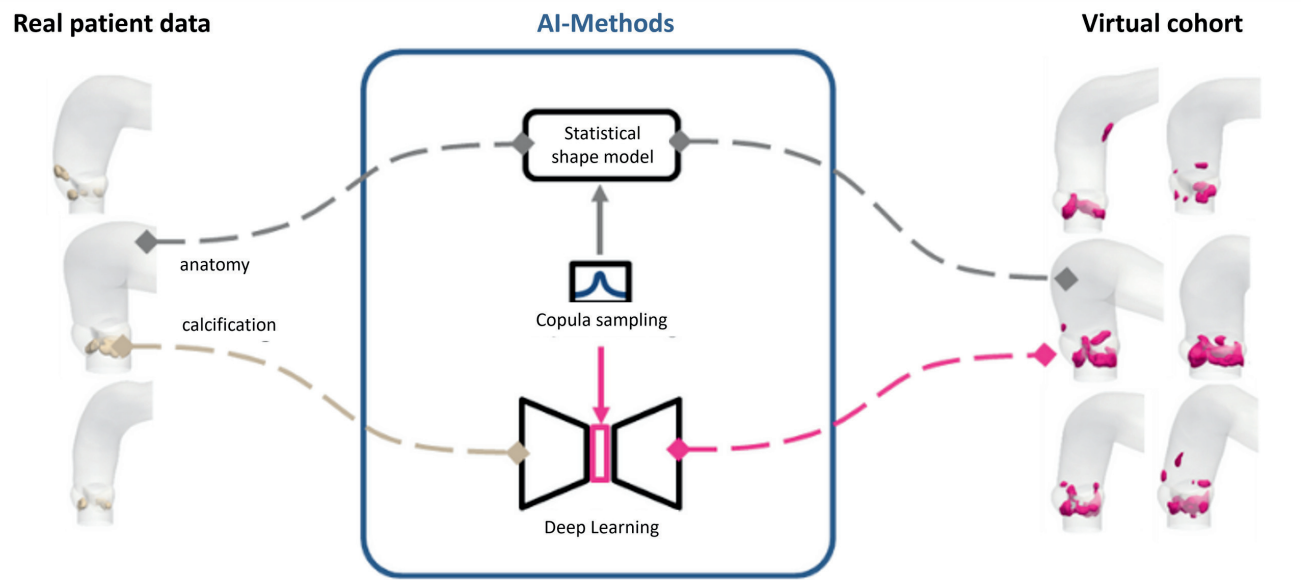
Thanks to comprehensive testing and manufacturing facilities plus many years of experience, IIB e.V. ensures a close integration of virtual, experimental, and clinically oriented product development.

# METHODOLOGICAL PORTFOLIO

The development and application of **virtual clinical trials** (*in silico* clinical trials, ISCT) is another focus at IIB e.V. Using real patient data IIB generates virtual cohorts through statistical and AI-based methods. These cohorts enable automated testing of implant prototypes on a large number of virtual patients in a digital environment. This approach allows systematic assessment of safety and efficacy across a wide range of anatomical variations while also significantly reducing animal experiments, associated risks, and the scope of real clinical studies.

Like real clinical trials, virtual clinical trials also require structured study planning. First, a scientific hypothesis is defined, which the simulations are intended to test. Next, the virtual patient cohort, relevant simulation parameters, and study design are determined to ensure a systematic and traceable evaluation of the medical product.

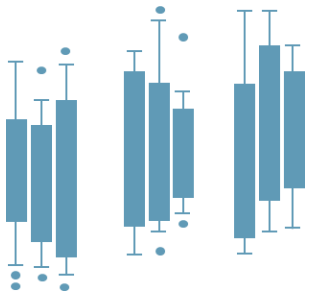
The foundation of virtual clinical trials is formed by virtual cohorts. These can either be patient-specific, reconstructed from clinical imaging data (e.g., CT), or generated synthetically using AI-based methods. Synthetic virtual cohorts allow the targeted inclusion of subgroups or rare edge cases that are often excluded from real trials for ethical reasons or due to low numbers. In addition, extensive virtual populations can be generated from a few real datasets, enabling statistically robust conclusions regarding implant design.




*Workflow for generating synthetic cohorts using AI methods: example of the human aorta in the region of the aortic valve in patients with calcific aortic valve stenosis*

High computational efficiency is essential for virtual clinical trials, as simulations are performed on a large number of virtual patients. Therefore, structural and fluid dynamic models are purposefully simplified to reduce computation time without compromising the validity of the results. Simulations are also built using scripted workflows, allowing automated execution and flexible application to different geometric models. This enables efficient calculation of large virtual cohorts while ensuring that all clinically relevant steps - from implantation to interaction with the surrounding tissue - are represented in the model.

Following the simulations, the results are statistically processed and interpreted to reveal relationships between design parameters and the clinical behavior of the implant. This allows for a targeted assessment of the safety and efficacy of the medical product.
As in real clinical trials, hypotheses, endpoints, and patient cohorts are defined in advance. Parameter studies, sensitivity analyses, and plausibility checks are performed to identify the factors that most significantly influence the outcomes. Comparison with real data and validation steps ensure robust and traceable results, supporting the further development and regulatory approval of medical products.



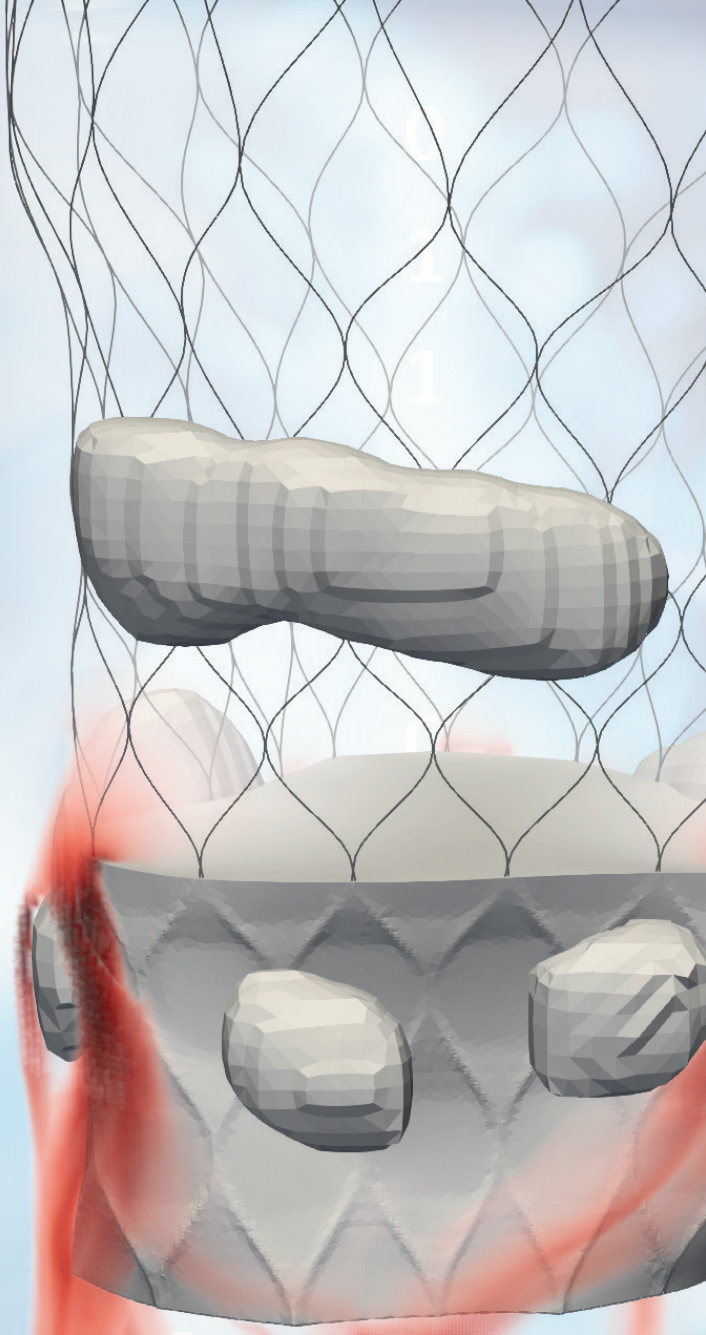
# Virtual Clinical Trial for the Evaluation of the Safety of an Aortic Valve Prosthesis

**Transcatheter aortic valve implantation** is a minimally invasive procedure for replacing the aortic valve with an aortic valve prosthesis. Due to patient-specific anatomical conditions and calcifications of the aortic root, leakage can occur after implantation, causing blood to flow back into the ventricle through a closed aortic valve prosthesis.

To evaluate the design of the aortic valve prosthesis with respect to blood regurgitation using a virtual clinical trial, hundreds of real patients were incorporated into a statistical model representing the anatomy of the aortic root. From this model, an arbitrary number of virtual patients can be generated, reflecting the anatomical variations of the real patients.

In the next step, the aortic valve prosthesis is implanted in the virtual patients using structural mechanical simulations and subsequently perfused with blood through flow simulations. This allows evaluation of the position and rate of blood regurgitation. Since this procedure is performed on a large number of virtual patients, the analysis can be conducted analogously to real clinical trials.

This approach enables, for example, the determination of which aortic valve design is best suited for a specific patient. It also allows assessment of whether new prosthesis designs outperform already clinically established commercial products.



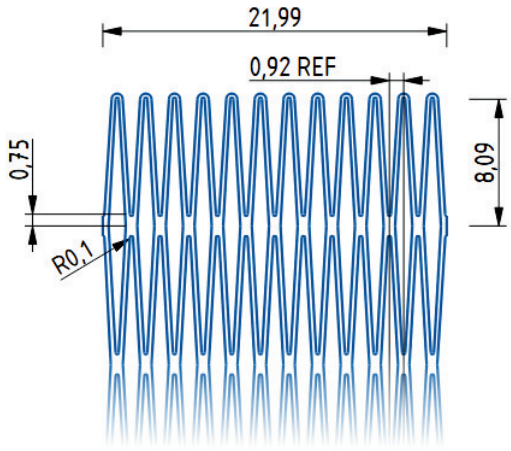
*Computational fluid dynamics analysis of blood regurgitation in a virtual patient treated with a transcatheter aortic valve prosthesis*

# Prototyping of Medical Devices

Following virtual product development, prototyping represents the crucial step for transforming digital concepts into physical implants or medical devices and for testing their functionality under realistic conditions. At IIB e.V., a fully in-house workflow enables rapid, safe, and reproducible production of functional implant prototypes.
Thanks to the close integration of simulation, manufacturing, and testing, design adjustments can be directly implemented in prototypes and evaluated within short development cycles. A wide range of biocompatible materials are available, including biostable polymers, bioresorbable materials, and metallic materials.
Prototyping at IIB e.V. covers all stages of product development and is tailored individually to the requirements of innovative implants and medical devices.

## DESIGN FOR MANUFACTURING

After virtual product development, in which the component geometry is created using CAD models and evaluated through simulations, the design is transferred into a manufacturing-ready model. The virtual design is adapted to serve as a template for production. Depending on the tube material and manufacturing process - for example, during shape setting of Nitinol stents - the geometry may change during fabrication. Therefore, the design must be adjusted in CAD prior to manufacturing to ensure the desired final geometry and functionality of the implant.




*CAD design of a stent for manufacturing*

*Production of a polymer semi-finished product by dip coating*

## TOOL DEVELOPMENT AND MANUFACTURING

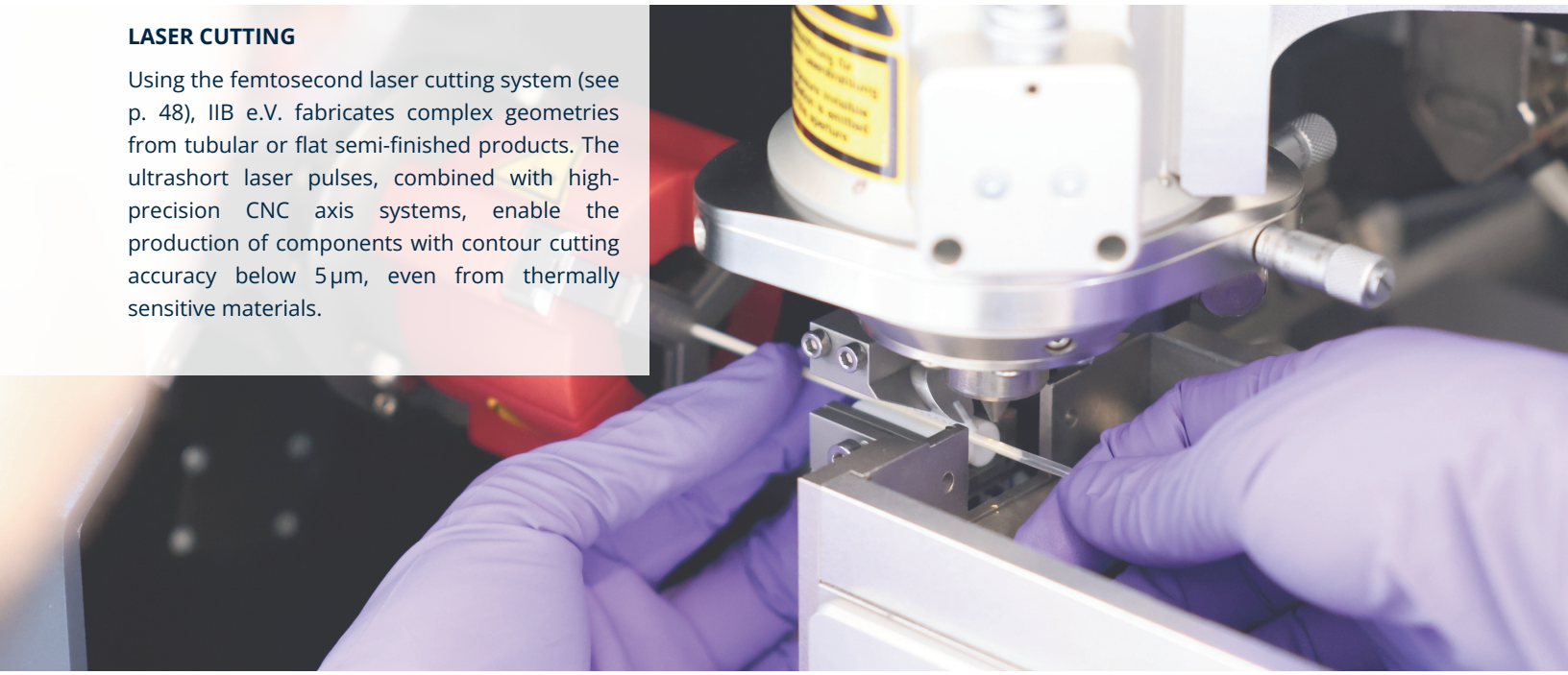
IIB e.V.'s in-house equipment is used to develop and manufacture both product-specific molding tools and industrially scalable manufacturing equipment as a basis for medical device prototyping. This enables a high degree of design freedom while maintaining short development times.

## SEMI-FINISHED PRODUCT MANUFACTURING

IIB e.V. produces polymer semi-finished products, in particular precision polymer tubes. Geometric parameters, such as inner diameter and wall thickness, can be precisely defined to ensure batch-to-batch quality consistency. Another core competency is the adjustment of polymer morphology - e.g., on the surface or within the bulk material (porosity) - for the production of biostable or biodegradable polymer structures.

## LASER CUTTING

Using the femtosecond laser cutting system (see p. 48), IIB e.V. fabricates complex geometries from tubular or flat semi-finished products. The ultrashort laser pulses, combined with high-precision CNC axis systems, enable the production of components with contour cutting accuracy below 5 µm, even from thermally sensitive materials.

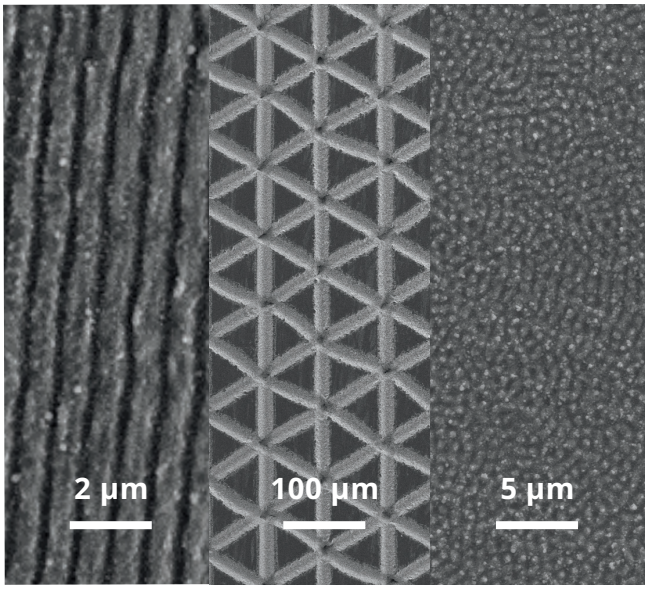


## DESIGN

Various technologies are available for implant prototyping:

- Braiding: Wires made of Nitinol, stainless steel, cobalt-chromium, or polymers are spirally interwoven around a core. The result is flexible mesh structures that are ideally suited to conform to curved or mobile anatomical target structures.
- Thermal Shape Setting: Through controlled heat treatment - e.g., of NiTi structures in a forced-convection chamber furnace (see p. 49) with defined temperature profiles - shape memory properties and austenite finish (Af) temperatures are precisely set. These can be verified using our optical system for Af temperature determination (see p. 62).
- Additive Manufacturing: Rapid prototyping using 3D printing (see p. 47) enables fast production of components from plastic or ceramic, including patient-specific designs based on imaging data (e.g., CT).
- Conventional Methods: For simple geometries, classical manufacturing techniques such as turning, milling, or drilling are employed.

*Process steps for the fabrication of stent structures using femtosecond laser cutting – from cutting of tube semi-finished products through mechanical post-processing to shape setting by heat treatment*




*Example surface structuring of metallic semi-finished products fabricated using ultrashort-pulse laser technology*

## SURFACE TREATMENT

The following surface treatment methods are available at IIB e.V. to optimize implant properties:

- **Microblasting:** Used to remove burrs and homogenize surface roughness, for example to increase the effective surface area.
- **Laser Processing:** Ultrashort-pulse lasers enable the targeted creation of micro- and nanostructures on implant surfaces. In particular, LIPSS (Laser-Induced Periodic Surface Structures) allow surface topographies to be generated at the nanometer scale. Surface structuring can optimize implant–tissue interactions.

## COATING

At IIB e.V., implant structures are coated with polymers as well as polymer–drug mixtures. Both the coating thickness and the drug loading can be precisely controlled. For this purpose, a high-precision ultramicrobalance is used (see p. 61).

*In-house developed system for coating implants*

## ASSEMBLY

Individual components can be assembled into complete prototypes - for example, using adhesive bonding, screws, or press fits, depending on the material combination and functional requirements. To optimize assembly quality or to assemble complex sub-assemblies, intricate work steps can be guided and verified through interaction with virtual, visual, and auditory tutorials (see p. 58).

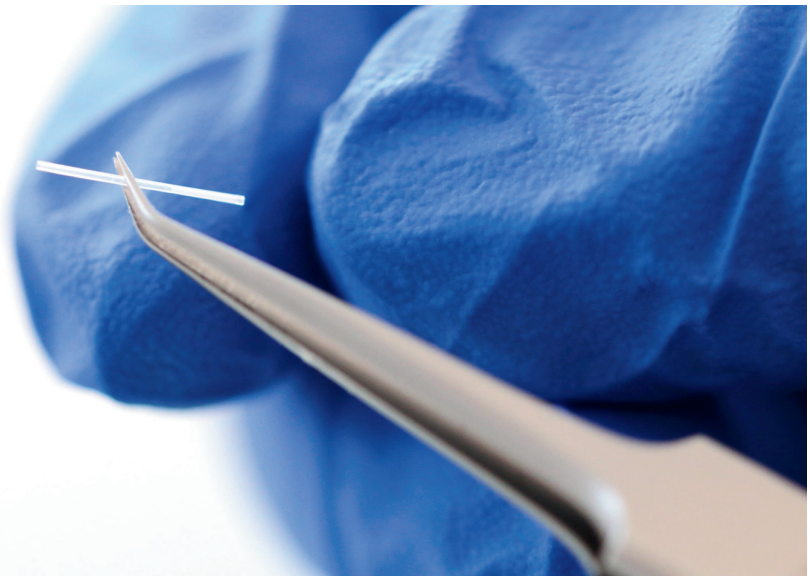
## VERIFICATION

Finally, a comprehensive technical evaluation of the prototypes is carried out in IIB e.V.'s accredited testing laboratory. This includes dimensional verification (e.g., wall thickness, strut width), material analyses, and functional tests (e.g., Af temperature, radial force, crush resistance). This ensures that the prototypes meet the specified requirements.

# Manufacturing of a Drug-Eluting Microstent for Glaucoma Therapy

The use of state-of-the-art stents offers unprecedented prospects for success in numerous medical applications including therapy for glaucoma. At IIB e.V., an innovative drug-eluting microstent for glaucoma treatment is being developed.

The microstents are fabricated from polyurethane granules, which are dissolved in chloroform and processed into dimensionally precise tubes with reproducible inner and outer diameters using a fully automated dip-coating process. The resulting geometric parameters are verified with a laser measurement system. Functional elements, such as a micromechanical valve mechanism, are manufactured with high precision using a femtosecond laser cutting system. Subsequently, the implant is coated with a drug that inhibits excessive tissue reaction in the eye. The microstent has a diameter of approximately 360 µm and can be implanted minimally invasively using a custom-designed, 3D-printed applicator system.



*Microstents for glaucoma therapy*

Glaucoma is the leading cause of irreversible blindness worldwide. To prevent glaucomatous damage, specialized therapeutic approaches aim to reduce intraocular pressure to a defined, patient-specific target level.

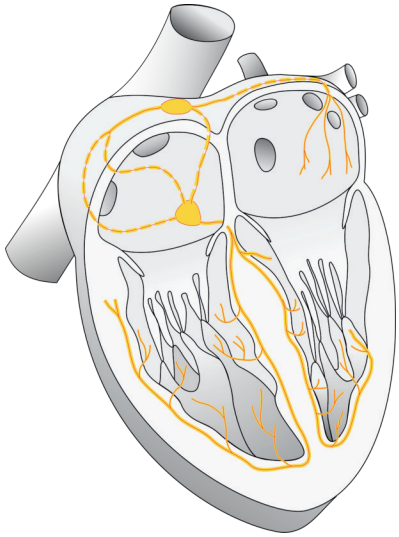
*Position of the microstent with drug coating highlighted in orange in the eye*

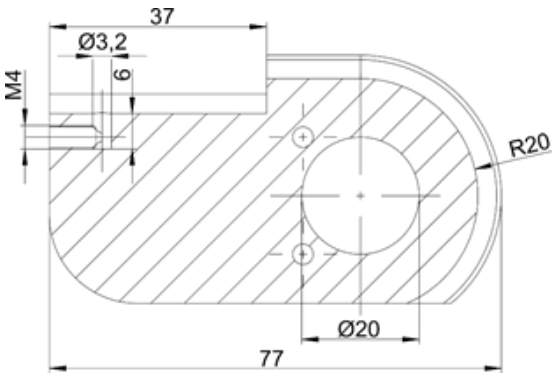
# Development of Measurement Methods and Special Equipment

At IIB e.V., in addition to biomedical implants, test setups and validated testing methods are developed for the standards-compliant physical characterization of a wide range of medical devices.
For innovative medical products, standardized methods for analysis generally do not exist. In such cases, appropriate testing methods and specialized test setups are established. The need for custom-designed test rigs may also arise from an improved measurement principle of an existing method.
Expertise in biomedical test equipment development is based on an experienced interdisciplinary team from the fields of electrical engineering, computer science, and mechanical engineering. A modern precision mechanics workshop is available at IIB e.V. for implementation.
Starting from the medical-technical research question, measurement concepts are developed, then measurement technology and sensors are assembled, and the concepts are implemented in a functional test setup controlled by customizable testing software. Both physiological boundary conditions and high-precision measuring instruments are taken into account. Reproducibility and comparability of measurement results are key requirements.
Additionally, the requirements of various quality management systems (e.g., ISO 9001, ISO 17025, ISO 13485) are considered from the outset. Corresponding documentation is then prepared for the qualification of the test rig and the validation of the measurement methods, which provides an ideal solution for use in quality assurance processes or for regulatory approval.

## Processes for the Development of Measurement Methods and Specialized Devices

**DEFINITION OF REQUIREMENTS** The development of testing methods and test rigs begins with a requirements analysis, as presented in the chapter on Product Development and Prototyping. This analysis takes into account both normative standards (e.g., ISO and ASTM standards) and specific properties of the implant to be tested, such as geometry, material, and loading conditions. In addition, the highest safety and quality standards are considered.

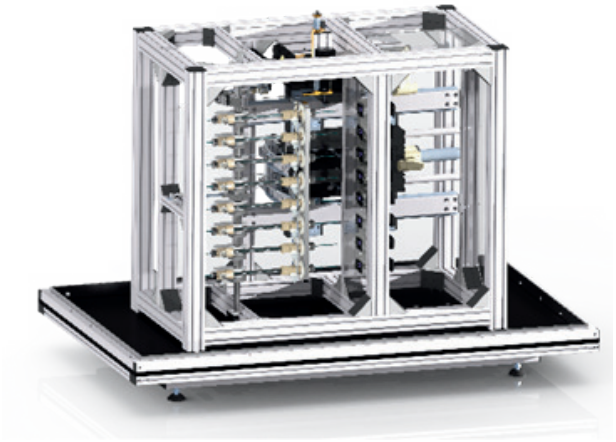


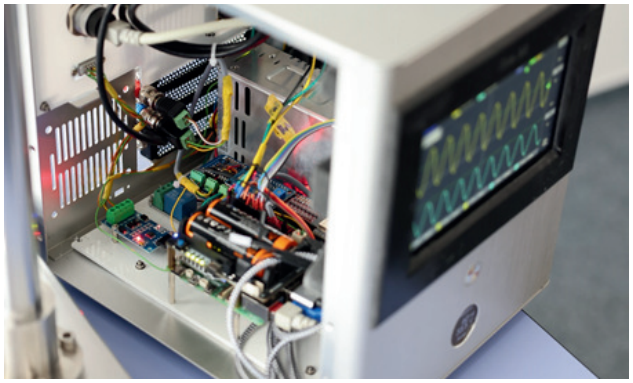



**TEST RIG DESIGN** Based on the defined requirements, a comprehensive measurement concept is developed in the next step. The definition of the required measurement accuracy is crucial for selecting suitable measurement principles. Different measurement concepts are compared and evaluated in terms of feasibility, precision, and cost-effectiveness. Taking safety requirements into account, the preferred concept is translated into a test rig design. Technical details are developed using CAD software. In addition, the control electronics, including safety circuits are designed.

*Precision mechanical machining of a plastic component using a three-axis CNC milling machine – the technical implementation at IIB e.V. is carried out by experienced electronics and software engineers as well as designers and precision mechanics.*

**TECHNICAL IMPLEMENTATION** In the technical implementation phase, the mechanical and electronic components are realized. The focus is on precise manufacturing and assembly to ensure that defined test modes can be reproduced reliably. A wide range of high-precision measurement devices and electronic components - such as the impedance analyzer (see p. 59), laser distance sensors, and the benchtop multimeter (see p. 60) - provides great flexibility in test rig design. The highest care and quality in the fabrication of test rigs are essential, as many medical devices must be tested reliably over hundreds of millions of cycles. At IIB e.V., experienced staff from precision mechanics to software development work together in an interdisciplinary manner.





**SOFTWARE DEVELOPMENT** In parallel with the technical implementation, the software architecture is developed and tailored to the specific requirements of each testing procedure. Considerations include interface compatibility, data security, access rights, and user-friendliness.

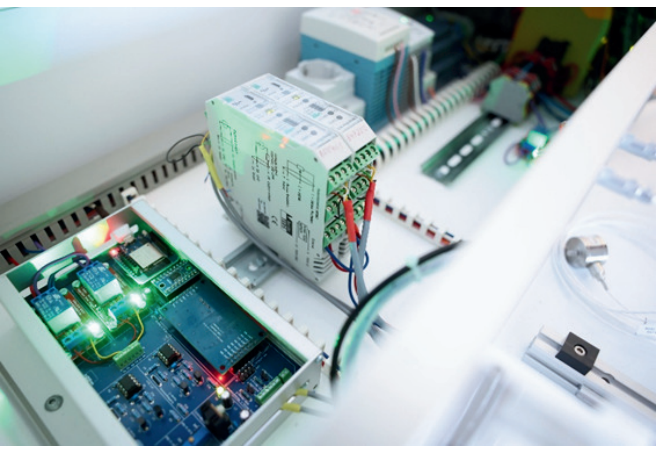
**QUALIFICATION AND VALIDATION** Conformity of the test rig with respect to the Machinery Directive and machine safety is documented as part of the qualification process. Compliance with the relevant standards is demonstrated through validation measurements.

# Special Test Rig for the Analysis of Pushability and Trackability of Cardiovascular Implants

Application-oriented investigations of cardiovascular products, in particular stents, stent delivery systems, and balloon catheters, represent a key focus at IIB e.V. An excellent example of the development of in-house measurement methods and specialized equipment is the trackability test rig. This rig is used to examine the push characteristics of catheter-based delivery systems in anatomical vessel models. Forces at the proximal catheter handle during advancement (trackability) as well as the force ratio between the proximal handle and the distal catheter tip (pushability) are measured as indicators of the catheter's guiding and pushing performance. These measurements are applied both in the context of regulatory testing and in comparative product evaluations of different manufacturers (benchmark tests).

**A linear actuator with clamping and kink protection** allows the system under test to be individually secured and advanced at a constant feed rate into an anatomical model derived from the requirements analysis. Force sensors are used to measure distal and proximal forces during catheter advancement. The water bath with integrated heating enables the simulation of physiological conditions and the integration of different anatomical vessel models.

**Anatomical models of the vascular system** allow the complex *in vivo* loading conditions of the implant systems under test to be taken into account. The two- or three-dimensional models are manufactured for example using CNC milling or 3D stereolithography printing. After computer-aided model development, a wide variety of implantation pathways can thus be made available quickly and cost-effectively.



**CONTROL ELECTRONICS AND SOFTWARE** At IIB e.V., the control electronics and software were developed in-house by experienced electronics and software engineers. They ensure reproducible control of the drive axis and force sensors. The user software enables the execution of defined and reproducible measurement sequences to determine the push characteristics, which are derived from the measured force–displacement curves. The integrated emergency stop circuit guarantees user safety.

**SPECIFICATIONS**

- Continuously adjustable linear actuator with Hall sensors
- Travel range ≤ 450 mm
- High-precision force sensor technology
- Force measurement range ±10 N
- Control electronics
- Precision-engineered catheter guides
- Temperature-controlled water bath
- Camera system for visual documentation
- User safety mechanisms
- Emergency stop

# Biomaterials and Polymer Chemistry

In the field of modern implant technology, the focus is on materials that are precisely tailored to their specific medical application. A key objective is not only to optimize implant design but, above all, to functionalize the surfaces in a targeted manner to improve biocompatibility and actively promote tissue integration. For this reason, the methodological spectrum is concentrated on the development, processing, and characterization of polymer-based biomaterials for implants.

A particular focus is placed on **material development, surface modification and functionalization, drug incorporation and release, as well as material characterization.** This approach enables the creation of tailored material solutions for a wide range of medical applications.

**Material Development**

The development of suitable materials is crucial for the performance of modern implants. Materials must, on the one hand, withstand high mechanical and chemical stresses, and on the other hand, allow controlled interaction with the biological environment. Depending on the application, both permanently stable and deliberately degradable polymers may be required. At IIB e.V., material systems are investigated to evaluate their stability and degradation behavior, and methods are developed to precisely tailor surfaces and properties to meet medical requirements. In this way, the foundation is laid for implants that are both safe and functionally effective. The following are key focus areas of IIB e.V.'s research:

- Development of new implant materials based on:
  - Biodegradable polymers (e.g., polylactide, polyglycolide)
  - Biostable polymers (e.g., polyurethanes)
  - in pure form, as polymer blends, or as copolymers
- Processing via solvent-based methods

**Material Characterization**

Material characterization plays a central role in the development and quality assurance of polymer materials. Targeted analytical methods allow the physical, chemical, and structural properties of polymers to be determined, enabling a well-founded assessment of their suitability for specific applications. Characterization is typically carried out using mechanical, morphological, and thermal methods.

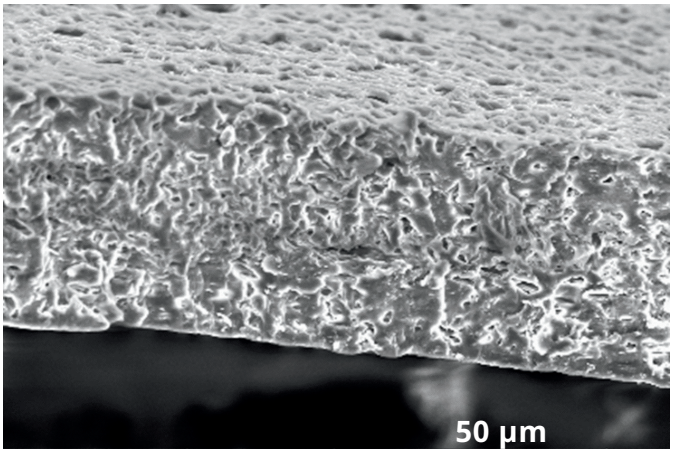
**CHEMICAL TESTING METHODS** These methods enable the targeted analysis of substances with respect to their composition, structure, and concentration. A distinction is made between qualitative methods, which provide information on the type of substances present, and quantitative methods, which determine their exact amounts. Instrumental techniques such as spectroscopy and chromatography play a key role in this context.

**MECHANICAL TESTING METHODS** provide information on the strength, stiffness, and elongation properties of polymers. Standard procedures include:

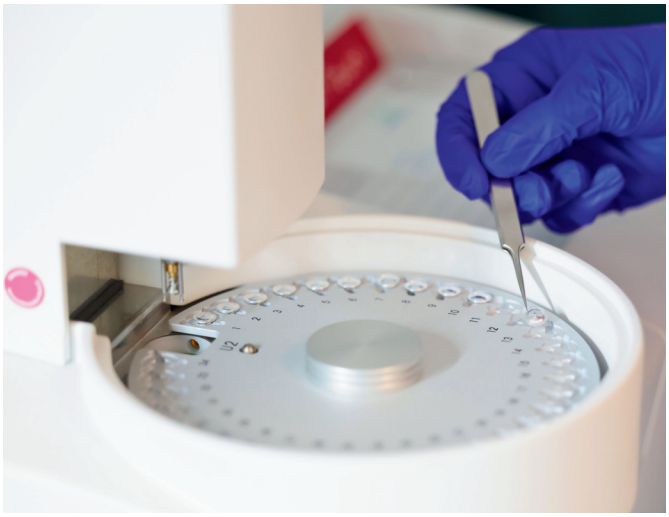
- Tensile testing (according to DIN EN ISO 527): Determination of tensile strength, elastic modulus, and elongation at break using a universal testing machine (see p. 39)
- Compression and bending tests: Evaluation of behavior under compressive or bending loads using static and dynamic testing machines (see pp. 38–39)
- Torsion tests: Analysis of the mechanical behavior of materials under shear stress - relevant for loaded implant and instrument components - using a static testing machine (see p. 38)
- Hardness testing (e.g., Shore hardness): Determination of surface hardness

The **morphology** of a polymer, i.e., the spatial arrangement and structure at the microscopic level, plays a decisive role in the mechanical, thermal, and functional properties of the material. It thus has a major influence on characteristics such as strength, elasticity, transparency, density, and diffusion behavior. To gain a precise understanding of this internal structure, various microscopic techniques are employed:

- Scanning Electron Microscopy (SEM): High-resolution imaging to visualize surface and fracture structures (see p. 40)
- Transmission Electron Microscopy (TEM): Analysis of internal structures, such as phase boundaries or crystallites (see p. 41)




**Thermal methods,** such as Differential Scanning Calorimetry (DSC) (see p. 62), are used for detailed analysis of the temperature behavior of polymers. They examine how a polymer responds to controlled temperature changes and which energetic processes occur within the material. This method allows key parameters related to thermal stability, melting behavior, and glass transition to be determined. By recording heat flows during heating or cooling, characteristic transitions in the polymer can be identified, such as the point at which the material changes from a solid to a viscous state or at which crystalline structures melt. This information provides valuable insights into the internal structure, processability, and operational limits of the polymer under thermal stress.



**Surface Modification and Functionalization, Drug Incorporation and Release**

Essential for projects in the field of material development and drug incorporation is chemical analytics. These analyses are applied at various stages of a project and cover different tasks depending on the specific requirements:

- Polymer Analysis
  - Gel Permeation Chromatography (GPC): Determination of molecular weights (see p. 64)
  - Viscosity measurements using GPC and capillary viscometry (see p. 64)
  - Polymer identification using Raman spectroscopy (see p. 65)

- Drug Analysis and Release
  - Quantitative analysis of active agents using high-performance liquid chromatography (HPLC) (see p. 63)
  - *In vitro* release studies and determination of the amount of incorporated drug
  - Establishment of specific release conditions by selecting appropriate media

- Additional Analytical Methods and Applications
  - Identification of unknown materials and by-products using Raman spectroscopy
  - pH measurement and control
  - Quality assurance as well as surface modification and functionalization (particularly via coatings)

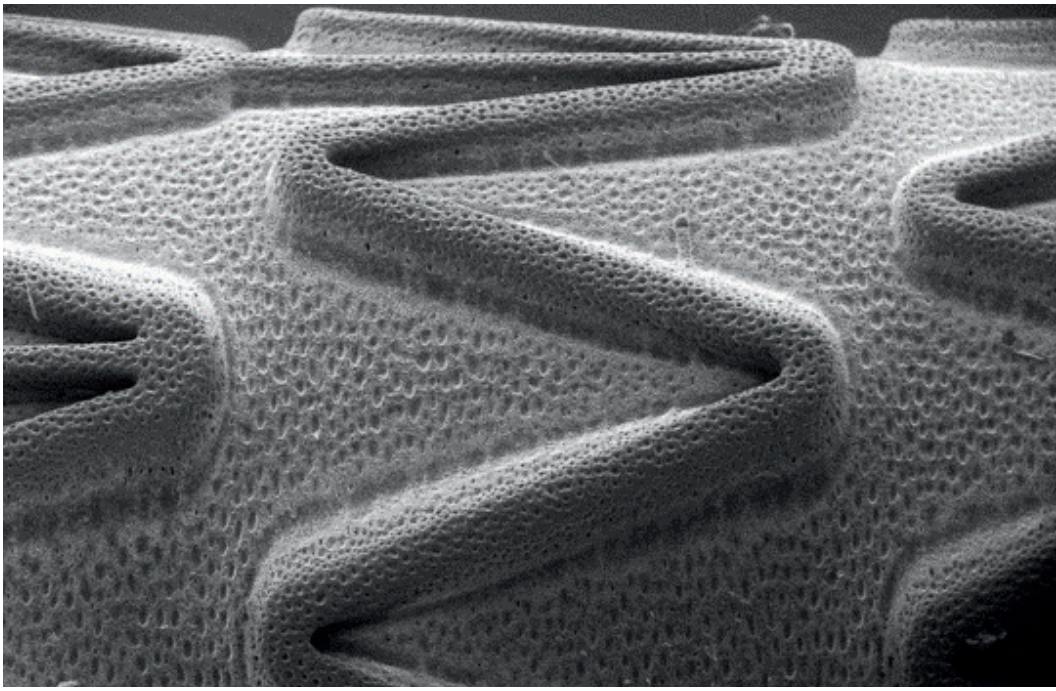

*Quality control after the manufacturing of a covered stent at IIB e.V.*

# Development of a Polymer-Based Cover for Stents

A key application area of polymer-based biomaterials is cardiovascular implant technology. Covered stents are used to seal vascular injuries or to treat aneurysms. In this context, the choice and functionalization of the cover play a decisive role.

Highly flexible, biocompatible polymers, such as polyurethanes, are used for stent coverings. These materials withstand the mechanical demands of the vascular system while providing a reliable barrier function. The polymer surface can be tailored to support endothelialization. By embedding active agents, such as antiproliferatives or antithrombotics, into the polymer matrix, the risk of restenosis and thrombosis can be reduced. Controlled release ensures that the drugs act precisely during the critical period following implantation. Extensive analyses of mechanical properties, drug release kinetics, and biological interactions are conducted to ensure the performance of the covered stent.

Through this combination of tailored polymer development and targeted surface functionalization, a stent is created that not only withstands the high mechanical stresses during implantation and expansion while sealing the vessel, but also supports healing processes and minimizes complications.



*SEM images of the porous structure of the cover embedding the stent*

# Biological Testing of Materials and Implants

Even at the early stages of implant development, the analysis of implant–tissue interactions constitutes an important part of the research work. The materials and active agents used in implant fabrication should, as far as possible, be free of cytotoxic substances and allow good integration of the implant into the surrounding tissue. Healing processes after implantation should be completed quickly, the implant function should be maintained over a long period, and adverse effects, such as excessive cell proliferation or inflammation, should be avoided.

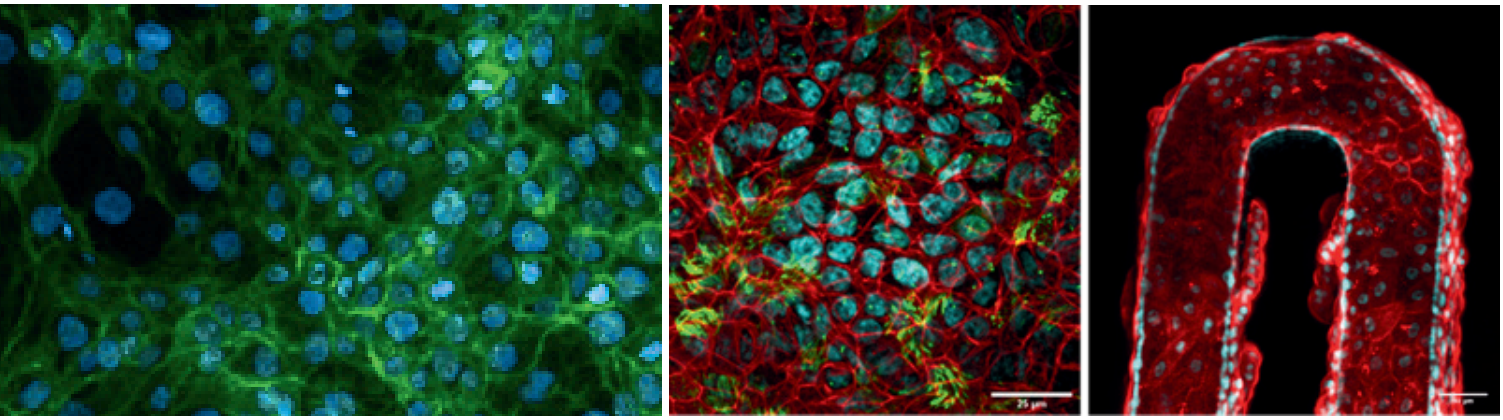
Targeted endothelialization of implants is a central strategy in cardiovascular implant development. Endothelial cells, which form a thin boundary layer between blood and tissue in the body, are encouraged to selectively colonize the implant surface. The goal is to prevent undesired interactions with components of the immune system as well as with blood cells such as platelets or erythrocytes.

The methodological spectrum of the **Biomedical and Biomaterials Research Group at IIB e.V.** focuses on the development and application of *in vitro* methods to characterize biomaterials and medical devices, particularly implants. Key aspects include **cytotoxicity and proliferation testing according to DIN EN ISO 10993-5, microscopic and molecular analyses of cell–biomaterial interactions, 3D cell culture models, feasibility studies using animal tissue, and HET-CAM assays (Hen's Egg Test – Chorioallantoic Membrane).** This approach enables the identification of suitable biocompatible materials depending on the implantation site and intended function of the implant.

**Cytotoxicity**

Cytotoxicity is typically assessed by measuring metabolic cell activity followed by detection of the biochemical response using a plate reader (see p. 68) or by imaging-based methods. In addition, the effects of substances or materials on cell proliferation, function, and morphology can be determined (see pp. 67–69). Implants, biomaterial extracts, and biologically active substances are tested for potential cytotoxic effects using cultured cells. Both primary cells and immortalized cell lines are employed for these assays. Cytotoxicity testing is performed in accordance with DIN EN ISO 10993-5 (Biological evaluation of medical devices – Tests for *in vitro* cytotoxicity). This ensures early in the project that no materials with cytotoxic potential are selected for implant development.

*Representative fluorescence microscopy images of cells after contact with biomaterial extracts, as well as in direct contact with an implant structure*



### 3D Cell Culture Model

**In order to** study implant–tissue interactions as realistically as possible, a specialized cell culture model, the Air-Liquid Interface (ALI) model, has been developed.

At IIB e.v., cells from the porcine oviduct are freshly isolated from tissue samples. These cells grow in the laboratory in a three-dimensional structure that closely resembles the natural architecture of the oviduct.

This testing system allows implants, such as an oviduct stent, to be evaluated *in vitro* for their compatibility with the tissue. Various advanced analytical methods are employed:

- Real-time microscopy provides insights into physiological cell function and cell–implant interactions within the culture (see p. 67).
- Scanning Electron Microscopy (SEM) reveals ultrastructural details (see p. 40).
- Confocal Laser Scanning Microscopy enables the examination of cell architecture and specific functional markers.

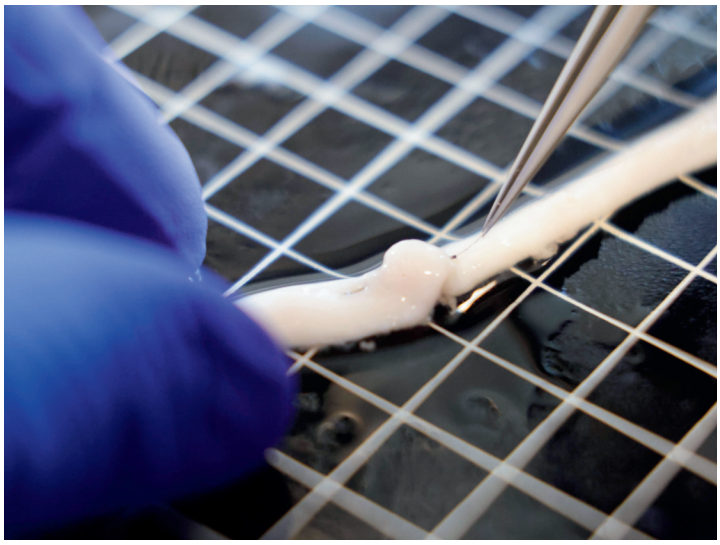
Additionally, immune signaling molecules are measured, and the gene expression profile of the cells is analyzed. This approach allows a deeper understanding of how implants interact with tissue and which biological mechanisms are involved.

*Aseptic work under the safety cabinet: preparation of a biological experiment at IIB e.V.*

**Feasibility Studies on Animal Tissue and *ex vivo* Investigations**

Feasibility studies play an important role in the development of new implants or surgical techniques. These investigations are conducted on animal cadavers or readily accessible animal tissue.

Thanks to the extensive scientific network of IIB e.V., particularly the long-standing collaboration with the Research Institute for Farm Animal Biology (FBN) in Dummerstorf, targeted implantation studies can be carried out in the IIB e.V. laboratory (see p. 44). Such studies help to make research more efficient while minimizing the number of necessary animal experiments in later preclinical studies in accordance with the 3R principle (Reduce, Replace, Refine).



*Representative ex vivo analyses at IIB e.V.*

*Micro-CT image of an implanted polymer stent*

**Hen's Egg Test (HET-CAM Model)**

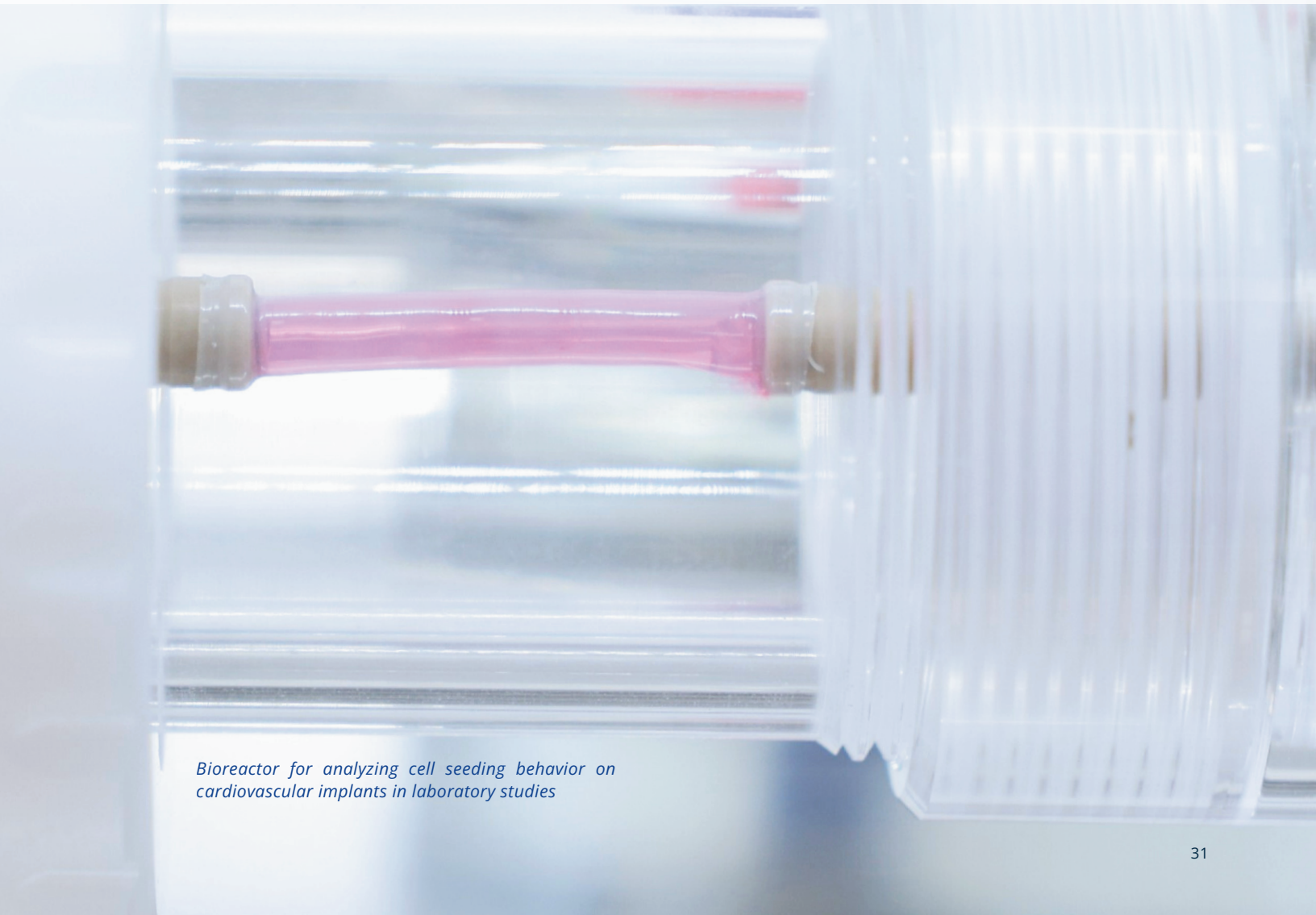
The Hen's Egg Test (HET) on the extraembryonic chorioallantoic membrane (CAM) is, strictly speaking, a method positioned at the interface between *in vitro* and *in vivo* studies and can help minimize the number of animal experiments in accordance with the 3R principle. For the assay, fertilized chicken eggs are opened to expose the CAM, which is responsible for efficient gas exchange between the embryo and the environment. The now easily accessible CAM contains numerous blood vessels with a dense capillary network and can be used for biocompatibility analyses (see p. 43). In addition to its significance in tumor research, the CAM test is also applied to evaluate the biocompatibility of biomaterials and nanoparticles.

# Implant-Specific *in vitro* Testing Systems Using the Example of Covered Stent Testing Technology

The use of cell culture plates, including multiwell plates, is a standard method in cell biology. Multiwell plates allow multiple cell cultures to be investigated simultaneously under identical conditions, saving time, conserving reagents, and providing precise comparative data.
However, these experiments are conducted under static conditions, meaning that flow conditions, as they occur in the cardiovascular system, cannot be reproduced. Flow conditions do have a significant impact on cell function - for example, endothelial cells respond to specific shear stress and flow patterns.

To analyze the endothelialization of cardiovascular implants, such as covered stents, a bioreactor system has been developed that simulates physiological blood flow conditions. Specially fabricated polymer tubes are used as scaffolds, with material properties optimized to support the attachment and growth of endothelial cells on the surface. A motorized rotation system ensures uniform cell seeding.

For long-term studies, parameters such as flow rate, cell density, and incubation time can be precisely controlled. Endothelialization is then assessed using fluorescence microscopy of the cytoskeleton and scanning electron microscopy (SEM) (see pp. 40 and 69). This system enables preclinical investigation of tissue–implant interactions under physiologically relevant conditions.



*Bioreactor for analyzing cell seeding behavior on cardiovascular implants in laboratory studies*

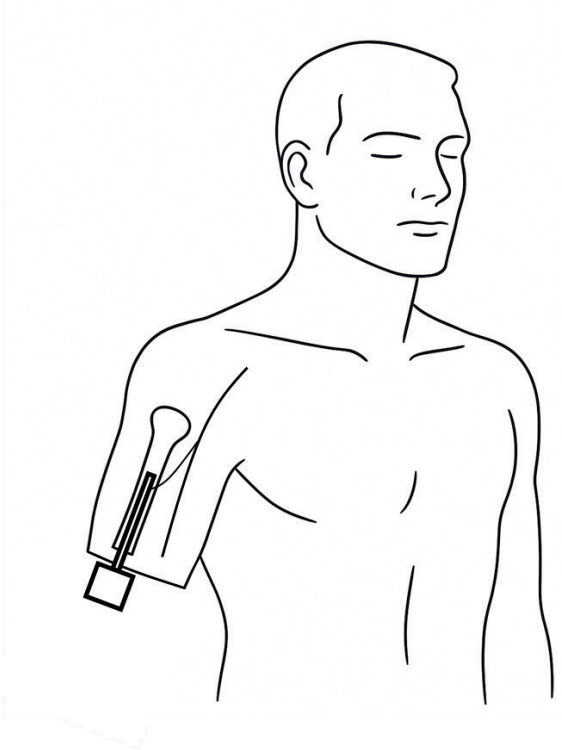
# Regulatory Requirements and Approval Preparation

High regulatory standards apply to the research, development, and testing of implants and biomaterial-based medical devices. In particular, the European Medical Device Regulation (MDR 2017/745) requires manufacturers to provide comprehensive technical documentation, conduct standard-compliant testing, and implement a validated risk management system.
In Mecklenburg-Western Pomerania, IIB e.V. serves as the central MDR competence center and as a point of contact for companies and research institutions for the regulatory-compliant implementation of medical device processes. With its interdisciplinary expertise, the institute supports all phases of product development - from preclinical testing and clinical evaluation to preparation for regulatory approval.

**MDR Center at IIB e.V. for Strategic Support of Companies**

IIB e.V. provides comprehensive support to manufacturers throughout the entire product lifecycle - from early risk classification and selection of the conformity assessment procedure (e.g., MDR Annex IX/XI) to its implementation. Based on structured gap analyses of the Technical Documentation, fundamental General Safety and Performance Requirements (GSPR) are derived and linked to verification and validation (V&V) plans.
In addition, the institute addresses usability (IEC 62366-1), unique device identification (UDI), labeling, EUDAMED actor obligations, and post-market surveillance requirements.

Benefits for manufacturers: A clearly defined regulatory pathway reduces time and regulatory risks, minimizes deviations in Notified Body audits, and provides cost predictability through planned testing and documentation milestones. The consistent, scalable documentation architecture also facilitates the transition to production.



**Strategic Preparation for Regulatory Approval**

- Support in defining risk classification, conformity assessment procedures, and MDR requirements
- Development of individual Regulatory Roadmaps

**Design/Development Planning**

- Define requirements, risks, and verification/validation (V&V) strategy
- Establish and maintain technical documentation from the outset

**Preclinical Verification and Validation**

- Provide biological, mechanical, and MR evidence to demonstrate GSPR compliance
- Consistently maintain evidence within the Technical Documentation

**Clinical Evaluation and Post-Market Surveillance**

- Clinical Evaluation in accordance with Article 61 and Annex XIV (Part A), and design post-market clinical follow-up (PMCF) in accordance with Annex XIV (Part B)
- Benchmarking of the “state-of-the-art” therapy

**Clinical Investigation**

- Plan prospective clinical studies
- Conduct retrospective data analyses
- Support the development of study protocols in accordance with ISO 14155

**Standard-Compliant Testing Expertise and Methodological Development**

A key distinguishing feature of IIB e.V. is the development and application of standard-compliant testing methods. Wherever available, investigations are conducted in accordance with relevant international standards and guidelines (e.g. DIN EN ISO 527, ASTM F2182-19, ISO 10993 series). Where suitable standards do not exist, indication-specific test protocols are developed and validated. These protocols are subsequently documented in compliance with the MDR (Annex II) and translated into a regulatory-acceptable evidence base. Testing can be performed either in the accredited test laboratory or in non-accredited environments, while consistently ensuring clear, traceable evidence of safety and performance.

Benefits for manufacturers: High acceptance of results by Notified Bodies, shorter development iterations without re-testing, accelerated evidence generation - even for novel implant technologies - and seamless integration of test reports into the Technical Documentation, resulting in a measurable advantage in time to approval and competitive differentiation.

**Clinical Study Planning & Network Expertise**

As a translational partner, IIB e.V. translates clinical questions into feasible study designs at an early stage - ranging from feasibility / first-in-human studies to confirmatory clinical trials. In collaboration with University Medical Centers in Rostock and Greifswald, IIB e.V. defines endpoints, inclusion/exclusion criteria, follow-up schedules, statistical plans, develops ISO 14155-compliant study protocols (including monitoring, data management, and safety/reporting procedures), and supports ethics committee and regulatory submissions in accordance with MDR / MPDG. Where appropriate, retrospective data, registry data, and real-world evidence are integrated, and post-market clinical follow-up (PMCF) measures are closely aligned with the post-market surveillance system.

Benefits for manufacturers: Realistic, regulatorily accepted endpoints and a robust operational workflow accelerate patient recruitment and data generation, reduce study risks (protocol deviations, drop-outs), and enable predictable timelines, ensuring that clinical evidence is available faster and more reliably for regulatory approval.

**Clinical Evaluation & Literature Review**

Clinical evaluation is a central component of medical device approval. At IIB e.V., this process is conducted in accordance with current European regulatory requirements, ensuring that the safety, performance, and benefit of the product are transparently and comprehensibly documented. The approach involves systematic literature research and assessment, analysis of study results, and comparison of the product with existing market solutions. This creates a clear understanding of efficacy, risks, and competitive positioning. The insights gained are directly incorporated into the required technical and regulatory documentation. This includes the clinical evaluation report, evidence for General Safety and Performance Requirements (GSPRs), and planning of post-market activities.

Benefits: A robust, well-documented evidence base accelerates the approval process, reduces queries from regulatory authorities, may eliminate the need for additional studies, and strengthens the case toward customers, investors, and payers. This establishes the foundation for stable regulatory approval and efficient product development.

## Examples of Developing and Implementing National Standards

- Derivation of new test methods for load testing of bone anchoring systems for the humerus
- Investigations on the MR safety of implants
- Clinical planning of regulatory approval studies in accordance with Article 62 MDR
- Development of a national standard DIN SPEC 13259: “Reusable tourniquets for hygienic blood collection – Requirements”
- Development of new test methods for leadless pacemaker fixations

# Bone-Anchored Prosthetic System for Upper-Arm Amputees

### Strategic Regulatory Approval Preparation

IIB e.V. supports the regulatory approval preparation of an innovative bone-anchoring system for transhumeral (upper-arm) amputees. The system enables direct, osseointegrated attachment of an external prosthesis to the humeral stump, providing a functional alternative to conventional socket prostheses.
As part of the strategic regulatory planning, the risk classification and conformity assessment procedure are derived and justified in accordance with the MDR. Furthermore, the structured derivation of regulatory requirements is performed, covering risk management (ISO 14971), usability (IEC 62366-1), biocompatibility (ISO 10993), mechanical and fatigue testing, as well as the clinical evaluation in accordance with Annex XIV MDR and ISO 14155.

### Design and Development Planning

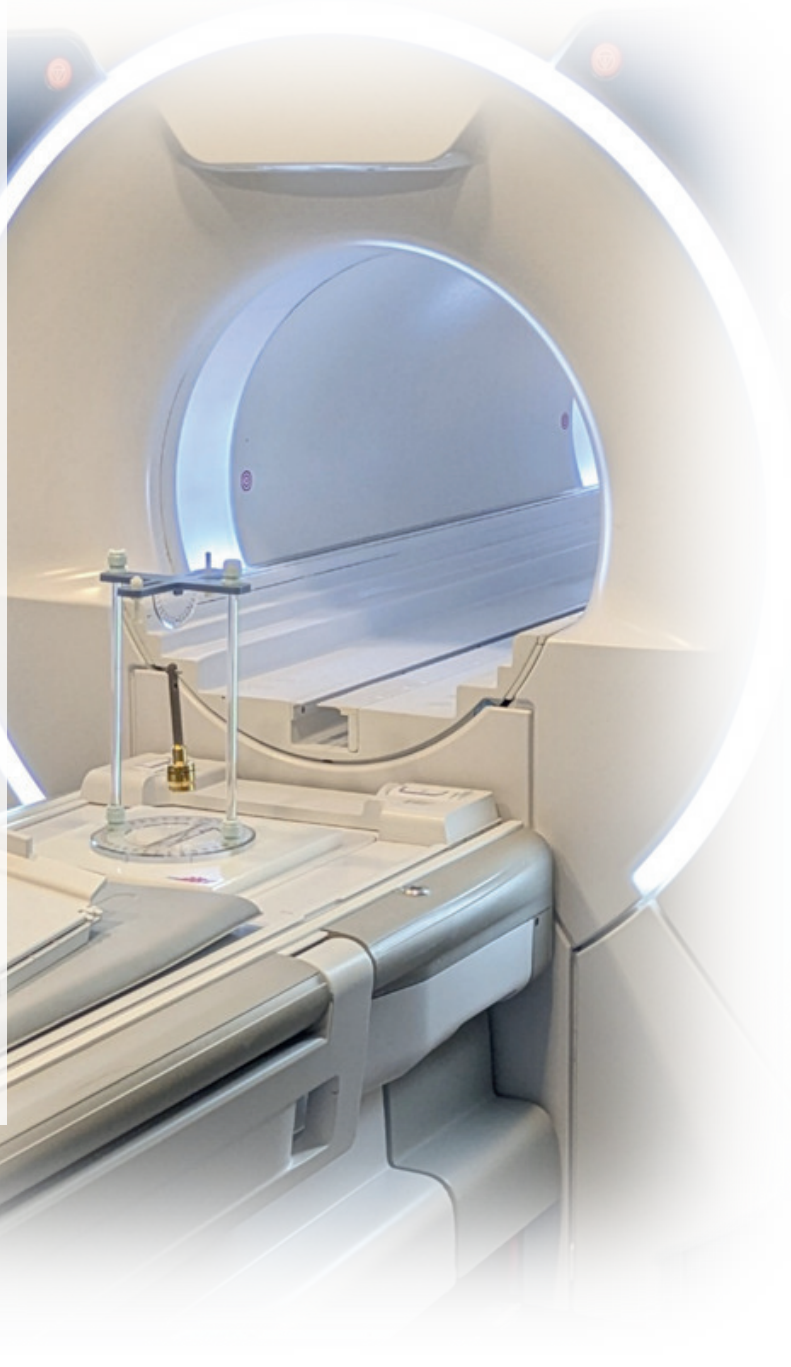
The development planning established at IIB e.V. consistently links requirements, risks, and verification & validation (V&V) strategies. Medical and functional requirements are derived, for example, from image-based data (CT, MRI) and anatomical studies.
In the case of the bone-anchoring system, design specifications for the modular, conical shaft components were derived from parameters such as cortical thickness and medullary canal diameter. These specifications enable an anatomically adapted fit, simplified implantation, and reduced manufacturing efforts.

### Preclinical Verification and Validation

Preclinical V&V follows a risk-based approach to address the General Safety and Performance Requirements (GSPRs). This includes a biocompatibility program in accordance with ISO 10993, mechanical testing to evaluate stability, fatigue, and torsion, as well as evidence of MR safety and compatibility. All tests are performed according to validated protocols and are fully documented.

### Clinical Evaluation and Post-Market Follow-Up

IIB e.V. supports the planning of the Clinical Evaluation in accordance with MDR Article 61 and Annex XIV (Part A), as well as the design of post-market clinical follow-up (PMCF) according to Annex XIV (Part B). This involves a systematic analysis of the state-of-the-art and clinical benchmarks to contextualize the benefit, risks, and performance parameters of the product in comparison with established therapies.



*Analysis of MR safety of a bone-anchoring system using a clinical 3T MRI system*


*Development of informational materials and facilitation of patient questionnaires by IIB e.V.*

**Clinical Investigation**

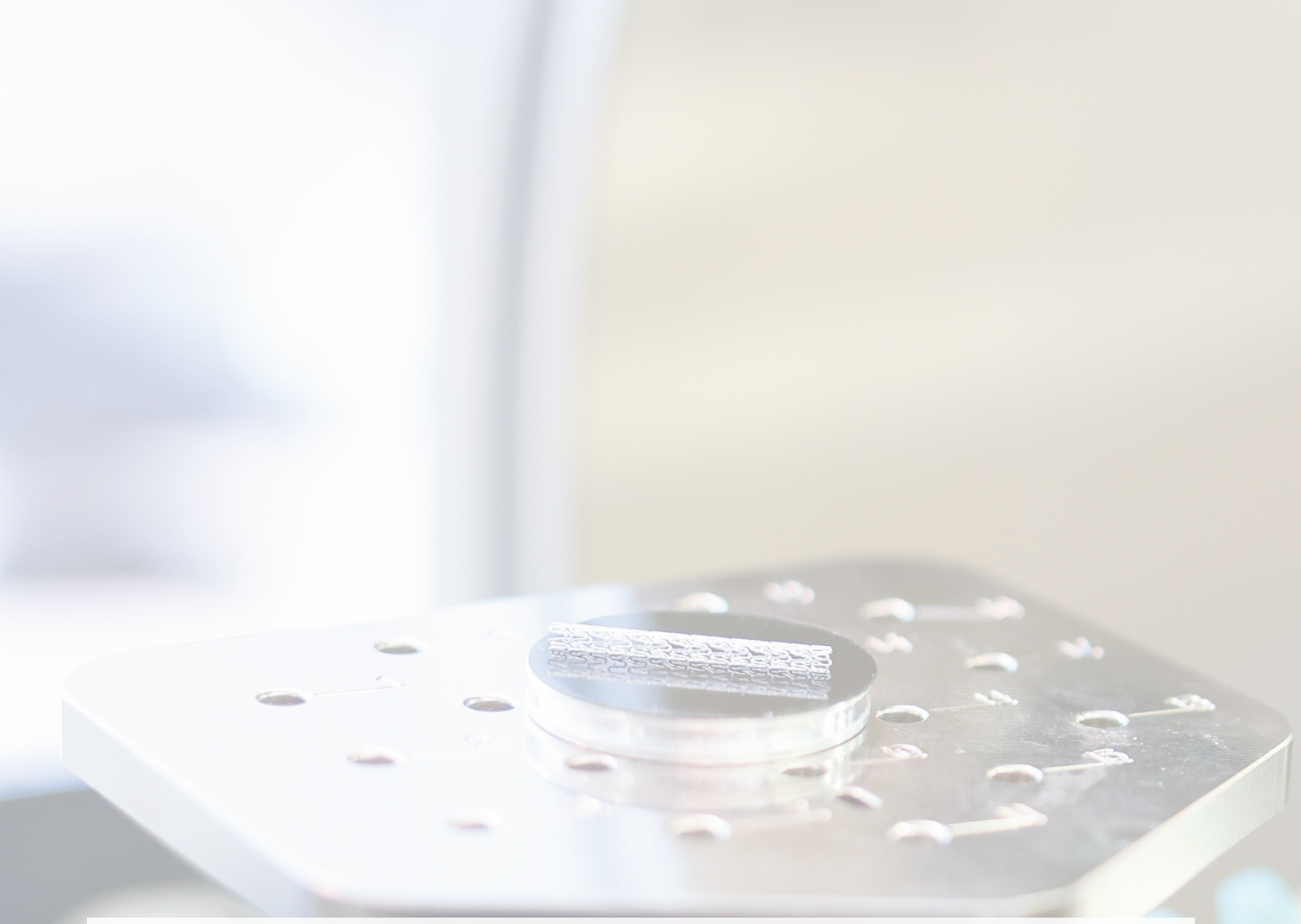
The generation of clinical evidence is achieved through the planning and execution of prospective and retrospective studies conducted in accordance with ISO 14155 standards. The primary performance endpoint is the implant survival rate over a defined study period without mechanical or septic failure.

In addition, functional and safety-relevant endpoints are collected, such as prosthesis usage duration, reportable clinical events, and re-interventions. Furthermore, a validated assessment approach is implemented to analyze activities of daily living with a prosthesis.

IIB e.V. supports the human factors/usability process in accordance with IEC 62366-1 by conducting formative and summative evaluations (simulation-of-use). For this purpose, a simulated surgical procedure was performed and evaluated at IIB e.V., with the results integrated into the Instructions for Use (IFU), training concepts, and risk controls.

The clinical rationale for the regulatory study links durability, benefit, and safety with the GSPRs and ISO 14971, thereby establishing a robust regulatory foundation for the study.

*Artificial bone for testing newly developed implants in the laboratory*



# Technical Equipment

The equipment at IIB e.V. forms the core of its research and development activities. It combines state-of-the-art technologies from various disciplines and makes it possible to support implant development across the entire value chain - from the initial idea through to comprehensive preclinical research. The equipment infrastructure at IIB e.V. is divided into several thematic areas that optimally complement one another.

The extensive technical infrastructure provides the foundation for the development of innovative implants. By closely integrating manufacturing, testing, analysis, and documentation, IIB e.V. establishes the basis for safe, high-performance, and clinically relevant implant solutions.

Part of the equipment was financed with the support of the State of Mecklenburg-Western Pomerania - particularly the Ministry for Economic Affairs, Infrastructure, Tourism and Labour - as well as through federal funding programs. This has sustainably strengthened the technical infrastructure at IIB e.V. and specifically supported the development of innovative implants.

**Mechanical testing systems** are used to investigate the strength, durability, and functional safety of implants. Different load scenarios can be realistically simulated in order to reliably assess the behavior of materials and designs.

**Imaging techniques and microscopic analyses** enable the precise investigation of materials, structures, and tissue–implant interfaces - from fine surface details to three-dimensional representations. These methods support quality assurance and provide important insights into the interaction between implants and the biological environment.

The **Manufacturing and Prototyping** division combines creativity and precision. Additive and high-precision manufacturing processes enable the rapid production and adaptation of implant prototypes as well as patient-specific models. This allows new concepts to be implemented promptly and tested in the laboratory.

**Material analysis and chemical characterization** enable the detailed investigation of the physical and chemical properties of biomaterials. This allows biocompatibility, stability, and functionality to be specifically assessed and improved.

A particular focus is on **hydrodynamic analyses**, which realistically simulate flow conditions and stresses in the laboratory - especially for cardiovascular implants.

Powerful **workstations** and specialized software environments enable complex numerical simulations, such as the analysis of stresses, flows, or material behavior. By linking design data with virtual models, implants can be digitally designed, evaluated, and optimized before physical implementation.

The equipment is further complemented by precise **measurement technology and sensors** that capture electrical, thermal, and mechanical parameters. Modern impedance analyses, multimeters, and sensor systems provide essential data for evaluating implants and testing setups, contributing significantly to the understanding of each system.

# Electrodynamic Testing Machines

***Models: E1000 by Instron & LTM3 by ZwickRoell***

To analyze the mechanical behavior of materials and components under cyclic loading, IIB e.V. relies on two high-precision electrodynamic testing machines. These systems enable both quasi-static and dynamic tests, even under variable environmental conditions such as temperature or liquid testing media, thanks to an integrated medium chamber.
The institute has the following systems available for this purpose: the ZwickRoell LTM3 HR and the INSTRON ElectroPuls E1000. These machines are characterized by their compact design, low-maintenance drive concept, precision and highly repeatable control. The electrodynamic linear drive allows the application of variable load profiles - from sinusoidal to arbitrarily complex load signals - enabling realistic simulation of dynamic stresses. Due to their high control quality and the ability to accurately regulate force, displacement, or strain, the electrodynamic universal testing machines are particularly suitable for demanding tasks in research, development, and quality assurance.

**Technical Specifications**

| | INSTRON E1000 | Zwick LTM3 HR |
|---|---|---|
| Test Frequency | up to 100 Hz | up to 120 Hz |
| Force Transducer | Two Force Transducer, 250 N & 2000 N | Three Force Transducer, 70 N, 500 N & 3000 N |
| Piston Stroke | 60 mm | 60 mm |
| Medium Chamber | Test medium up to 40 °C with a volume of 3.1 L | Test medium up to 45 °C with a volume of 6 L |
| Clamping Devices | Pneumatic clamping devices, max. 250 N, for use in the medium chamber; mechanical wedge clamp, 1000 N | Mechanical T-sample holders, max. 3000 N, for use in the medium chamber |


## Application Examples

- Testing the lifespan under high cyclic loading of bone plates, screws, or stents
- General material testing of metals, plastics, or composites under controlled laboratory conditions
- Assessment of long-term stability under repeated tension and compression
- Comparison of different alloys regarding their fatigue resistance
- Evaluation of bioresorbable polymer materials for degradation behavior under dynamic loading

# Static Universal Testing Machines

***Models: ZwickiLine 0.5 kN, 2.5 kN and 5 kN by ZwickRoell***

The static universal testing machine is used in medical technology for the mechanical characterization of biomaterials as well as implants and implant components. It enables the precise determination of typical material properties such as tensile strength, modulus of elasticity, fracture strain, torsion modulus, and other material-specific parameters required for the development and quality assurance of medical devices. At IIB e.V., the universal testing machines are used, among other applications, for the analysis of polymers and metals, as well as for prototype testing of stents, catheter shafts, or micro-implants. The flexible adaptability of the testing configuration and force measurement range makes the universal testing machines an important component in product development, materials research, and standardized testing of medical components. Tests can be conducted at room temperature as well as under physiological conditions (37 °C air or 37 °C aqueous test medium). Another special feature is the available torsion setup.

| Technical Specifications | |
|---|---|
| Force Transducer | 20 N; 100 N; 500 N; 2,5 kN; 5 kN |
| Torsion Transducer | 0,2 Nm & 20,0 Nm |
| Environmental Conditions | 37 °C air or 37 °C aqueous test medium |
| Crosshead Speed | 0,0005 - 600 mm/min |
| Rotational Speed | 0,01 - 20 U/min |
| displacement resolution | 0,02 µm |
| Test Setups | Tensile Test, Compression Test, 3-Point Bending Test, 4-Point Bending Test, Torsion Test, Pure Shear, Special Test Setups |

## Application Examples

- Uniaxial tensile test of shoulder rod or wire samples made of polymer-based or metallic materials to determine standard material properties such as modulus of elasticity, tensile strength, fracture strain, etc.
- 3-point / 4-point bending test of material samples or on stents and catheter sections
- Determination of the force required to detach a stent axially from a balloon catheter (stent removal force)
- Determination of torsional stiffness and strength of catheters

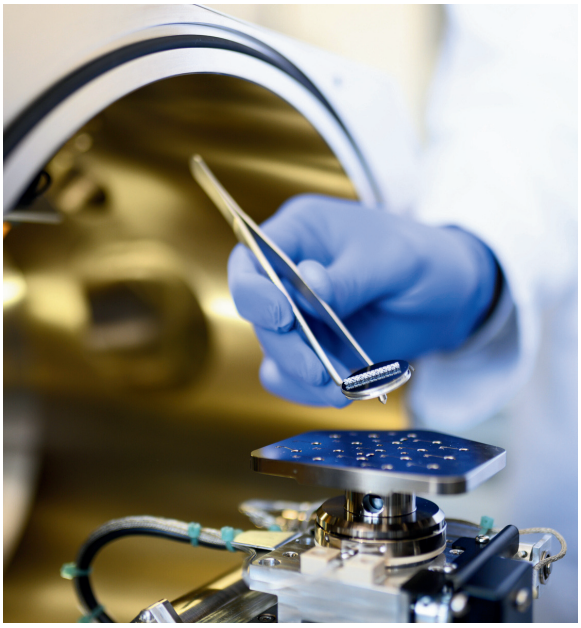
# Scanning Electron Microscope

***Model: Thermo Fisher Quattro S***

The Thermo Fisher Quattro S is a state-of-the-art scanning electron microscope (SEM) designed for multidimensional materials characterization in medical device research. An SE2 detector delivers high-resolution images of the finest surface morphologies, while the CBS detector generates material-dependent backscattered electron contrast, enabling precise structural and material-contrast-based imaging. The integrated energy-dispersive X-ray spectroscopy (EDX) allows qualitative and quantitative elemental analysis directly within the SEM - crucial for implant surfaces, nanoscale coatings, or particle contamination. In low-vacuum mode, non-conductive and sensitive samples can be examined without conductive coating; the ESEM mode additionally enables in-situ observations under variable gas atmospheres, for example for hygroscopic or hydrated structures. The robust platform offers fast, reliable, and high-throughput analyses, forming a central foundation for microscopic and chemical characterization during the development, optimization, and regulatory validation of medical devices.

**Technical Specifications**

| | |
|---|---|
| Accelerating Voltage | 200 V up to 30 kV |
| Sample Stage | XY travel: 110 mm × 110 mm, stage tilt: –15° to +90° |
| Detectors | Backscattered electrons: CBS<br>High vacuum: < 6 × $10^{-4}$ Pa<br>Low vacuum: up to 200 Pa<br>ESEM: up to 4000 Pa |
| Resolution | up to 1 nm |
| Additional Options | Energy-dispersive X-ray analysis, Peltier-cooled sample holder (–20 °C to +60 °C), Electron beam deceleration from –4 kV to +50 V |



## Application Examples

- Measurement of implant and medical device dimensions on the micrometer and nanometer scale
- Qualitative and quantitative analysis of particles in the nanometer and micrometer range
- Qualitative surface analysis with a focus on structural details at the nanometer scale and optically transparent coatings
- Elemental analysis of metallic and ceramic medical devices as well as particles on surfaces
- Visualization of structural and chemical material changes following mechanical and functional stress testing of medical devices

# Transmission Electron Microscope

***Model: JEM-1400 von JEOL***

The JEOL JEM-1400 transmission electron microscope (TEM) is particularly well suited for the visualization of fine structural details in biological samples as well as for the analysis of particles at the nanometer scale. Owing to its high image contrast and its ability to resolve delicate internal structures, the JEM-1400 makes a significant contribution to the characterization of biomaterials, cells, nanoparticles, and tissue samples. In medical device development, the system enables, among other applications, the investigation of biocompatibility, the analysis of particulate contamination, and the morphological assessment of functional nanoscale components. The JEM-1400 provides a robust yet highly sensitive platform for standardized and reproducible analyses, particularly in preclinical research, drug delivery and release studies, the development of bioactive surfaces, and novel functionalized nanoparticles.


| Technical Specifications | |
|---|---|
| Accelerating Voltage | 80 - 120 kV |
| Resolution | up to 0,38 nm |
| Electron Gun | $LaB_6$ cathode |
| Camera System | Gatan ORIUS CCD-Camera |

## Application Examples

- Morphological analysis of micro- and nanoparticles, including magnetic nanoparticles
- Visualization of functional surface modification of nanoparticles
- Particle size analysis in accordance with DIN ISO 9276
- Visualization of the morphological properties of cells and tissue samples, as well as the incorporation of nanoparticles

# Reflected Light Microscope

***Model: AxioScope 7 by Zeiss***

The Zeiss AxioScope 7 is a modern reflected light microscope and, due to its flexible configuration, it enables a wide range of high-contrast imaging techniques. Using brightfield, darkfield, and polarized light contrast as well as fluorescence imaging, both structural and optical properties of materials can be characterized in a differentiated manner.
Through the combined use of reflected and transmitted light illumination, the system is suitable for a broad variety of sample types, ranging from polished metal surfaces to transparent biological sections. In particular, in the development and investigation of medical devices, the AxioScope 7 enables reliable evaluation of material microstructures, coating systems, particles, and fluorescence-labeled biological components. The high image quality and modular, adaptable design make it a valuable instrument for interdisciplinary research at the interface of materials science and biomedicine.

**Technical Specifications**

| | |
|---|---|
| Illumination | White-light LEDs for reflected and transmitted light measurements |
| Sample Stage | XY travel range: 80 mm × 60 mm, max. working distance: 12 mm Maximum sample height: 70 mm |
| Camera System | 5 Megapixel CMOS color camera |
| Measurement Modes | Imaging modes – reflected light: brightfield, darkfield, polarized light contrast, fluorescence; transmitted light: brightfield, polarized light contrast |
| Additional Options | Z-axis motorization for extended depth-of-field imaging |

## Application Examples

- Visualization of implant components using cross-sectional samples and determination of their dimensions
- Analysis of material changes and material defects in medical devices, as well as contamination and wear on their surfaces
- Particle analysis using fluorescence and darkfield imaging
- Visualization of tissues, cells, and microorganisms in the context of medical device development

# Stereo Microscope

***Model: Discovery.V20 by Zeiss***

The Zeiss Discovery.V20 stereo microscope provides high-resolution, three-dimensional visualization of macroscopic samples, offering excellent depth of field and high optical precision. It is ideally suited for the examination of surface structures of larger components, complex medical devices, and delicate samples where non-destructive and spatially differentiated analysis is required.
Particularly in medical technology research and development, the Discovery.V20 enables reliable visual inspection of surface conditions, assembly quality, material transitions, and defects or damage. Owing to its large working distance, even bulky or irregularly shaped samples can be analyzed and prepared for subsequent investigations. The system therefore represents an important tool for macroscopic characterization and quality assurance throughout the medical device development process.

| Technical Specifications | |
|---|---|
| Illumination | Reflected light LED ring illumination and LED transmitted light illumination |
| Zoom Range | 7,5x to 150x |
| Camera System | 8,3 Megapixel Ultra HD CMOS colour camera |
| Measurement Modes | Brightfield and darkfield modes available for reflected and transmitted light illumination |
| Additional Options | LED line light for high-contrast surface imaging |

## Application Examples

- Quality assurance in the manufacturing of medical devices and implant prototypes
- Sample preparation for biocompatibility studies within the framework of in ovo experiments
- Preparation of samples of microimplants and their components, such as glaucoma stents and microelectrodes
- Visualization of manufacturing defects in the context of process development

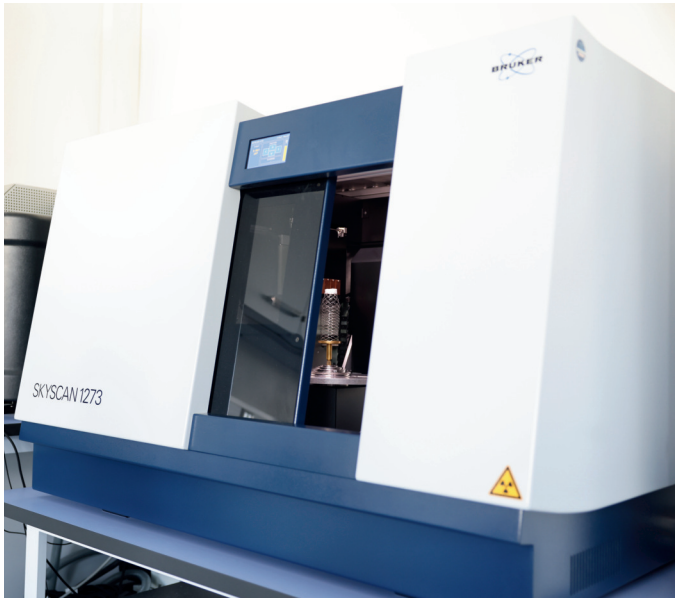
# µCT-Scanner

***Model: SkyScan 1273 Desktop-Mikro-CT by Bruker***

Micro-computed tomography (µCT) is a three-dimensional imaging technique that uses X-rays to enable the analysis of medical components, tissue samples, and technical parts. The Skyscan 1273 micro-computed tomography system from Bruker Corporation (Billerica, USA), including its evaluation software, is equipped with a 130 kV X-ray source, a 6 MP X-ray detector, and a positioning stage with mounting fixtures. The Skyscan 1273 allows the scanning of specimens with object dimensions of up to 250 mm in length and diameter. Using the evaluation software, two-dimensional cross-sectional images are generated and subsequently reconstructed into three-dimensional models. In addition, the software enables various analyses, such as fracture analysis and geometrical characterization. The scanned specimens can ultimately be further processed as surface geometry models, enabling direct comparison between research data and prototyping workflows.

**Technical Specifications**

| | |
|---|---|
| X-ray Source | 40 - 130 kV<br>39 W |
| Detector | Active-pixel CMOS flat-panel detector, 6 MP (3072 × 1944) |
| Object Size | 250 mm diameter<br>250 mm height |
| Resolution | Voxel size (X-ray source):<br>≥ 5 µm |
| Software | NRecon, CTAn, CTVox, CTVol, DataViewer |




## Application Examples

- Reconstruction of existing implants and medical devices within the framework of reverse engineering
- Geometrical measurement of medical devices, e.g. strut width, cell size, or stent wall geometry
- High-resolution 3D analysis of bone trabecular density, bone volume (BV) / total volume (TV), structure model index (SMI), as well as finite element–based derivations for strength prediction

# Optical Coherence Tomography System

***Model: ILUMIEN Optis by Abbott Medical***

Intravascular optical coherence tomography (OCT) is a high-resolution, catheter-based imaging technique used in medicine - particularly in cardiology - to visualize the internal structure of blood vessels in real time. A flexible catheter equipped with a thin optical fiber delivers near-infrared light (typically at a wavelength of 1300 nm) into the hollow organ under investigation. A prism at the catheter tip deflects the light radially toward the vessel wall.
The light reflected from the surrounding tissue is guided back through the catheter to the evaluation unit. OCT imaging is based on the principle of interferometry between the light reflected from tissue layers and a reference beam, resulting in depth-resolved cross-sectional images of the examined regions.


| Technical Specifications | |
|---|---|
| Outer Diameter | 1,0 mm |
| Image Resolution | 10 - 20 µm |
| Tissue Penetration | 1,0 - 2,5 mm |
| Image Acquisition Rate | 180 images/s |
| Pullback Speed | 18 mm/s |
| Longitudinal Resolution | 10 images/mm |
| Pullback Length | 54 mm |

## Application Examples

- 3D visualization and geometrical measurement of tubular biological structures (e.g. blood vessels, fallopian tubes, etc.)
- Visual representation of morphological features in high-resolution cross-sectional images

# Thermal Imaging Camera

***Model: VarioCAM HDx by InfraTec***

Infrared thermography is a non-contact imaging measurement technique used for the analysis of surface temperatures. It is based on the detection and evaluation of infrared radiation emitted by an object. The acquired signals are converted into thermal images that make temperature distributions and thermal changes visible.
At IIB e.V., a professional thermography system from InfraTec (Dresden, Germany) is used for this purpose. The system consists of a compact industrial camera (VarioCAM HDx head 675 GW) and the corresponding evaluation software IRBIS 3.1 plus.

**Technical Specifications**

| | |
|---|---|
| Detector type | Low-noise detector with micro-scanning |
| Thermal resolution | up to 0,03 K |
| Frame rate | 30 Hz (full-frame format) |
| IR image resolution | 640 x 480 IR-Pixel |
| Lens | Precision lens, 20 mm focal length |

## Application Examples

- Heating analysis of active medical implants, e.g. battery components of modern pacemaker systems
- Non-destructive and contactless thermal analysis for material characterization under static and dynamic mechanical loading
- Characterization of material samples and components by means of thermal stress analysis
- Micro-thermography analysis of electronic assemblies, components, and subcomponents

# High-Speed Imaging Technology

***Model: IDT Kamera Os7-V3-S2 by Imaging Solution GmbH***

When motions occur too rapidly for the human eye or conventional cameras to resolve, high-speed camera systems combined with appropriate analysis software provide a non-contact optical measurement technique for analyzing motion sequences.
At IIB e.V., a high-speed imaging system from IS – Imaging Solution GmbH (Eningen unter Achalm, Germany) is available, together with the analysis software ProAnalyst (Xcitex Inc., Woburn, USA). The system consists of the high-speed camera IDT OS7-V3-S2 (shock resistance up to 200 g, 1920 × 1280 pixels; Integrated Design Tools, Inc., Pasadena, USA), the associated illumination, and multiple optical lenses. The camera captures motion sequences at high frame rates and reproduces them in slow motion for detailed evaluation. Using the analysis software, movements can be evaluated on a pixel-by-pixel basis, enabling quantitative measurement and characterization of the dominant motion patterns.

| Technical Specifications | |
|---|---|
| Detector type | CMOS Polaris II |
| Resolution | 1920 x 1280 Pixel |
| max. Frame rate | up to 2700 fps |
| Minimum exposure time | 1 µs |
| Analysis software | ProAnalyst (Xcitec Inc., USA) |
| Vibration resistance | 200 G |

## Application Examples

- Analysis of the opening and closing behavior and determination of the geometric orifice area of heart valve prostheses under simulated cardiac cycle conditions in a pulse duplicator system
- Deformation analysis of anchoring structures made of nitinol
- Investigation of the fatigue properties of cyclically loaded implant components
- Validation of finite element simulations of movable implant components

# Macro Photography and High-Resolution Imaging Systems

***Model: EOS R5 & R5 Mark II and 70D by Canon***

For the professional visual documentation of implants, test results, and development processes, IIB e.V. utilizes a comprehensively equipped camera system. The setup includes modern mirrorless full-frame cameras and DSLR models from the Canon EOS series, complemented by a selection of high-quality macro and zoom lenses.
The system is used both for technical macro photography in laboratory environments and for the production of high-quality image and video formats for public relations, research communication, and training purposes. The camera technology is further enhanced by studio accessories such as light boxes, LED lighting, tripods, macro rails, and gimbal stabilization systems. Of particular note is the Canon EOS R5, which enables professional motion picture formats for tutorials and scientific applications through its 8K video resolution. This media infrastructure allows for detailed visual representation of complex implant structures and research results - practical, high-resolution, and tailored to specific target audiences.

| Technical Specifications | |
|---|---|
| Camera models | Canon EOS R5 (2x),<br>Canon EOS R5 Mark II,<br>Canon EOS 70D |
| Macro lenses | Canon RF 100mm f/2.8L Marco IS USM,<br>Tamron SP 90mm f/2.8L, Di Macro 1:1 |
| Zoom lenses | Canon RF 24-70mm f/2.8L,<br>RF 70-200mm f/2.8L,<br>EF-S 18-55/135/200mm |
| Studio equipment | Havox Photo Studio Box,<br>macro rail with illuminated stage |
| Lighting | 2x GVM 800D-RGB LED-Lights |
| Recording | Rode VideoMic Pro - Directional microphone |


## Application Examples

- Macro photography of implant prototypes
- Video documentation of technical processes
- Creation of multimedia content for research and teaching
- Visualization of laboratory processes and equipment usage
- High-resolution visualization of complex implant designs

# Liquid Particle Counter

***Model: Syringe particle counter from Markus Klotz GmbH***

The “Syringe” particle counter from Klotz uses the principle of light obscuration to determine particle size and count in liquids. In this process, a particle-containing dispersion flows through an optical flow cell that is illuminated by a laser. The resulting light obscuration pulses detected are proportional to the particle size and enable precise analysis of particles in the range from 5 µm to 100 µm, extendable up to approximately 400 µm.
The detected particles are subsequently classified into defined size classes, allowing a detailed representation of the particle size distribution. The method enables rapid and standard-compliant assessment of particulate contamination in liquid-based samples - particularly in accordance with USP 788, an established pharmaceutical standard.
This technology is especially relevant for medical devices intended for implantation or insertion into the human body. It is used to evaluate potential particle release and to assess coating integrity, for example in coated stents or catheters in order to minimize risks such as thrombogenicity.


| Technical Specifications | |
|---|---|
| Particle diameter | 5 - 400 µm |
| Particle size categories | User-defined, up to 256 size classes |
| Sample type | clear liquids |
| Measurement principle | light obscuration |
| Applicable standards | USP 788 |

## Application Examples

- Determination of the particle distribution in liquid samples generated during simulated use of vascular implants
- Compliance testing according to USP 788
- Assessment of the cleanliness of the implant manufacturing process

# Dynamic Image Analysis

***Model: FlowCam 8100 by Yokogawa Fluid Imaging Technologies, Inc.***

The FlowCam 8100 uses the method of dynamic image analysis (Flow Imaging Microscopy) for quantitative and morphological characterization of particles in liquids. In this process, a particle suspension is manually introduced into the injection port and conveyed through an optical flow cell via a syringe pump. A high-speed camera captures images across the entire width of the flow cell. The particle images are then automatically segmented and individually analyzed for morphological parameters. The FlowCam 8100 is employed in medical device research and development, for example to evaluate wear particles generated during simulated use of medical devices. Particles in the size range of 2 µm to 1 mm can be detected. By combining high-resolution imaging with powerful data analysis, the system provides a standards-compliant, visual, and practical method for assessing diverse particle populations.

| **Technical Specifications** | |
|---|---|
| Particle diameter | 2 µm - 1 mm |
| Flow cell width / optical magnification | 300 µm / 40× magnification<br>80 µm / 100× magnification |
| Camera | High-resolution monochrome CMOS sensor (1920 × 1200 pixels) |
| Measurement principle | Optical trigger and digital image capture |
| Applicable standards | USP 788, ASTM E3060 |
| Analysis parameters | Count, Area, Area-equivalent diameter, Ferret diameter, Transparency, Circularity, Ovality, Edge sharpness |


## Application Examples

- Morphological characterization of wear particles after simulated use of vascular implants
- Particle classification based on morphological parameters (e.g., circularity, transparency, length/width ratio, edge sharpness, area)

# 3D Printer

***Model: Form 3B+ by FormLabs & Objet30 Prime by Stratasys***

Additive manufacturing is a central process at IIB e.V. for the rapid, precise, and flexible production of medical device components, prototypes, or visual functional models. Two 3D printing systems are available for this purpose: the Formlabs Form 3B+ and the Stratasys Objet30 Prime. The Form 3B+ operates using stereolithography (SLA), in which a liquid resin is precisely cured by a laser. This process produces highly durable, smooth, and dimensionally accurate functional parts - including silicone-like flexible components, for example for vascular models. The Objet30 Prime uses the PolyJet process, in which liquid photopolymer is deposited layer by layer through print nozzles and then cured. This method allows the production of complex geometries with fine details. Both systems complement each other perfectly in prototype development: they enable rapid design iterations, validation of design concepts, and production of application-relevant test structures in the laboratory - making them a key technology for modern implant development.


**Technical Specifications**

| | Form 3B+ | Objet30 Prime |
|---|---|---|
| Printing method | Stereolithography (SLA) | PolyJet-Technology |
| Resolution (XY) | 25 µm | 42 µm |
| Layer height (Z) | 25 - 300 µm | 16 µm |
| Build volume | 145 x 145 x 185 mm | 294 x 192 x 148,6 mm |
| Advantages | Smooth surfaces, High dimensional accuracy, Wide range of materials | Very high level of detail, Smooth or matte surfaces, depending on the application |

## Application Examples

- Production of functional prototypes of mechanically load-bearing components for test setups
- Prototypes of implant structures for iterative development of stents, heart valve components, etc.
- Visualization of complex designs during the implant development phase
- Support for technical outreach by presenting complex technologies at trade shows, in training sessions, or videos

# FS Laser Cutting System

***Model: StarCut Tube Monaco by Coherent Inc.***

The StarCut Tube femtosecond laser cutting system from Coherent Inc., equipped with a powerful 60 W infrared ultrashort-pulse laser, enables high-precision processing of metallic and polymeric materials in the micro- and submicrometer range. The ultrashort laser pulses, with a pulse duration of 300 fs, achieves the highest processing quality by directly evaporating the material to be processed. Combined with minimal thermal impact, this technology is ideal for the development and production of delicate medical devices.
Furthermore, the system allows targeted surface structuring, for example for the functional modification of implant surfaces with respect to cell adhesion, fluid interaction, or osseointegrative properties. The laser system thus represents a central technology platform for systematically researching and implementing state-of-the-art manufacturing processes and innovative material concepts in medical technology.

| Technical Specifications | |
|---|---|
| Laser wavelength | 1035 nm |
| Pulse duration | 300 fs up to 10 ps |
| Repetition rate | max. 1 MHz and single-pulse operation |
| Laser power | max. 60 W |
| Pulse energy | 1 - 80 µJ |
| Axes | X = 300 mm, Y = 75 mm, Z = 40 mm at max. 250 $mms^{-1}$ |
| Process gas | Argon and Nitrogen, up to max. 24 bar |
| Tube diameter | max. 30 mm |
| Additional options | water-based tube cooling |

## Application Examples

- Production of functional prototypes of mechanically load-bearing components for test setups
- Prototypes of implant structures for iterative development of stents, heart valve components, etc.
- Visualization of complex designs during the implant development phase

# Forced Convection Chamber Oven

***Model: forced convection chamber oven NA 15/65 by Nabertherm***

Forced convection chamber ovens are an essential tool in medical technology and implant development, particularly for reproducible thermal processes such as material modification, shape stabilization, or heat treatment. The forced air circulation within the oven chamber ensures very uniform temperature distribution - a key requirement for controlled processes such as curing polymer coatings, pre-treating metals thermally, or shaping thermoelastic alloys like Nitinol.
At IIB e.V., the NA 15/65 forced convection chamber oven from Nabertherm is used for these purposes. With a maximum temperature of 650 °C, a temperature accuracy of ±4 °C, and programmable time-temperature profiles, this compact benchtop oven supports a wide range of standardized applications in research, development, and quality assurance. It has proven particularly effective for imprinting shapes into Nitinol components, such as self-expanding stents, as well as for thermally curing implant-specific coatings.

| Technical Specifications | |
|---|---|
| max. Temperature | 650 °C |
| Temperature uniformity | ± 4 °C (according to DIN 17052-1) |
| Interior | 340 mm x 295 mm x 170 mm |
| Usable volume | approx. 15 L |
| Heating system | horizontal forced convection with stainless steel air baffles |
| Programmability | time-temperature profiles |

## Application Examples

- Shape setting of Nitinol stents through targeted thermal treatment with defined temperature profiles
- Thermal curing of bioresorbable polymer coatings on implant surfaces
- Solution and stress annealing of metal samples (e.g., titanium, stainless steel) prior to further processing steps

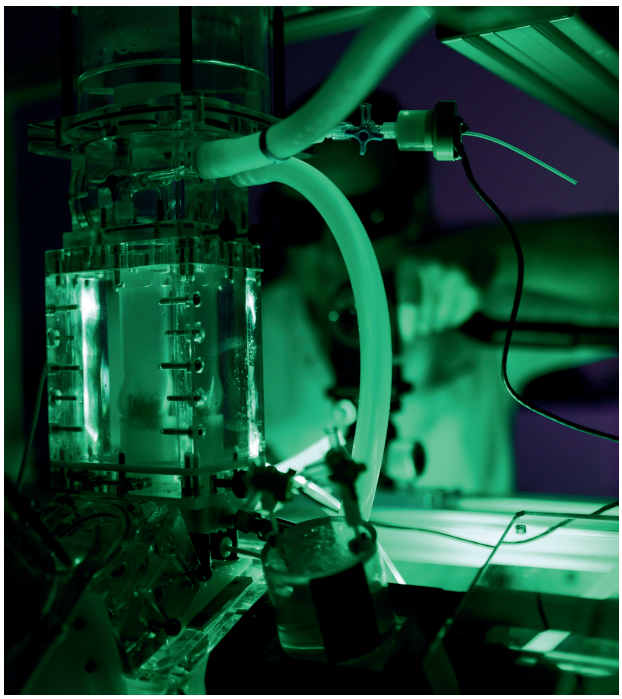
# Particle Image Velocimetry-System

***Model: PIV-System by Dantec Dynamics***

Particle Image Velocimetry (PIV) is a non-contact, optical method for analyzing velocity fields in flowing liquids and gases. At IIB e.V., particle motions are captured using a state-of-the-art PIV system from Dantec Dynamics, consisting of a Nd:YAG double-pulse laser (532 nm, 145 mJ) and high-speed CMOS cameras. Data evaluation is performed with the DynamicStudio software using cross-correlation of consecutive image pairs. This system enables precise flow analysis - particularly in combination with pulsatile flow sources, such as a pulse duplicator system. Velocity and shear fields can thus be reconstructed to assess hemodynamic properties and identify thrombogenic regions, which is especially relevant for ISO 5840-compliant testing of heart valve prostheses.

## Technical Specifications

| | |
|---|---|
| Laser source | Nd:YAG double-pulse, 532 nm, 145 mJ, 15 Hz (Litron Laser Ltd., UK) |
| Camera system | Mikroton EoSens 12CXP+, Highspeed-CMOS 12MP |
| Objectives | Zeiss 50 mm f/1.4 ZF.2<br>Zeiss 85 mm f/1.4<br>Zeiss 100 mm f/2.0 |
| Laser optics | Light sheet optics – base module with 5:1 volume illumination |
| Particles | PS-FluoRot 10 µm, 20 µm, 50 µm microparticles GmbH, DE |
| Objective filter | long-pass 590 nm (AHF Analysetechnik AG, DE) |
| Software | DynamicStudio 7.6 |



## Application Examples

- Flow analysis in heart valve test rigs (according to ISO 5840) for visualization and quantification of velocity and shear fields
- Detection of vortices and secondary flows to investigate hemodynamic stresses and thrombogenic risk
- Generation of an experimental data set for CFD validation

# Pulse Duplicator System

***Model: Pulse Duplicator System by ViVitro Labs Inc. and HDTi 6000 by BDC Laboratories***

Pulse duplicator systems simulate the hydraulic properties of the human cardiovascular system and enable testing of heart valve prostheses under realistic, dynamic pressure and flow conditions. At IIB e.V., two advanced test systems are available: the ViVitro Pulse Duplicator System and the HDTi 6000 from BDC Laboratories. Both systems can simulate physiological as well as pathological circulatory scenarios (e.g., hypotension, hypertension, arrhythmias).
These systems allow standardized testing in accordance with DIN EN ISO 5840-3, including the measurement of key hydrodynamic parameters such as effective orifice area (EOA), pressure gradients, regurgitant volume, and flow profiles. In combination with high-speed cameras, opening and closing behavior can be analyzed. Together, they provide an essential platform for the development, characterization, and regulatory approval of heart valve prostheses.

**Technical Specifications**

| | ViVitro Pulse Duplicator System | HDTi 6000 BDC Laboratories |
|---|---|---|
| Simulation medium | fluid with blood-like viscosity | fluid with blood-like viscosity |
| Operating frequency | 3 - 200 bpm | 2 - 240 bpm |
| Flow rates | 0 - 15 L/min | 0 - 10 L/min |
| Measurement parameters | Pressure profile, Forward flow time & volume, EOA, Regurgitant volume | Pressure profile, Valve opening times, EOA, Regurgitant volume |
| Camera integration | High-speed camera viewing window | Integrated high-speed cameras |
| Standards compliance | Compliant with ISO 5840 for mechanical and biological heart valves | Compliant with ISO 5840 for mechanical and biological heart valves |

## Application Examples

- Analysis of effective orifice area (EOA), pressure gradients, and regurgitant volume of heart valve prostheses under (patho-)physiological loading conditions
- Use of high-speed cameras to analyze valve opening and closing kinematics
- Comparative studies of different valve designs and materials
- Support of preclinical and regulatory processes

# Heart Valve Durability Tester

***Model: VDT-3600i by BDC Laboratories***

Heart valve durability testers are used to demonstrate the long-term functionality and mechanical robustness of heart valve prostheses under realistic, yet accelerated conditions. Testing is conducted in accordance with ISO 5840, which requires that a valve successfully withstand at least 200 million cycles - equivalent to approximately five years of clinical use.
At IIB e.V., several VDT-3600i durability testing systems from BDC Laboratories (USA) are available for this purpose: three 6-channel systems and one 2-channel system. These allow parallel durability tests under controlled hydrodynamic conditions and at frequencies of up to 50 Hz, significantly reducing the total testing time. Each system features independently controllable test chambers, enabling flexible scheduling and reproducible results.

| **Technical Specifications** | |
|---|---|
| Available systems | 3x 6-channel,<br>1x 2-channel |
| Frequency range | up to 50 Hz |
| Test chamber setup | independently adjustable test chambers |
| Measurement parameters | Failure analyses |
| Test fluid | physiological test fluid |
| Standards compliance | Compliant with ISO 5840 |

## Application Examples

- Demonstration of the structural durability of heart valve prostheses for regulatory approval
- Long-term testing of surgical and transcatheter heart valve prostheses
- Detection of valve failure and material fatigue

# High-Performance Workstations

***Model: Z8 Workstations by HP***

In modern medical technology, and particularly in the field of implant development, numerical methods, computer-aided design, and artificial intelligence (AI)-driven image and data analyses are becoming increasingly important. High-performance computing forms a central technical foundation, as many underlying tasks demand significant computational power, memory, and specialized hardware.
At IIB e.V., high-performance computing also plays a key role in research and development. Multiple custom-configured high-performance workstations are available for diverse tasks in CAD design, numerical simulation, image processing, and AI applications. Each system is tailored to specific use cases and provides a robust platform for data- and compute-intensive applications through multi-core processors (CPU), large memory (RAM), modern graphics processors (GPU), and fully integrated SSD storage to enhance I/O performance.
The institute employs both established commercial software such as ANSYS Mechanical, ANSYS Fluent, Abaqus/CAE, and Creo Parametric, as well as open-source solutions like OpenFOAM and Python-based AI frameworks. This ensures that a wide range of requirements - from implant development to data-driven research - can be effectively addressed.

**Technical Specifications (Excerpt)**

| Field of application | CPU | RAM | GPU |
|---|---|---|---|
| FEA simulations | 2x Intel(R) Xeon(R) Gold 6154, 18 Kerne @ 3 GHz | 384 GB | NVIDIA Quadro P 4000, 8 GB |
| CFD simulations | 2 x Intel (R) Xeon (R) Gold 6226R, 16 Kerne @ 2,9 GHz | 375 GB | 2 x NVIDIA Quadro RTX 5000, 16 GB |
| FSI simulations | 2 x Intel(R) Xeon (R) Gold 6246R, 16 Kerne @ 3,4 GHz | 768 GB | NVIDIA Quadro RTX 6000, 24 GB |
| KI / Deep Learning | 2 x Intel(R) Xeon (R) Gold 6246R, 16 Kerne @ 3,4 GHz | 786 GB | NVIDIA Quadro RTX 6000, 24 GB |
| Image analysis | 2x Intel(R) Xeon(R) Gold 6154, 18 Kerne @ 3 GHz | 192 GB | NVIDIA Quadro P 4000, 8 GB |

## Application Examples

- FEA simulations for evaluating stress distributions in implant designs
- CFD simulations for analyzing hemodynamic flows through implants
- FSI simulations for realistic modeling of the opening and closing behavior of heart valve prostheses
- Training and application of neural networks
- CAD-based design of test rigs and implant components

# Mixed Reality

***Model: HoloLens 2 by Microsoft and Apple Vision Pro by Apple***

AR and VR technologies offer a wide range of applications in medical device development - from visualizing complex geometries to supporting manufacturing processes. At IIB e.V., two systems with different approaches are in use. The Microsoft HoloLens 2 employs a transparent display to overlay digital content onto the real environment, making it particularly suitable for process-supporting applications that require location-based information. The Apple Vision Pro provides a fully immersive, high-resolution display, ideal for interactive simulations and the visualization of complex 3D models. Both systems support modern development and training scenarios in medical research and production.

**Technical Specifications**

| | HoloLens 2 | Apple Vision Pro |
|---|---|---|
| Technology | Augmented Reality | Mixed Reality |
| Display type | transparent waveguide | Micro-OLED-Display |
| Resolution | 2K (2048 × 1080) per eye | 4K, total 23 million pixels |
| Field of view (FOV) | approx. 52° | approx. 100° |
| Special features | Anchored content, hand & voice control | High detail, 3D spatial mapping, intuitive gesture control |

## Application Examples

- Visually guided assembly of medical device components using context-sensitive holographic overlays
- Creation and use of virtual 360° tours for personnel training, e.g., for orientation in laboratory structures, safety zones, and equipment setup
- Interactive VR training simulations, for example to visualize motion sequences or safety behavior in virtual scenarios

# Impedance Analyzer

***Model: MFIA 500 kHz by Zürich Instruments***

Impedance analyzers are an important tool in the development and quality assessment of active medical implants. They enable precise analysis of the electrical properties of materials, tissues, and interfaces - particularly where electrical signals are transmitted or measured. In implant development, impedance analysis is used, for example to evaluate insulation materials, characterize bioelectronic interfaces, or analyze electrochemical processes in implantable sensors.
At IIB e.V., the MFIA 500 kHz impedance analyzer from Zurich Instruments is used for these tasks. The system allows high-precision measurements across a frequency range of 1 mHz to 500 kHz with an accuracy of up to 0.05 %. Thanks to its wide impedance measurement range from 1 mΩ to 1 TΩ, the device is suitable for both low- and high-resistance samples. Software-based control enables automated measurement sequences, phase analyses, and long-term studies under controlled conditions - making it ideal for material diagnostic and electrochemical investigations in medical technology.


| Technical Specifications | |
|---|---|
| Frequency range | 1 mHz up to 500 kHz |
| impedance range” | 1 mΩ to 1 TΩ |
| Impedance range | up to ± 0,05 % |
| Measurement parameters | Impedance, Phase, Capacitance Inductance, Resistance, Conductance |
| Measurement methods | Frequency sweeps, Time–potential protocols, Phase analysis |

## Application Examples

- Characterization of bioelectronic interfaces of implantable electrodes
- Investigation of the electrical conductivity and insulation properties of polymer coatings
- Frequency-dependent material analysis of electroactive materials
- Aging tests and monitoring of electrical properties under long-term stress
- Impedance spectroscopy on implantable sensors for detecting tissue changes

# Benchtop Multimeter

***Model: 34470A by Keysight***

In the development and validation of medical implants as well as sensitive electronic systems, precise electrical measurements are essential. Benchtop multimeters with high resolution and stability enable reliable detection of even the smallest electrical signals - whether for analyzing current traces in sensor circuits, verifying calibration standards, detecting minimal temperature or drift changes in long-term stressed components.
At IIB e.V., the high-resolution Keysight 34470A benchtop multimeter is used for these tasks. With a resolution of 7.5 digits and very low measurement noise, the device is ideally suited for precise DC and AC voltage and current measurements down to the microvolt and picoampere range. Its wide dynamic range and integrated temperature compensation allow accurate characterizations under variable environmental conditions. Due to its DAkkS calibration, the system also meets the requirements for standardized laboratory applications and long-term monitoring - such as in product testing, prototype development, reference measurements, or documentation of regulatory-relevant properties.

| **Technical Specifications** | |
|---|---|
| Display resolution | 7,5 Digits |
| Voltage range | DC: 100 nV - 1000 V<br>AC: 1 µV - 750 V |
| Current measurement range | DC: 100 pA - 3 A<br>AC: 1 µA - 3 A |
| Resistance measurement | 1 mΩ - 1 GΩ |
| Accuracy | up to ±0,0015 % |


## Application Examples

- Characterization of low-current sensors
- Long-term monitoring of drifting components in implants or test rigs
- High-precision resistance measurements for material characterization (e.g., insulation testing)

# Ultramicrobalance

***Model: XPR6UD5 by Mettler Toledo***

For the precise dosing and control of extremely small samples and active ingredient quantities, we use the XPR6UD5 ultra-microbalance from METTLER TOLEDO. It enables highly precise weighing in the micro- and sub-microgram range and is therefore a key tool for applications in which even the smallest deviations are measurably relevant.
The balance allows reliable determination of active ingredient masses, for example in the manufacture of drug-eluting stents or other medical technology products. To ensure maximum measurement stability, the balance is equipped with an anti-vibration platform and an anti-static system with ionizer, minimizing the effects of vibrations and electrostatic charging. Constant temperature control and a motorized draft shield with touchless operation ensure contamination-free handling under stable conditions.
The balance can be integrated into existing digital laboratory and production systems via various interfaces. In combination with LabX software, all measurement data are automatically documented and stored in a tamper-proof manner, making an important contribution to traceability and quality assurance in regulated environments.


**Technical Specifications**

| | |
|---|---|
| Capacitance | 0,5 µg - 6,1 g |
| Resolution / Repeatability | 0,5 µg / 0,3 µg |
| Stabilization time | < 8 s |
| Draft shield | Motorized, non-contact control, easy-to-clean design |
| Temperature control | Active Temperature Control |
| Accessories | Antistatic kit (ionizer), anti-vibration plate |

## Application Examples

- Precise determination of minute active ingredient quantities in pharmaceutical and biomedical samples
- Dosing and investigation of nanopowders, biomaterials, or coatings in medical technology
- Measurement of residues, additives, or contaminants in research and production environments
- Determination of mass changes in drying, sorption, or reaction processes in the µg range

# Differential Scanning Calorimeter

***Model: DSC 5+ by Mettler Toledo***

Differential scanning calorimetry (DSC) is a thermal analysis technique for the quantitative determination of physical and chemical material transitions, such as melting, glass transition, crystallization, or decomposition processes. Heat flows resulting from temperature-induced changes in the sample are measured, enabling precise determination of reaction enthalpies even with very small sample quantities.
In medical technology, DSC is particularly used to assess the thermal stability, crystallinity, and aging resistance of polymer-based materials - both for biostable and biodegradable implant materials. For materials intended for use in the body, understanding the thermal behavior of polymers is essential, for example regarding deformation, crystallization, or thermally induced degradation. DSC provides crucial information on processability and the potential lifespan of materials. Due to its high sensitivity and reproducibility, DSC is an indispensable tool in materials science research, development, and quality assurance.

| **Technical Specifications** | |
|---|---|
| Temperature range | -150 °C to +700 °C |
| Temperature accuracy /<br>Temperature precision | ± 0,2 K<br>± 0,02 K |
| Heating rate /<br>Cooling rate | 0,001 to ≈ 200 K/min<br>0,001 to ≈ 50 K/min |
| Measurement modes | power compensation mode<br>and heat flow mode |
| Sample robot capacity | max. 96 samples + 7<br>reference crucibles |
| Crucible sizes | 20 - 160 µL |


## Application Examples

- Analysis of crystallinity, reaction enthalpies, or thermal degradation is of central importance, for example in the development of new composite materials or in the assessment of manufacturing quality
- Determination of decomposition or glass transition temperature (Tg) to define processing/sterilization parameters
- Monitoring thermal changes during aging or hydrolysis
- Investigation of polymer, filler, or drug carrier blends for thermal interactions

# High-Performance Liquid Chromatography System

***Model: HPLC-System by KNAUER Wissenschaftliche Geräte & UHPLC-System Nexera by Shimadzu Corporation***

High-performance liquid chromatography (HPLC) is a key analytical technique for the qualitative and quantitative determination of active ingredients and impurities in solutions. In medical technology and implant development, HPLC is particularly used for analyzing drug release, monitoring coating processes, or characterizing complex substance mixtures. IIB e.V. has access to the following powerful liquid chromatography systems: a classic HPLC system from KNAUER Wissenschaftliche Geräte GmbH, known for its robustness and reliable UV/Vis detection, and a Nexera UHPLC system from Shimadzu Corporation, offering ultrahigh resolution, fast run times, and high sensitivity. Both systems enable reliable analysis of low-concentration active ingredients - down to 0.1 µg/mL - supporting analytical studies in research, development, and quality assurance.

| Technical Specifications | HPLC (KNAUER) | UHPLC (Shimadzu) |
|---|---|---|
| Detection | UV/Vis diode array detector | UV/Vis diode array detector |
| Limit of detection | to 0,1 µg/mL | < 0,05 µg/mL |
| Minimum required sample | 20 µL | 5 µL |
| Measurement duration | 8 - 30 min | 5 -10 min |
| Number of available methods | > 30 | > 10 |
| Software | EZ Chrom Elite | LabSolutions |

## Application Examples

- Drug release studies of coated stents, implants, or bioactive carrier systems
- Quantification of pharmaceutical active ingredients such as sirolimus, paclitaxel, insulin, or acetylsalicylic acid
- Separation and analysis of complex mixtures in biological or aqueous matrices
- Long-term monitoring of substance stability in storage or release studies

# Gel Permeation Chromatography System

***Model: PSS SECurity GPC-System by Agilent***

Gel permeation chromatography (GPC), also known as size-exclusion chromatography, is a specialized form of liquid chromatography used to determine molecular weight distributions and structural parameters of macromolecules. Unlike classical HPLC, separation is not based on interactions with the stationary phase but solely on the size (or hydrodynamic volume) of the dissolved molecules.
In implant development, GPC plays a crucial role in characterizing permanent and (bio)degradable polymers, coating materials, and biofunctional carrier structures. Typical analytes include synthetic polymers, biopolymers, or proteins, for which molecular weight averages (Mn, Mw, Mz), polydispersity, intrinsic viscosity, structural and size distributions can all be determined.
At IIB e.V., access is provided to a PSS SECurity GPC system from Agilent as part of the institute-wide infrastructure. It combines high-resolution separation columns with a viscometer and a refractive index detector. This setup allows universal calibration without the need for specific standards and enables comprehensive molecular characterization. For example degradation analyses, quality control, or shelf-life studies of polymeric materials.

| **Technical Specifications** | |
|---|---|
| Separation principle | Size exclusion based on hydrodynamic volume |
| Detectors | Refractive index detector, viscosity detector |
| Analytical parameters | $M_n$, $M_w$, $M_z$, Polydispersity, η, Rg, Rh |
| Typical samples | Polymers, biopolymers, proteins |
| Software | WinGPC UniChrom (PSS) |

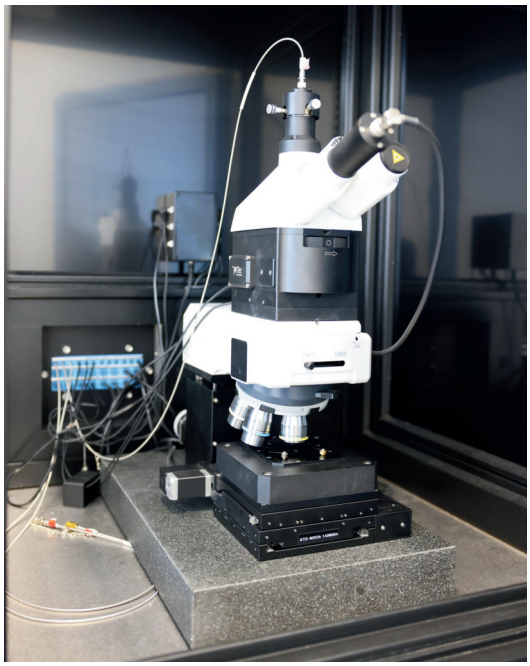

## Application Examples

- Determination of molecular weights and polydispersity of degradable implant materials
- Characterization of degradation kinetics in polymer degradation studies
- Quality control and structural comparison of polymers for coating systems
- Shelf-life testing: aging and stability of polymeric implant components

# Raman Microscope

***Model: alpha 300 by WITec / Oxford Instruments***

Raman spectroscopy enables contact-free qualitative material analysis by evaluating the characteristic Raman spectrum, often referred to as the “molecular fingerprint”. Raman spectroscopy is particularly suitable for identifying polymer types, active ingredients, crystallinity, or impurities - frequently for particle sizes as small as approximately 10 µm. In implant technology, the method can be used to analyze polymer structures, drug distributions, and surface states without extensive sample preparation.
At IIB e.V., access is provided to the confocal Raman microscope alpha 300 R from WITec / Oxford Instruments. It combines Raman spectroscopy with high-resolution microscopy and allows Raman imaging with a full spectrum per pixel. This enables visualization of drug distributions in implant coatings or multilayer structures. It also allows the monitoring of polymer conformations and degradation states - non-invasive, three-dimensional, and with high spectral resolution.



| Technical Specifications | |
|---|---|
| Wavelengths | 532 nm, 785 nm |
| Spectrometer / detector | fiber-coupled UHTS spectrometer |
| Spatial resolution | < 200 nm lateral, < 900 nm axial bei 532 nm |
| Scan range | 25 x 25 mm (XY), 30 mm (Z); Step sizes: X/Y 100 nm, Z 10 nm |
| Scan speed | up to 1300 spectra/s |
| Software | WITec Suite |

## Application Examples

- Visualization of drug distribution in polymer coatings
- Analysis of multilayer systems, e.g., stacked polymer films
- Characterization of crystallinity and molecular conformation in implant-related polymers
- Chemical particle analysis (identification of microparticles)

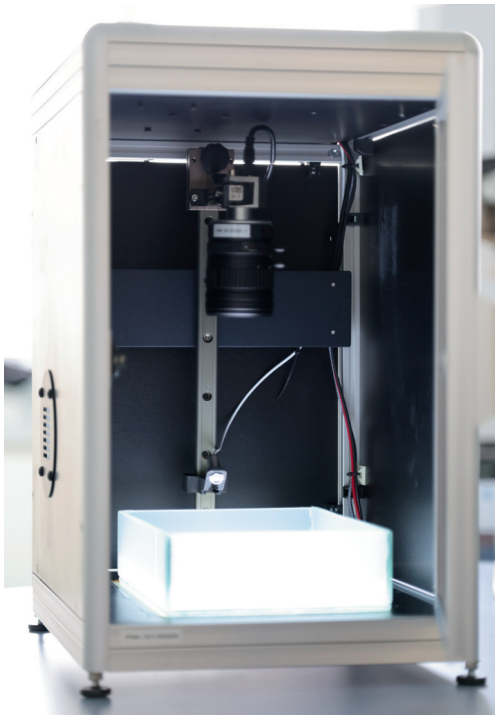
# Optical Measurement System for Determination of Af Temperature

***Model: NCAT-System by ANVLaser***

Optical measurement systems for determining the austenite finish (Af) temperature are essential tools in the material testing of shape memory alloys such as Nitinol. They non-contactly capture the thermally induced phase transition from the martensitic to the austenitic phase, which is crucial for the recovery behavior and function of medical components. These systems enable precise, standards-compliant measurements even on very small geometries, making them a key part of implant development.
At IIB e.V., the NCAT system from ANVLaser Industries is used for this purpose. It allows simultaneous, contactless analysis of multiple Nitinol samples with different geometries. Using a high-resolution camera and intelligent image analysis, deformation-dependent recovery processes during heating are documented, and the Af temperature is calculated precisely - compliant with ASTM F2082. The system thus enables rapid and reliable evaluation of the thermofunctional properties of Nitinol components for medical applications.

**Technical Specifications**

| | |
|---|---|
| Measurement method | Optical detection via digital camera & image analysis |
| Temperature range | -50 °C to +50 °C<br>±2 °C calibrated |
| Sample size & sample geometry | Simultaneous analysis of up to 10 samples with varying sizes and shapes |
| Operating range (L x W x H) | 205 mm x 190 mm x 65 mm |
| Standards compliance | ASTM F2082 |



## Application Examples

- Characterization of self-expanding Nitinol stents by determining the Af temperature to ensure reliable superelasticity in the body
- Support for medical product approvals in accordance with ASTM F2082
- Process control of thermal treatment steps

# Real-Time Cell Tomograph

***Model: 3D Cell Explorer by Nanolive***

The real-time cell tomograph enables the study of living cells without intervention or dyes in real time. This allows key cellular processes to be visualized and closely monitored.
At IIB e.V., the 3D Cell Explorer from Nanolive is used for this purpose. This advanced microscope employs a specialized 3D imaging technique (holotomography) and can additionally capture fluorescence images. The unique feature of the system is that it delivers high-resolution 3D images of cells in rapid succession and operates completely label-free - without any additives that could alter the cells. An incubation chamber also ensures that cells are maintained under stable conditions, such as temperature and $CO_2$ concentration, allowing reliable measurements over extended periods. With this setup, cell division and differentiation can be observed in real time in response to stimuli.


**Technical Specifications**

| | |
|---|---|
| Light source | Laser 520 nm, CoolLED pE300ultra |
| Detection | Laser-based hologram acquisition |
| Fluorescence filter | FITC: 474, 3/499,5-530; TRITC: 554,5/580-611; Cy5: 635/661-800 |
| Objectives | 60x (NA 0.8) |
| Camera | Sony IMX174 CMOS |
| Incubation | Stage-top incubation chamber (temperature and $CO_2$ gas control) from OKOLab |

## Application Examples

- Interaction between tissue-specific cell types and implant structures
- Analysis of cytotoxicity of material extracts and active ingredients
- Non-destructive single-cell analysis, including dynamics of cellular organelles

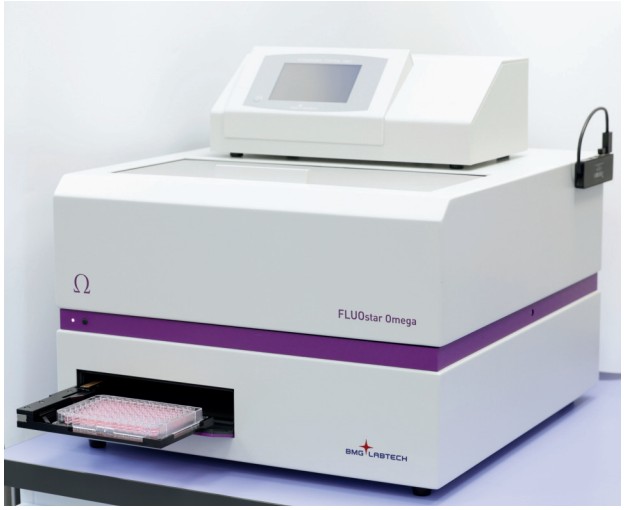
# Microplate Reader

***Model: FLUOstar Omega by BMT LABTECH***

A microplate reader is used to measure chemical, biological, or physical reactions, properties, and analytes within the wells of a microplate. For research and development work, IIB e.V. uses the FLUOstar Omega microplate reader from BMG-LABTECH GmbH (Ortenberg). This device allows the execution and evaluation of cell-based assays such as cell viability tests, ELISA (enzyme-linked immunosorbent assay), and the quantification of nucleic acids and proteins.
The system enables measurements of absorbance, fluorescence, and luminescence, both as endpoint and kinetic assays. Additionally, it maintains controlled environmental conditions during measurements, such as temperature and $CO_2$ concentration. This allows a wide range of quantitative biochemical and cell-based assays to be performed.
The microplate reader is indispensable for assessing cytotoxicity in accordance with DIN EN ISO 10993. It also enables the investigation of inflammatory processes in the context of foreign body reactions.

**Technical Specifications**

| | |
|---|---|
| Light source | High-energy xenon flash lamp |
| Detection | Absorbance, fluorescence, luminescence |
| Fluorescence filter | 400/505; 544/590; 485/520; 584/620 |
| Incubation | controlled temperature and $CO_2$ atmosphere, integrated shaking function |
| Measurement modes | top and bottom detection, well scanning, endpoint or kinetic assays |




## Application Examples

- Quantitative analysis of cytotoxicity of implants and biomaterials according to DIN EN ISO 10993
- Analysis of the impact of active ingredients and implant materials on cell proliferation
- Detection of inflammatory markers after contact with implant structures using ELISA

# Inverted Microscope System

***Modell: DMi8 by Leica***

Wide-field fluorescence microscopy is a key imaging technique in cell-based biomaterials research, as it provides high-resolution and dynamic insights into cellular processes.
At IIB e.V., the modular inverted microscope system Leica DMi8 is used for this purpose, combined with the highly sensitive Leica DFC9000 sCMOS camera. The system allows real-time imaging of living cells under physiological conditions and is ideally suited for analyzing cell migration, cytotoxicity, and morphodynamic changes. Thanks to motorized components, an integrated incubator, and fluorescence imaging capabilities, it provides a versatile platform for automated, reproducible measurement series - indispensable for studying cellular responses to biomaterials.

**Technical Specifications**

| | |
|---|---|
| Camera | Leica DFC9000 sCMOS |
| Resolution | 4,2 Megapixel |
| Frame rate | > 40 frames/s |
| Light source | LED- or laser-based fluorescence excitation |
| Objective turret | Motorized, with multiple objective positions |
| Incubation module | Temperature (up to 37 °C), $CO_2$ (up to 5 %), humidity controlled |
| Software | LAS X (Leica Application Suite X) |

## Application Examples

- Detection of morphological changes in fibroblasts or smooth muscle cells
- Analysis of macrophages or endothelial cells after stimulation with cytotoxic substances
- Identification of substances with cytotoxic or morphogenic effects

# The Accredited Testing Laboratory at IIB e.V.

The testing laboratory for cardio- and vascular products is an independent and autonomous laboratory integrated within IIB e.V. Its main focus is on physical testing of balloon catheters and stent systems used for the treatment of coronary heart disease and other arterial vascular conditions.

The core tests are standardized, norm-compliant procedures that have been established and validated within the laboratory. In accordance with Regulation (EU) 2017/745 (Medical Device Regulation – MDR), these tests are applied as part of product approvals. Additionally, the laboratory offers comparative studies with market-standard products, which are important for understanding their function, design verification, market studies, and the formulation of development objectives for various manufacturers.

For new safety and effectiveness requirements for implants, innovative testing methods are developed and standardized in close collaboration with the IIB e.V. Research, Development, and Technology Transfer division as well as with clients.

**Competence, Precision, Quality – Our Experience for Safety**

Since the mid-1990s, the testing laboratory has been conducting independent investigations on medical devices. The focus is on physical testing of stents and catheter systems. The essential tests are internationally standardized, particularly in ISO 25539-1/-2, ISO 10555-1/-4, as well as in various standards of the American Society for Testing and Materials (ASTM).

DAkkS
Deutsche
Akkreditierungsstelle
D-PL-13185-01-00

**Internationally Recognized Accreditation**

Accreditation as a testing laboratory by the German Accreditation Body (DAkkS) according to DIN EN ISO 17025 forms the basis for high quality and broad acceptance of our services.

Through the Mutual Recognition Arrangement (MRA), DAkkS accreditation is recognized worldwide in all member states of the International Laboratory Accreditation Cooperation (ILAC).

Taking into account current medical and technical knowledge, testing methods and the associated equipment are continuously revised or newly developed and implemented in practice.

The results produced by the testing laboratory are successfully used for obtaining CE approvals as well as for international product approvals by non-European authorities (USA – FDA, China – CFDA, Japan – PMDA, etc.).

**National and Internationally on the Safe Side**

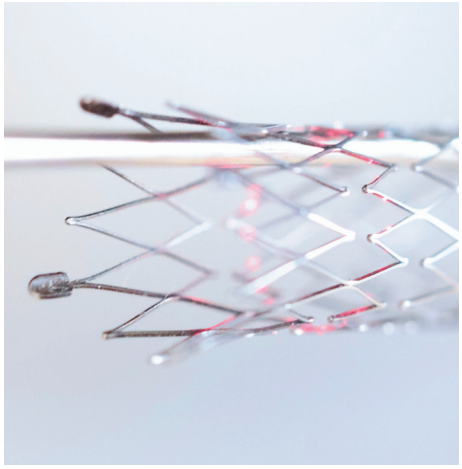
The testing laboratory has already collaborated with numerous medical device manufacturers worldwide – from Europe, North and South America, as well as Asia. At the same time, the IIB e.V. testing laboratory sees itself as a reliable partner and service provider for regional companies and research institutions in Mecklenburg-Vorpommern.

**Tests are offered for:**

- Formulation of development objectives
- Comparative studies for the scientific understanding of implants (benchmark studies)
- Medical device certification

# TESTING LABORATORY

In the testing laboratory, a comprehensive evaluation of implants - such as cardiovascular stents - is conducted, focusing on geometry, mechanics, morphology, as well as fatigue and functional tests. The goal is to realistically assess safety, reliability, and manufacturing quality over the entire service life.

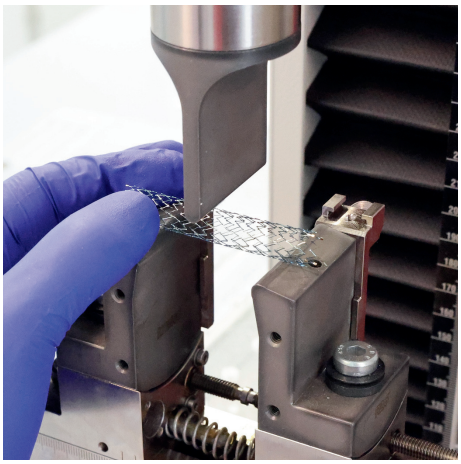


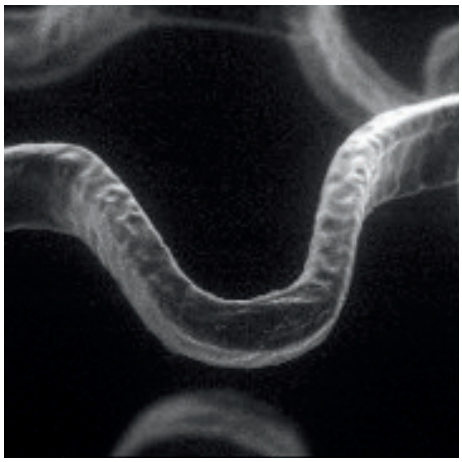
**GEOMETRIC PROPERTIES**

Within the scope of testing assignments for stents and catheter systems, key product dimensions such as outer diameter, length, strut dimensions, and wall thickness are determined. In addition, length changes upon deployment can be measured and side-branch accessibility can be assessed. For this purpose, various optical methods such as microscopy or laser measurement are available.

**MECHANICAL PROPERTIES**

At the core of the testing laboratory's work is the evaluation of mechanical properties, including resistance to deformation under radial and perpendicular loading as well as the radial force of self-expanding stents. In addition, the expansion behavior of balloon-expandable stents, elastic recoil, as well as buckling and bending stiffness are investigated.
Further key parameters include maximum tensile force, stent pull-off force, and balloon burst pressure to ensure safety, reliability, and quality.





**MORPHOLOGICAL PROPERTIES**

The testing laboratory offers a comprehensive portfolio of morphological analyses, including:

- Surface analysis by scanning electron microscopy (SEM),
- Surface analysis by light microscopy,
- Dynamic image analysis of particles,
- Investigation of coating integrity, and
- Photographic documentation.

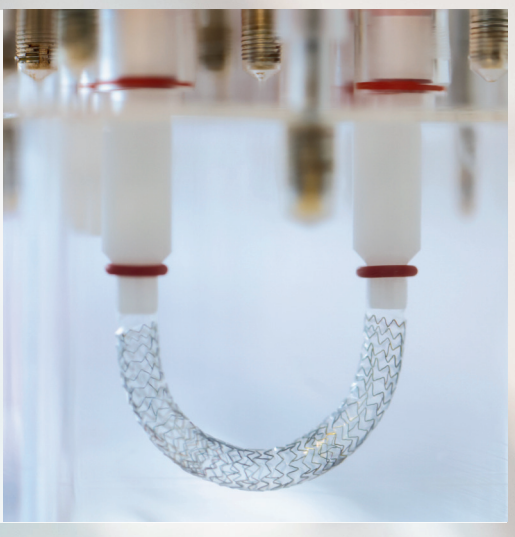
The objective is to assess surface quality, structural homogeneity, and particle distribution in order to evaluate manufacturing quality and durability.

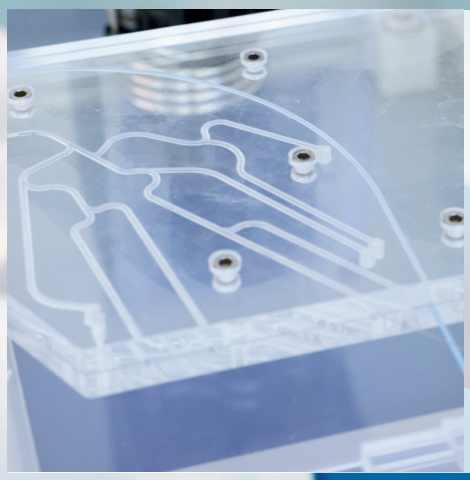
## FATIGUE TESTING

The testing laboratory offers reliable methods for determining the fatigue resistance of products. The following aspects are investigated:

- Radial loading
- Multiaxial loading (compression, bending, torsion)
- Chronic coating integrity including particle release
- Balloon fatigue as a specific fatigue indicator
- Long-term particle release and its impact on performance and reliability

The objective is to realistically estimate the service life and reliability of products and to ensure quality over the entire period of use.





## APPLICATION TESTING

The testing laboratory performs simulated applications in anatomical models to realistically evaluate trackability, pushability, and crossability. In this process, conformity to the vessel wall as well as the positioning accuracy of implant systems are assessed.

In addition, particle release is investigated both during simulated application and during stent deployment in order to identify potential risks at an early stage. The permeability properties of cover materials and membranes are also analyzed to reliably represent their behavior under real-use conditions.

## SPECIAL PARAMETERS

In addition, special parameters that significantly influence the performance and processing characteristics of implants can be determined. These include the determination of transformation temperatures of nickel-titanium alloys, the assessment of X-ray contrast, and seal seam testing. Furthermore, comprehensive testing of semi-finished products is carried out, for example to characterize manufacturing and processing influences.

# Competence, Independence, and Validity

## Quality Management in Accordance with DIN EN ISO/IEC 17025

Since 2010, the Testing Laboratory for Cardio and Vascular Products has been operating in accordance with the quality management system DIN EN ISO/IEC 17025 and has been accredited by the German Accreditation Body (DAkkS) since 2012. Competence, impartiality, and validity, as well as compliance with legal regulations, guidelines, and international standards in the performance of testing services, form the basis for a relationship of trust with medical device companies, clinics, and authorities.

Through a strict separation of tasks and responsibilities within IIB e.V., it is ensured that the personnel of the Testing Laboratory for Cardio and Vascular Products and the personnel from the research division of IIB e.V. are not subject to each other's technical authority. In addition, the personnel responsible for product testing have committed themselves to carrying out no medical device development within the scope of accreditation and to taking all necessary measures to ensure confidentiality regarding product and customer data and thus safeguard impartiality.

The personnel of the Testing Laboratory for Cardio and Vascular Products have extensive experience in the field of medical device testing, applied biomechanics and sensor technology, as well as the development of testing methods, based on many years of activity. By participating in specialist conferences, exchanging experience with other laboratories, and actively contributing to standards committees, it is ensured that the testing services offered correspond to the current state of the art. Regular internal training courses also ensure that the competence of the testing staff is consistently maintained at a high level.

All testing methods offered within the scope of accreditation are validated. To assess validity, for example, calibration results, systematic evaluations of influencing factors, and comparative measurements with other methods are used. The aim is always to minimize the sensitivity of the methods to external influences and to maximize reproducibility.

*Example: Use of a calibrated measuring device for determining the cover thickness of covered stents*


**All testing and measuring devices are routinely assessed for suitability.**

The testing laboratory ensures the metrological traceability of its measurement results through the regular execution of calibrations. As a rule, DAkkS-accredited calibration laboratories are commissioned to verify the laboratory's own testing equipment. In exceptional cases, such as for specialized measurement setups, internal calibrations are performed, taking into account the requirements of the calibration guidelines of DAkkS or the German Calibration Service (DKD).

## Quality Management System

The requirements of DIN EN ISO/IEC 17025, "General Requirements for the Competence of Testing and Calibration Laboratories," are implemented through an internal quality management system. Special regulations and procedures have been established that, on the one hand, define organizational and structural processes and their execution, and on the other hand, describe technical processes, particularly the testing methods, measuring equipment, and personnel.

The quality policy is based on the requirements of Regulation (EU) 2017/745 (MDR), the Medical Devices Implementation Act (MPDG), and DIN EN ISO/IEC 17025. Working according to standardized processes forms the foundation for consistently high quality in all operations within the testing laboratory. Technical procedures are documented in international standards, internal regulations, test instructions, validation reports, calibration records, or competency certificates. The Quality Management Manual (QMH) and procedural instructions regulate organizational processes. Forms and protocol templates enable effective documentation. Handling of faulty tests, the derivation of corrective actions, and the implementation of preventive measures are also part of the quality management system.

Through regular processes such as internal audits, inter-laboratory comparison tests, and management reviews, the quality management system - and thus the activities of the entire testing laboratory - is continuously optimized.

Not least, through regular on-site assessments (every 1.5 years), the testing laboratory is under continuous supervision by DAkkS, which consistently evaluates and confirms the conformity of the laboratory's work with the requirements of DIN EN ISO/IEC 17025.

## Relevant international standards applicable to the Testing Laboratory for Cardio and Vascular Products

Deutsche Akkreditierungsstelle D-PL-13185-01-00

| | |
|---|---|
| **ISO 25539-1** | Cardiovascular implants - Endovascular implants - Part 1: Endovascular prostheses |
| **ISO 25539-2** | Cardiovascular implants - Endovascular implants - Part 2: Vascular stents |
| **ISO 10555-1** | Intravascular catheters - sterile and single use catheters - Part 1: General requirements |
| **ISO 10555-4** | Intravascular catheters - sterile and single use catheters - Part 4: Balloon dilatation catheters |
| **ISO 14708-1** | Implants for surgery - Active implantable medical devices - Part 1: General requirements |
| **ISO 14708-2** | Implants for surgery - Active implantable medical devices - Part 2: Cardiac pacemakers |
| **ISO 7198** | Cardiovascular implants and extracorporeal systems - Vascular prostheses - Tubular vascular grafts and vascular patches |
| **ASTM E 3060** | Standard Guide for Subvisible Particle Measurement in Biopharmaceutical Manufacturing Using Dynamic (Flow) Imaging Microscopy |
| **ASTM F 2079** | Standard Test Method for Measuring Intrinsic Elastic Recoil of Balloon-Expandable Stents |
| **ASTM F 2081** | Standard Guide for Characterization and Presentation of the Dimensional Attributes of Vascular Stents |
| **ASTM F 2394** | Standard Guide for Measuring Securement of Balloon Expandable Vascular Stent Mounted on Delivery System |
| **ASTM F 2477** | Standard Test Methods for in vitro Pulsatile Durability Testing of Vascular Stents and Endovascular Prostheses |
| **ASTM F 2942** | Standard Guide for in vitro Axial, Bending, and Torsional Durability Testing of Vascular Stents |
| **ASTM F 3067** | Guide for Radial Loading of Balloon Expandable and Self Expanding Vascular Stents |
| **ASTM F 3505** | Standard Test Method for Stent and Endovascular Prosthesis Kink Resistance |
| **USP 788** | Particulate matter in injections |

# Services for the Regional Economy

The Institute for ImplantTechnology and Biomaterials (IIB e.V.) is a key partner for medical technology companies in Mecklenburg-Western Pomerania and beyond. With its modern research and laboratory infrastructure, the institute supports companies in all phases of product development – from the initial concept to market readiness. The goal is to make innovations more efficient, safer, and more economical, thereby sustainably strengthening the competitiveness of the regional medical technology sector.

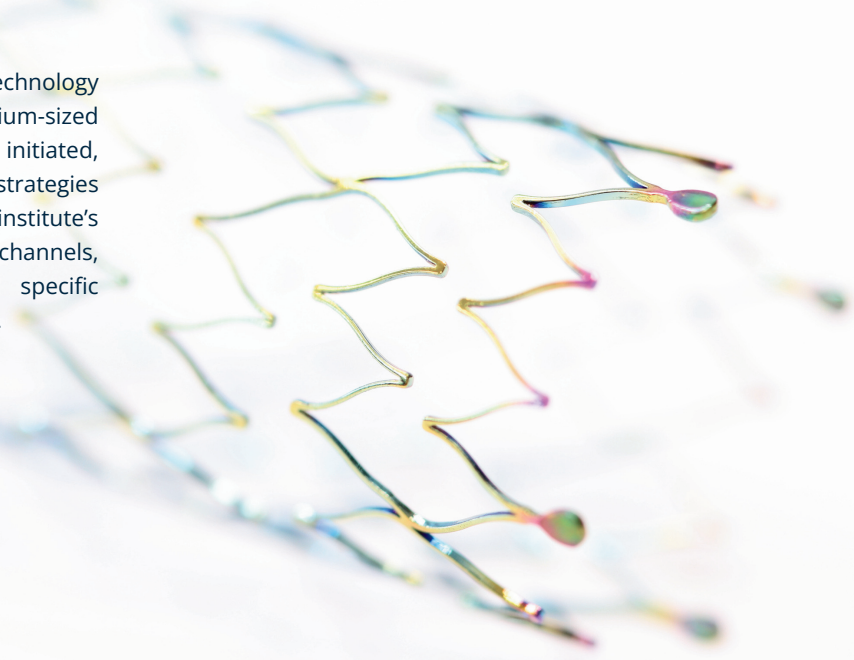
Companies benefit from a comprehensive offering that combines scientific depth with practical applicability. The range of services extends from material characterization and surface analysis to CAD-based design and numerical simulation, as well as the manufacturing and functional coating of implants. In addition, the accredited testing laboratory at IIB e.V. provides standardized testing procedures for cardiovascular implants.

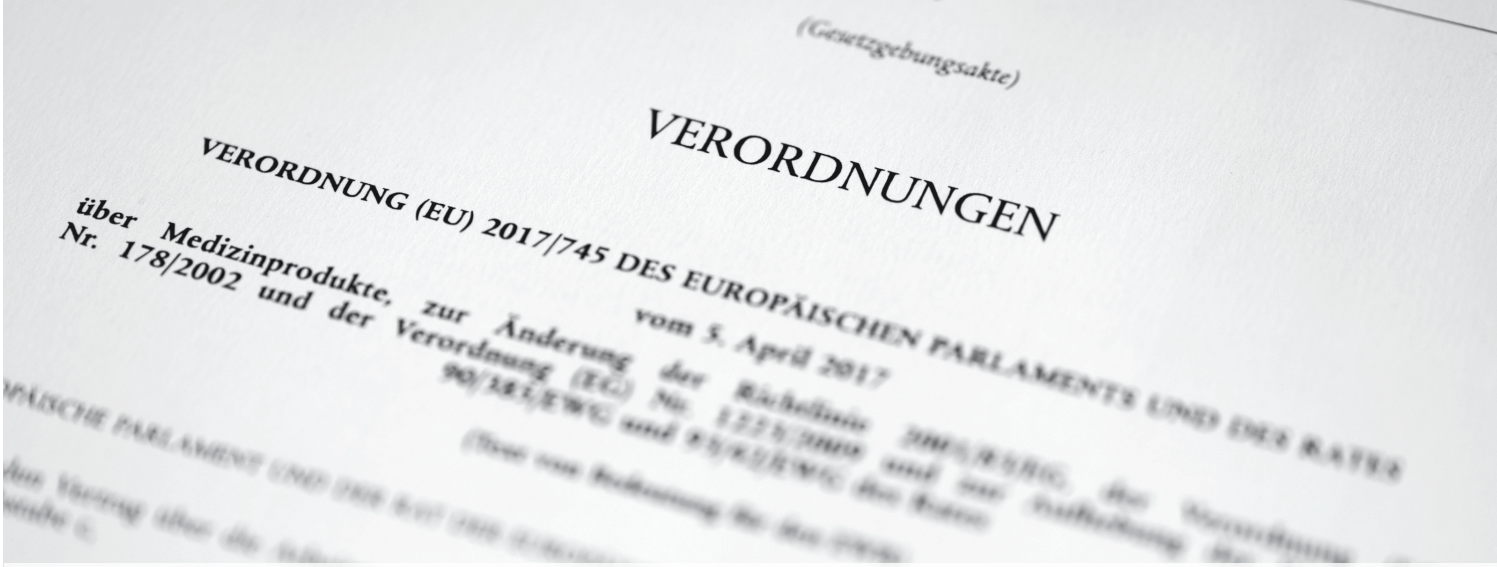
A particular advantage for companies lies in the institute's integrated process chain: research, development, prototyping, and testing are all carried out under one roof. This allows development times to be shortened, costs reduced, and innovation cycles significantly accelerated. Through the close integration of virtual product development, manufacturing, and experimental validation, companies receive rapid and reliable results, enabling them to secure design decisions early on.

Furthermore, IIB e.V. is actively engaged in technology transfer. In cooperation with small and medium-sized enterprises, practical development projects are initiated, feasibility studies conducted, and market entry strategies developed. Partners benefit from the institute's interdisciplinary expertise, short communication channels, and customized solutions tailored to the specific requirements and resources of regional companies.

In addition to its technical services, IIB e.V. also acts as a networking platform and driver of innovation for the medical technology sector in Mecklenburg-Western Pomerania. Through specialist events, workshops, and collaborations with universities, clinics, and industry partners, the institute promotes the exchange of knowledge and experience between science, industry, and healthcare. This fosters new innovation partnerships and sustainable value creation in the region.

With this combination of technical excellence, regional networking, and application-oriented research, IIB e.V. makes an important contribution to the further development of Mecklenburg-Western Pomerania as a medical technology hub and to the successful transformation into a knowledge-based, future-oriented economy.






# Medical Device Regulation (MDR) – Competence Center

The MDR Competence Center at IIB e.V. is the first point of contact for regional medical technology companies and start-ups seeking to bring their products to market safely and in compliance with regulations. The center consolidates expertise in regulatory affairs and biostatistics/statistics, providing companies with easily accessible information, thorough research, and data-driven analyses. Its goal is to create a clearly structured entry into MDR requirements – from an initial overview to concrete, actionable steps leading to market approval.

The focus is on strengthening the regional economy through research and development in medical technology. IIB e.V. primarily addresses companies in the fields of biomaterials, biomechanics, medical devices, and implants that aim to bring their solutions to the international market. The MDR Competence Center helps structure development pathways, leverage potential, and make the transition from prototype to market-ready solution predictable.

For small and medium-sized enterprises (SMEs) and start-ups, the center serves as a primary contact point: in collaboration, the product category of the project is determined, required evidence is defined, and the stepwise compilation of evidence is established. Based on this, realistic roadmaps are created, outlining clear milestones, priorities, and documented interim results. These roadmaps can later be directly integrated into the technical documentation. This approach provides companies not only with answers to specific questions but, more importantly, guidance through the entire process.

A central component is biometric and analytical support throughout the entire development cycle. This includes structured literature and standards research, data analysis from preliminary studies, and the planning of clinical trials – from exploratory concepts (e.g., for first-in-human applications) to the biometric design of protocols such as Clinical Development Plan (CDP), Clinical Investigation Plan (CIP), and Clinical Evaluation Plan/Report (CEP/CER). This creates a robust evidence base that makes risks visible early and accelerates subsequent regulatory submissions.

Furthermore, the MDR Competence Center promotes networking between science and industry in Mecklenburg-Vorpommern. It supports the transfer of research results into marketable products, guides the development of next-generation devices (e.g., smart implants), and contributes to industrial value creation in international markets. At the same time, it strengthens the region by establishing long-term research structures, fostering company settlements and spin-offs, and securing skilled personnel.

# From Warnemünde to the World

***Rostock***
*National Conference on Health Economy*

***Paris***
*Visit to Europe's Largest Specialist Conference "EuroPCR"*


***San Francisco***
*TCT-Conference*


***San Diego***
*IIB e.V. at the World's Largest Cardiology Conference "TCT""*

***Basel***
*Joint Conference of the Swiss (SSBE), Austrian (ÖGBMT) and German (VDE DGBMT) Societies for Biomedical Engineering*

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**Photos**
IIB e.V., Holger Martens



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