REMEDIS
Higher quality of life through novel micro-implants
Our society is undergoing far-reaching demographic changes: according to the Federal Statistical Office, Germany’s population will decrease by almost 22 percent to less than 65 million people by 2060. The number of 20-to-64-year-olds is set to decrease by six million people by 2030. The average age of the population is rising. At the same time, medical progress holds out the prospect of growing old with ever fewer health-related problems.

Apart from the opportunities that demographic change presents for individuals and the challenges it poses to society, it also offers new chances for doing business. Illnesses such as cataract, glaucoma or coronary heart disease, which are more prevalent in people of advanced age, will become increasingly common over the next few years. The key to curing such diseases, or at least alleviating their symptoms, is precisely the sort of high-tech medicine made in Germany that REMEDIS develops.

REMEDIS pools the efforts of outstanding natural and engineering scientists and medical experts from Germany and abroad. Building upon excellent basic research in biomedical technology, REMEDIS is conducting research into innovative products that could help patients all over the world within the next few years, and which thus have enormous business potential.

The Federal Ministry of Education and Research supports REMEDIS as part of its “Leading-Edge Research and Innovation in the New German Länder” programme. The funding amounts to €14 million over five years – an excellent investment; one that does not just have a positive effect on the Rostock region and the other research centres involved, but benefits everyone in our longer-living society.
REMEDIS combines the efforts of major companies with those of scientists specialised in the widest possible variety of disciplines. Engineering and natural scientists together with medical experts from all over Germany work in close collaboration to develop innovative implants. These include stents and stimulation electrodes for the circulatory system, glaucoma stents and intraocular lenses for the eyes as well as auditory tube stents for the ears. Through its efforts to combine a local drug release system into the functionality of implants, REMEDIS provides cutting-edge research into such medical technology.

Building on the excellent basic research already available in the area of biomedical engineering, REMEDIS focuses on applied research into the development of implants with major potential for market penetration. The direct involvement of medical experts allows for an input of their experience in everyday clinical practice to implant development as part of a seamless chain of research processes.

This facilitates the development of increasingly successful treatments for clinical symptoms that could not be treated or not satisfactorily treated 10 or 20 years ago and were thus inevitably associated with a poor long-term prognosis. In addition, ever older patients shall be treated using innovative, minimally invasive and gentler procedures, which is precisely what is increasingly needed given current demographic trends.

REMEDIS headquarters are based at the Institute for Biomedical Engineering at the University of Rostock. The REMEDIS spokesperson is Prof. Dr. Katrin Sternberg. The Chairperson of the REMEDIS Board is Prof. Dr. Klaus-Peter Schmitz, Director of the Institute for Biomedical Engineering.

REMEDIS is being supported by the Federal Ministry of Education and Research to the tune of € 14 million over five years. The State of Mecklenburg-Vorpommern provides another € 1.4 million for the research network.

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Prof. Dr. Katrin Sternberg,
Spokesperson for REMEDIS
University of Rostock, Institute for Biomedical Engineering

“Collaboration with scientists in the widest possible variety of disciplines and the development of novel implant prototypes – that is what is so special about the work of REMEDIS. By involving high-performance industrial partners as early as the basic research phase of development we can ensure the successful clinical implementation of such implants downstream. This is both our challenge and our motivation.”
Intraocular lenses

Intraocular lenses for the treatment of cataract are amongst the most important implants in use in ophthalmology. In Germany alone about 500,000 operations are conducted each year. The further development of such artificial lenses is helping to decisively reduce the risk of secondary cataract, which may result from strong cell growth on the lens surface, reducing the effectiveness of such lenses. REMEDIS is also researching injectable, accommodative lens systems. Such devices should especially help older patients to regain the ability of younger eyes to see objects at various distances in sharp focus.

Micro-stents

The use of stents in the eye and the middle ear and the development of the minimally invasive micro-surgical techniques for their implantation are opening up new therapeutic options for patients suffering from glaucoma or chronic middle ear inflammation. Due to the location in which they are implanted and to conditions in their immediate environment, both glaucoma stents – as implants used for reducing pressure inside the eye are called – and auditory tube stents, which are used for aerating the middle ear, need to be designed with particular care in terms of function and tissue tolerance. They can be made out of either shape-memory alloys or polymers. Due to their size, micro-structure and biofunctional surfaces, micro-stent systems pose formidable scientific challenges, challenges that are met by REMEDIS right up to the stage of producing prototypes.

Prof. Dr. Rudolf Guthoff
University of Rostock, Department of Ophthalmology

“We are faced every day with the task of reducing eye pressure in patients with glaucoma. Sometimes neither medicines nor operations can help. We are delighted when we receive offers from the engineering sciences for implants originally used, for example, in the treatment of heart attacks, but now so reduced in size that they become feasible for use in the eye. And this is precisely the level that REMEDIS is working at.”
Stents and drug-eluting stents

REMEDIS is working successfully on the further development of drug-eluting stents into what is generally referred to as multi-mode stents: next-generation stents used to minimise the risk of delayed thrombosis using multi-level, selective local drug delivery.

In the area of stent technology using absorbable magnesium alloys and high-performance polymers, REMEDIS sets a European benchmark. In addition, the Institute for ImplantTechnology and Biomaterials, also a member of the REMEDIS consortium, is specialised in approval testing and benchmarking of stent systems.

Stimulation electrodes

Stimulation electrodes deliver controlled electrical impulses to the body. They are essential components of pacemakers, defibrillators, neurostimulators and cochlear implants, assuring the effectiveness of these high-tech products.

REMEDIS is working on the development of new coatings containing active substances for stimulation electrodes capable of inhibiting the build up of connective tissue in the area of electrode tips and thus preventing changes that might affect device capacity to transmit electrical signals.
REMEDIS takes on the task of jointly developing existing implants and creating new ones by combining the use of implants with drug treatments. Such combined products have substantial benefits in that they can decisively improve tissue-implant interaction through the precise, implant-based release of drugs. In their efforts to satisfy the requirement for new types of implants providing great new benefits to patients, the consortium partners are therefore concentrating particularly on modifications to the surface of implants.

In the course of this research, REMEDIS can rely on the know-how accumulated by its members over many years. The Institute for Biomedical Engineering of the University of Rostock with its engineering and natural science network is closely interlinked with medical partners from the university hospitals in Rostock and Greifswald as well as Hannover Medical School. Our project structure, consisting of a seamless process chain – starting from basic principles, through applied research and leading up to and including pre-clinical trials of the implants – ensures the scientific success of REMEDIS.

The early involvement of clinical partners analysing medical needs on the one hand and of high-performance enterprises on the other facilitates a rigorous transfer process of the results of pre-competitive research conducted by REMEDIS into clinical practice. The individual technical and methodological development processes at the interface between medicine, natural and engineering sciences also underpin the innovative strengths of the consortium.
### Project Area A
**Basic development – Biomaterials and drug delivery systems**

In order to create new therapeutic methods, Project Area A is dedicated to the development of biomaterials likely to have particularly useful qualities for local delivery of active substances. Examples include research into crosslinkable polymers for their potential to provide new types of intraocular lenses for the treatment of cataract, and ionic liquids for their use in temporary coatings. In addition, participating scientists are gaining insights into the basic mechanisms of interaction between newly developed biomaterials and their target biological structures. The use of manufacturing processes such as laser technologies to create the micro- and nano-structures of implants complete the basic development tasks of this project area.
Project Area B

Applied research into medical products with major potential for market penetration – Innovative implants with controlled, localised delivery of active substances

Project Area B implements the results of basic research: The scientists develop implants capable of delivering active substances locally, such as multi-mode stents and bioabsorbable polymer stents for vascular use. In addition to this, the knowledge emerging from Project Area A is implemented in the development of bioabsorbable micro-implants for the treatment of glaucoma and of stimulation electrodes containing active substances for pacemakers and cochlear implants.

Project Area C

Preparation of clinical trials – Organ-specific in vivo models

An important step on the way to the final use of a newly developed implant on actual patients is the establishment of organ-specific in vivo models for pre-clinical trials. This is the goal of Project Area C. It includes the imaging and cell biological analysis of ocular implants using minimally invasive techniques, the in vivo testing of differential vascular responses to multi-mode stents and the development of pre-clinical trials of glaucoma and auditory tube stents with functionalised surfaces.
Project Area Q
Development of methodologies at the interface between medicine, pharmaceuticals and technology – Cross-sectional projects

Project Area Q utilizes the development of methodologies at the interface between medicine, natural sciences and technology. Implant-specific pharmaco-logical approaches are developed in order to influence the behaviour of target cellular structures. In addition, laser micro-sintering is used to create modified surface areas and other processing technologies are being established for the coatings of the micro-implants under development. Furthermore, for morphological characterisation of implant surfaces Project Area Q provides specially adjusted procedures for micro- and nano-structure analysis.

Prof. Dr. Werner Weitschies
Ernst Moritz Arndt University of Greifswald, Institute of Pharmacy

“As pharmaceutical technologists, my group and I are responsible for ensuring that active substances are released from the implant surface in the required manner. This is to ensure that no risks arise later for the patient and that the implant does its work safely. In close cooperation with other REMEDIS partners developing new, implant-based drug release systems, we put together methods for testing them in the laboratory, while also keeping an eye on the approval testing that will be required further down the line.”
The REMEDIS partners

REMEDIS successfully combines the ideal range of collaborating partners in order to bundle their expertise in the areas of engineering, medicine and natural sciences into an integrated whole. The goal of the REMEDIS consortium is to establish an international research structure at the leading edge and to significantly enhance development skills in the area of biomedical engineering. REMEDIS combines the efforts of the following German and international research and industrial partners:

University of Rostock in collaboration with:

- Ernst Moritz Arndt University of Greifswald
- Hannover Medical School
- University of Applied Sciences Wismar
- Laser Zentrum Hannover
- Hannover Medical School
- University Medical Center Groningen
- RWTH Aachen
- Bayer MaterialScience AG
- Tepha, Inc., Lexington, MA, USA
- Institute for Implant Technology and Biomaterials
- CORTRONIK GmbH
- BIOTRONIK
- CORTRONIK GmbH
- WARNEMÜNDE
- Ernst Moritz Arndt University of Greifswald

Prof. Prof. h. c. Dr. med. Thomas Lenarz
Hannover Medical School, Ear, Nose and Throat Clinic

“REMEDIS gives us the opportunity to work together with internationally recognised experts to jointly advance implant development. The consortium concentrates and unites the strengths of its members into an innovative international powerhouse in the area of biomedical engineering.”

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Research facilities in the Mecklenburg-Vorpommern region

University of Rostock
University Medicine
Institute for Biomedical Engineering
Prof. Dr. Klaus-Peter Schmitz,
Prof. Dr. Katrin Sternberg,
PD Dr. Marian Löbler, PD Dr. Heiner Martin,
Dr. Wolfram Schmidt, Dr. Niels Grabow,
Guest Professor Axel Haubold, USA

Institute of Anatomy
Prof. Dr. Andreas Wree

Department of Ophthalmology
Prof. Dr. Rudolf Guthoff, Prof. Dr. Oliver Stachs

Department of Surgery
Division of General Surgery
Prof. Dr. Wolfgang Schareck, PD Dr. Carsten Bünger

Department of Oto-Rhino-Laryngology
Prof. Dr. Hans Wilhelm Pau

Institute of Experimental Surgery
Prof. Dr. Brigitte Vollmar

Department of Internal Medicine,
Division of Cardiology
Prof. Dr. Christoph Nienaber, Prof. Dr. Hüseyin Ince

Department of Internal Medicine, Division of
Tropical Medicine and Infectious Diseases
Prof. Dr. Emil Reisinger

Faculty of Mechanical Engineering and
Marine Technology
Department of Fluid Dynamics
Prof. Dr. Alfred Leder

Department of Materials Technology
Prof. Dr. Olaf Kelller

Department of Fluid Technology and Microfluidics
Prof. Dr. Hermann Seitz

Hannover Medical School
Ear, Nose and Throat Clinic
Prof. Prof. h. c. Dr. med. Thomas Lenarz

Laser Zentrum Hannover
Prof. Dr.-Ing. Dr.-Ing. E. h. mult. Dr. med. h. c.
Heinz Haferkamp, Prof. Dr. Boris Chichkov,
Dr. Michael Hustedt

RWTH Aachen
Institute for Textile and Macromolecular
Chemistry, DWI at RWTH Aachen
Prof. Dr. Martin Möller, Prof. Dr. Doris Klee

International research facilities

University Medical Center Groningen
Netherlands
Department of Biomedical Engineering
Dr. Theo G. van Kooten

Department of Materials in Medical Engineering
Prof. Dr. Detlef Behrend

Faculty of Mathematics and Natural Sciences
Institute of Physics
Prof. Dr. Karl-Heinz Meiwes-Broer,
Prof. Dr. Stefan Lochbrunner

Institute of Chemistry
Prof. Dr. Udo Kragl, Prof. Dr. Peter Langer

Ernst Moritz Arndt
University of Greifswald
University Medicine
Institute of Pharmacology
Prof. Dr. Heyo K. Kroemer

Department of Internal Medicine
Prof. Dr. Stephan Felix, Dr. Rilla Busch

Institute of Diagnostic Radiology
Prof. Dr. Norbert Hosten

Faculty of Mathematics and Natural Sciences
Institute of Pharmacy
Prof. Dr. Werner Weitschies

University of Applied Sciences Wismar
Institute for Surface and Thin Film Technology
Prof. Dr. Marion Wienceke

Institute for Implant Technology and Biomaterials
Warnemünde
Prof. Dr. Klaus-Peter Schmitz,
Prof. Dr. Detlef Behrend

Industry partners

BIOTRONIK Group
BIOTRONIK SE & Co. KG, Berlin, Erlangen
BIOTRONIK AG, Bülach, Switzerland
Dr. Claus Harder, Erik Trip

CORTRONIK GmbH, Warnemünde
Dr. Carsten Momma, Dr. Daniel Lootz

Bayer MaterialScience AG
Leverkusen
Prof. Dr. Hans-Wilhelm Engels, Dr. Michael Mager,
Dr. Jürgen Köcher, Chris Koppenburg

Tepeha, Inc.
Lexington, MA, USA
Dr. Simon F. Williams, Dr. David P. Martin
REMEDIS – our approach also includes regular contact and close collaboration with our business partners. Renowned and market-leading businesses such as the BIOTRONIK Group, Tepha, Inc. and Bayer MaterialScience AG form part of our network. CORTRONIK GmbH, an affiliate of the BIOTRONIK Group, is based in Warnemünde in the immediate proximity of the Institute for Biomedical Engineering of the University of Rostock.

An example of the successful development of a medical device ready for the world market is the “ORSIRO” stent manufactured by REMEDIS consortium member BIOTRONIK. The “ORSIRO” stent developed jointly at the Bülach, Erlangen, Rostock and Greifswald sites is a drug-eluting stent system for treating narrowing of the coronary arteries. It is a hybrid technology, consisting of passive and active components.

Prof. Dr. Klaus-Peter Schmitz
University of Rostock, Institute for Biomedical Engineering

“The cooperation of science with business is part of the REMEDIS consortium’s everyday life. For our academic partners, this means maintaining an orientation towards industry and markets, developing products and therapeutic procedures and preparing them for clinical use. Business partners are attracted by the skills of scientists and the facilities available at research centres and university hospitals at the REMEDIS sites. Together we have excellent chances for successfully introducing new medical devices, and thus for helping patients.”
REMEDIS is a research consortium of the University of Rostock – the oldest University in the Baltic area, founded in 1419.

The Institute for Biomedical Engineering (Director: Prof. Dr. Ing. K.-P. Schmitz), in which the REMEDIS headquarters are based, can look back on a long research tradition in the area of artificial organ replacement and biomaterials in Rostock. As a bridging institute between University Medicine and the Faculty of Mechanical Engineering and Marine Technology, the institute encompasses multiple specialties, providing the foundations needed for the work of the interdisciplinary REMEDIS consortium.

REMEDIS is also valuable to the University of Rostock for its ability to connect research and academic teaching. For example, research content flows directly into the "Biomedical Engineering" interdisciplinary Bachelor/Master degree course. In addition, REMEDIS offers upcoming scientists excellent prospects for qualification and participation in innovative research projects in the area of biomedical engineering.