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Medical Delta

Technological solutions for sustainable healthcare

Medical Delta – Life Sciences, Health & Technology

Content

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Colophon

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Technological solutions for sustainable healthcare

The COVID-19 pandemic has underlined the urgency of achieving a healthcare transition in the coming years. It has accelerated this transition by boosting the digitalization of healthcare and created new opportunities to get the right care in the right place.

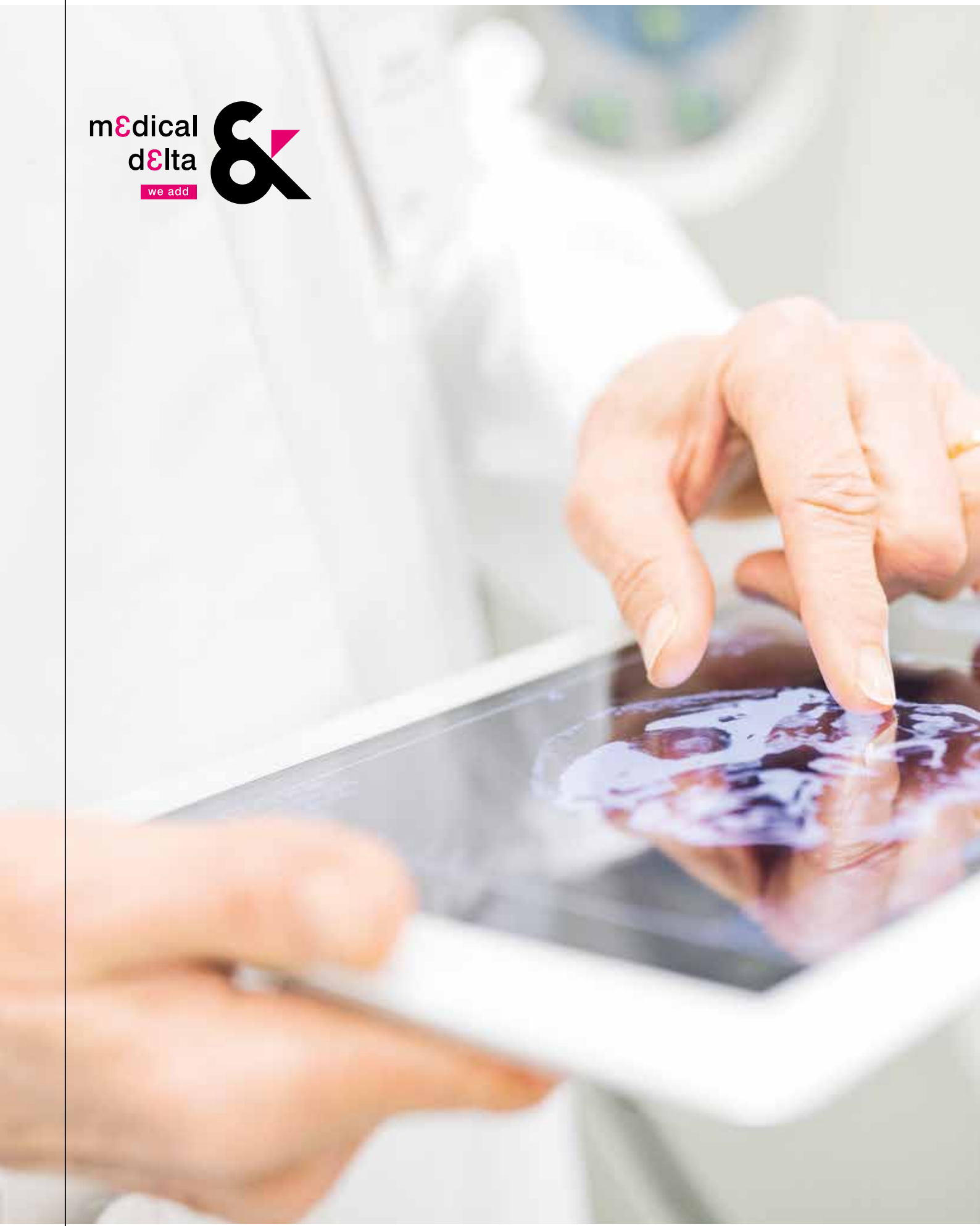
In the meantime, the average life expectancy in Europe is increasing. Due to the aging of our population and other factors, such as the increase in chronic diseases, the demand for specific care will increase in the coming years, as will the costs. At the same time, we want to live longer, in good health and condition and in a sustainable world, but the number of caregivers is declining. To keep our healthcare system sustainable, a transition is needed. In our opinion, technology plays an indispensable role in this transition.

To push this transition forward, the regional MedTech ecosystems in The Netherlands, in collaboration with universities, companies and governmental organizations, set up the MedTechNL Agenda. This agenda highlights the ambition that the MedTech sector wants to deliver: more focus on prevention and early diagnosis, more operations with minimal trauma and more care at home. Demand-driven innovation is crucial in realizing these ambitions and thus in realizing Medical Delta's contribution to the healthcare transition. Technological innovations are key, and it is of great importance that the technology itself fits into daily healthcare practice. This is only possible if scientists from different disciplines work together. Engineers and healthcare professionals collaborate, and patients' perspectives should also be taken into account from the beginning of each innovation process.

Over the past 15 years, Medical Delta has brought together scientists, engineers, medical doctors, small and medium enterprises, large companies, municipal and provincial governments, science funders and many others to collaborate. Medical Delta has captured the best scientists in their fields in 16 different consortia that are working together on 16 interdisciplinary scientific programs. Their research takes place at locations such as the BioScience Park in Leiden, the TU Delft campus and the Convergence HealthTech campus in Rotterdam. Acceleration of innovation takes place in 9 Medical Delta Living Labs, where scientists, companies, healthcare professionals and patients collaborate.

This magazine introduces the Medical Delta scientific programs. Each program aims to achieve ambitious goals in the coming years. You will learn how these Medical Delta programs are helping to accelerate technological solutions for sustainable healthcare.

Prof. dr. Frank Willem Jansen
Chairman Medical Delta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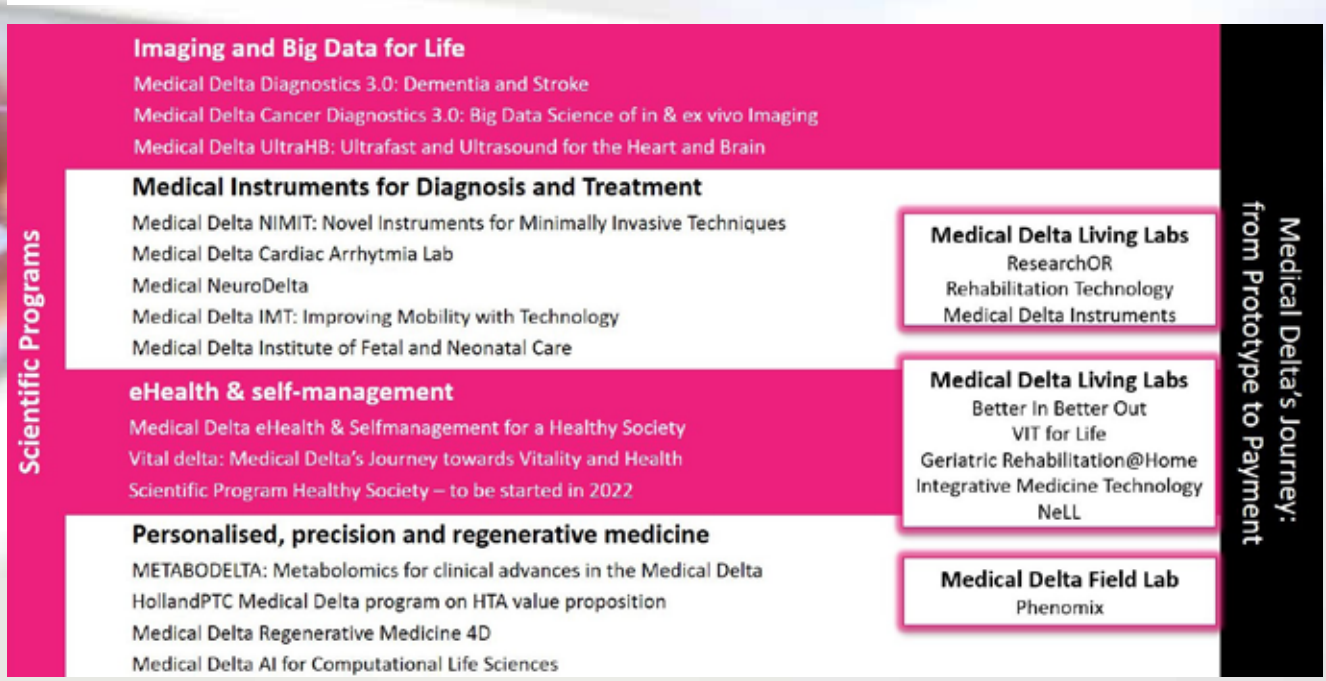
Medical Delta overview

Medical Delta brings together knowledge and experience from three universities, two academic medical centres and four universities of applied sciences in the province of Zuid-Holland. Top researchers from these institutions work together on technological solutions for sustainable healthcare, from molecule to reimbursement. A strong, outstanding scientific and business community, Medical Delta aims at creating and exchanging knowledge, stimulating and facilitating talent, and accelerating the valorisation and implementation of research results and innovations into healthcare practice. To ensure this, collaborations include several living labs, real-life settings in which healthcare innovators develop and test new ideas together with end-users.



Medical Delta Diagnostics 3.0: Dementia & Stroke

Dementia and stroke: how deep learning algorithms make faster diagnoses

Prof. dr. Wiro Niessen
Biomedical Image Analysis (EMC/TUD)

Dr. Frans Vos
Imaging Physics/Radiology (TUD)

Prof. dr. Mark van Buchem
Radiology (LUMC)

Dementia and stroke impose an enormous burden on individuals and society. To address this challenge, tools are required to identify individuals at risk – ideally very early in the disease process, to support the trend towards prevention.

Image-based techniques are among the most promising of the technologies available to improve diagnosis, prognosis and treatment selection. In particular, the application of imaging technology combined with the use of advanced data analytics, such as deep learning, will be helpful. This way, imaging biomarkers will be combined with other biomarkers and clinical data. Initially, dementia and stroke will be addressed in the Medical Delta Diagnostics 3.0 program.

Dementia

Dementia is a brain disorder characterized by loss of cognitive function such as thinking and remembering, which affects people's daily functioning. Using MRI imaging techniques and advanced analysis techniques, researchers want to understand better how dementia, such as in Alzheimer's disease, develops. In this project, the researchers are especially interested in changes in the micro- and macrostructure of the brain, as measured with diffusion MRI, MR fingerprinting and other quantitative techniques. Using images and data from large population studies and techniques such as deep learning and multi-component parameter mapping, they estimate novel imaging biomarkers such as the microstructure within white matter tracts, tissue volume fraction, myelin water fraction, and small vessel disease imaging markers such as lacunar infarcts and white matter hyperintensities. These imaging biomarkers are expect to lead to more accurate and faster diagnosis and prognosis to improve disease treatment and support steps towards disease prevention.

Stroke

A stroke occurs when the blood flow to parts of the brain is cut off. This can happen due to a blood clot that blocks the blood flow or due to bleeding in the brain. These two different types of stroke require different treatments, and the right treatment must be selected.

Accurate and objective imaging systems can support treatment selection in the acute stage of stroke by determining which type of stroke the patient has dealt with, thus optimizing the treatment selection process.

Future perspective

In the future, a scan of a patient will not only be inspected and interpreted by the doctor quantitatively; clinical decision making will be supported qualitatively based on deep learning algorithms that have been trained on previous cases.

In this way, doctors can detect a disease in an early phase, make a diagnosis faster, determine the best possible treatment more precisely and monitor the disease over a longer time.

“In this program we aim to learn optimally from imaging and healthcare data from previous patients, to treat the next generation of patients more effectively”, says Wiro Niessen, professor in Biomedical Image Analysis at Erasmus MC and TU Delft.

Collaboration

This program brings together experts in different fields, such as imaging physicists, medical image analysis experts and clinicians, with the joint aim of developing, implementing and validating imaging techniques to improve patient care. The research relies on data and clinical expertise available through collaborations with population and clinical studies.

“Through the collaboration across the different disciplines of the Medical Delta institutes, we create a whole which is greater than the sum of its parts,” concludes Niessen.

Using images and data researchers can estimate if a person is at high risk of developing dementia

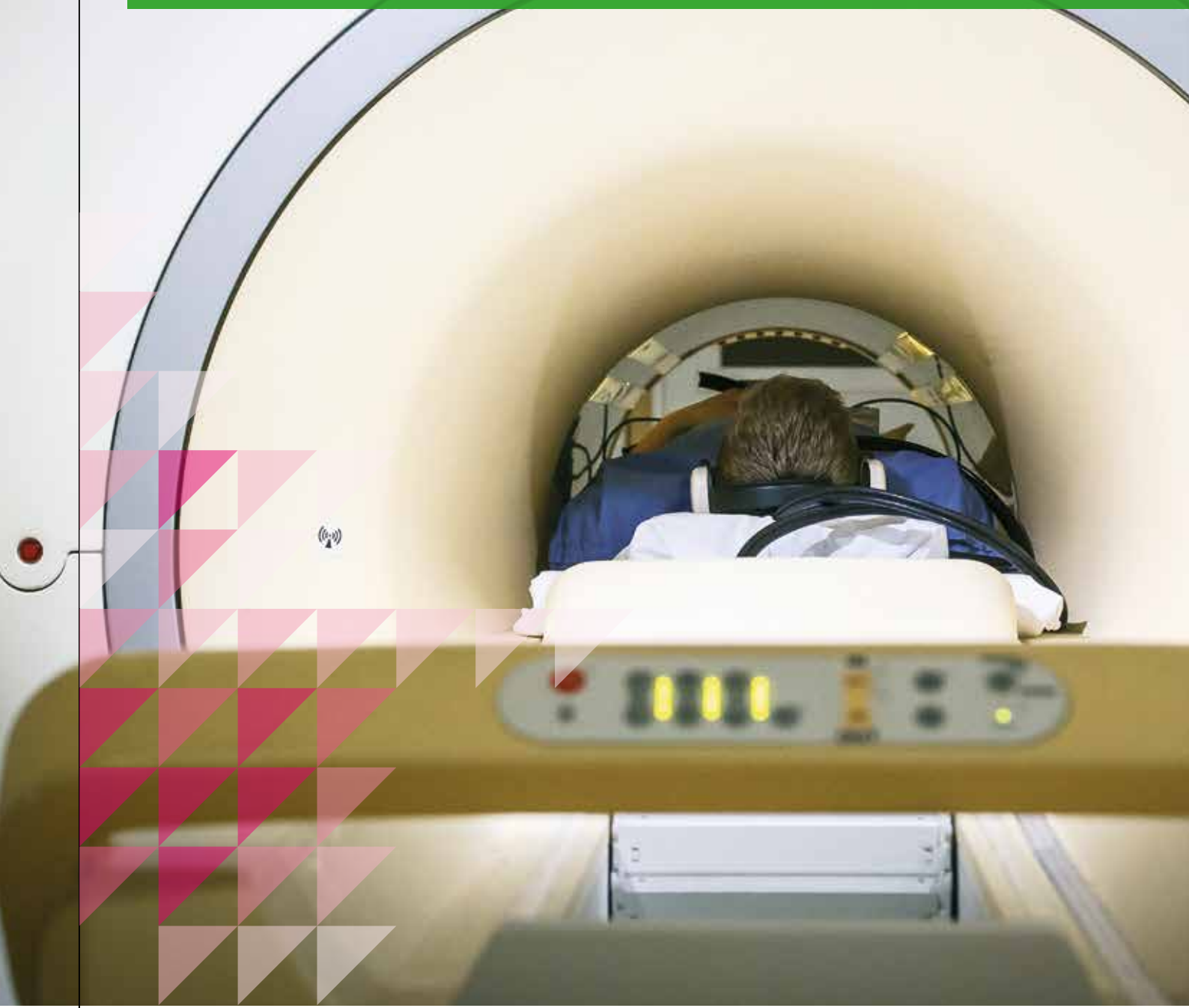
Medical Delta Cancer Diagnostics 3.0: Big Data Science of in & ex vivo Imaging

Faster and better cancer diagnostics with the help of advanced imaging techniques and machine learning

Prof. dr. ir. Matthias van Osch
Radiology (LUMC)

Prof. dr. Marion Smits
Radiology and Nuclear Medicine (EMC)

Dr. Jeroen Kalkman
Imaging Physics, Computational Physics (TUD)



Different patients with the same type of cancer can respond very differently to a specific treatment, and as a result, outcomes vary greatly between patients. Many clinical, pathological, and genetic factors make the diagnosis and choosing the right treatment for an individual patient increasingly complex.

In Medical Delta Cancer Diagnostics 3.0, the newest imaging techniques will be used together with machine learning to provide diagnosis faster and better.
At the moment, biopsies are taken to obtain information about the morphological, genetic and molecular characteristics of the tumor. Taking a biopsy is an invasive method and typically only a few 2D slices of the biopsies are imaged and analysed. Researchers from the Medical Delta Cancer Diagnostics 3.0 program believe diagnosing tumours could be improved by characterizing brain tumors and biopsies in 3D and extracting more information from them. The researchers do this by applying new MRI and optical imaging techniques.

Advanced MRI techniques

Within this program, which initially focusses on brain tumors, advanced MRI techniques are used to gather relevant information about the tumor. The researchers do this using standard in vivo MRI scans, as well as the newest MRI techniques and hardware. “For example, we will use a 7 Tesla MRI, which has a higher magnetic field and provides images with a better resolution and more information,” says Thijs van Osch, professor in the radiology department at LUMC.
The aim of comparing information gathered through conventional biopsies and information visible on the MRI scans is to deduce the genetic and molecular characteristics of the tumor from the MRI-data: a ‘virtual biopsy’.

Machine learning

In addition to obtaining better MRI images, this Medical Delta research program links them to machine learning to unlock all the information hidden in the different MRI-contrasts. Ultimately, this is expected to contribute to an even better treatment choice tailored to the individual patient, and to enable better monitoring of the tumor during treatment.
“It would be of enormous added value if we were able to better predict on the basis of all those MRI characteristics how the tumor will evolve and what that means for the patient in the future,” says Johan Koekkoek, neuro-oncologist in LUMC and MC Haaglanden.
For doctors it would very helpful to get guidance in making the right diagnosis and selecting the best treatment. “Currently, diagnosis is based on a visual assessment of the MRI scan by a radiologist,” says Marion Smits, professor of Neuroradiology at Erasmus MC. “Machine learning techniques will help us to include a lot more information from the MRI scan in our assessment, and to make such diagnoses more objectively.”

Optical imaging

A problem with ex-vivo conventional biopsies is that it is based on the processing and inspection of only a few 2D slices. This is making this technique slow, costly and destructive. In addition, only a minute fraction of the entire tissue is inspected and large scale structures can be easily missed or misidentified.
In this program the researchers will work on developing 3D imaging of whole tissue biopsies. “Imaging of the tissue in its native 3D state is expected to be more information rich and is expected to improve clinical diagnosis, and thereby facilitate treatment selection,” says dr. Jeroen Kalkman, Associate Professor in the Department of Imaging Physics (TU Delft).

Collaboration

The close collaboration that has been established between Erasmus MC, TU Delft and LUMC with MRI experts, computational scientists, engineers and clinicians is a key success factor for realizing the ambition to realize 3D image-based diagnosis of cancers. The support to provide a personalized treatment selection and treatment monitoring of brain tumors is envisioned as a template for similar Medical Delta innovations in the care of other cancer types.

Medical Delta ultraHB: Ultrafast and Ultrasound for the Heart and Brain

Ultrafast ultrasound for the heart and brain

Dr. David Maresca
Imaging Physics (TUD)

Dr. Annemien van den Bosch
Cardiology (EMC)

Prof. dr. Aad van der Lugt
Radiology & Nuclear Medicine (EMC)

Renewing ultrasound techniques will open doors for a whole range of diagnostic and therapeutic possibilities in the cardiovascular and neurological field. The Medical Delta program Ultrafast Ultrasound for the Heart and Brain offers excellent opportunities to tackle the major existing and evolving healthcare threats.

In the Netherlands, it is expected that 195,000 people will be diagnosed with heart failure in 2025, leading to a high number of hospitalizations and deaths. Atherosclerosis is a disease in which plaque builds up inside arteries. If plaque ruptures in an artery linked to the brain, this can lead to stroke. In neurology, brain tumors are also a large threat. In the Netherlands alone, more than 1,000 patients were diagnosed with a brain tumor in 2018.

The program focuses on three healthcare threats: heart failure, atherosclerosis and neurological disorders.

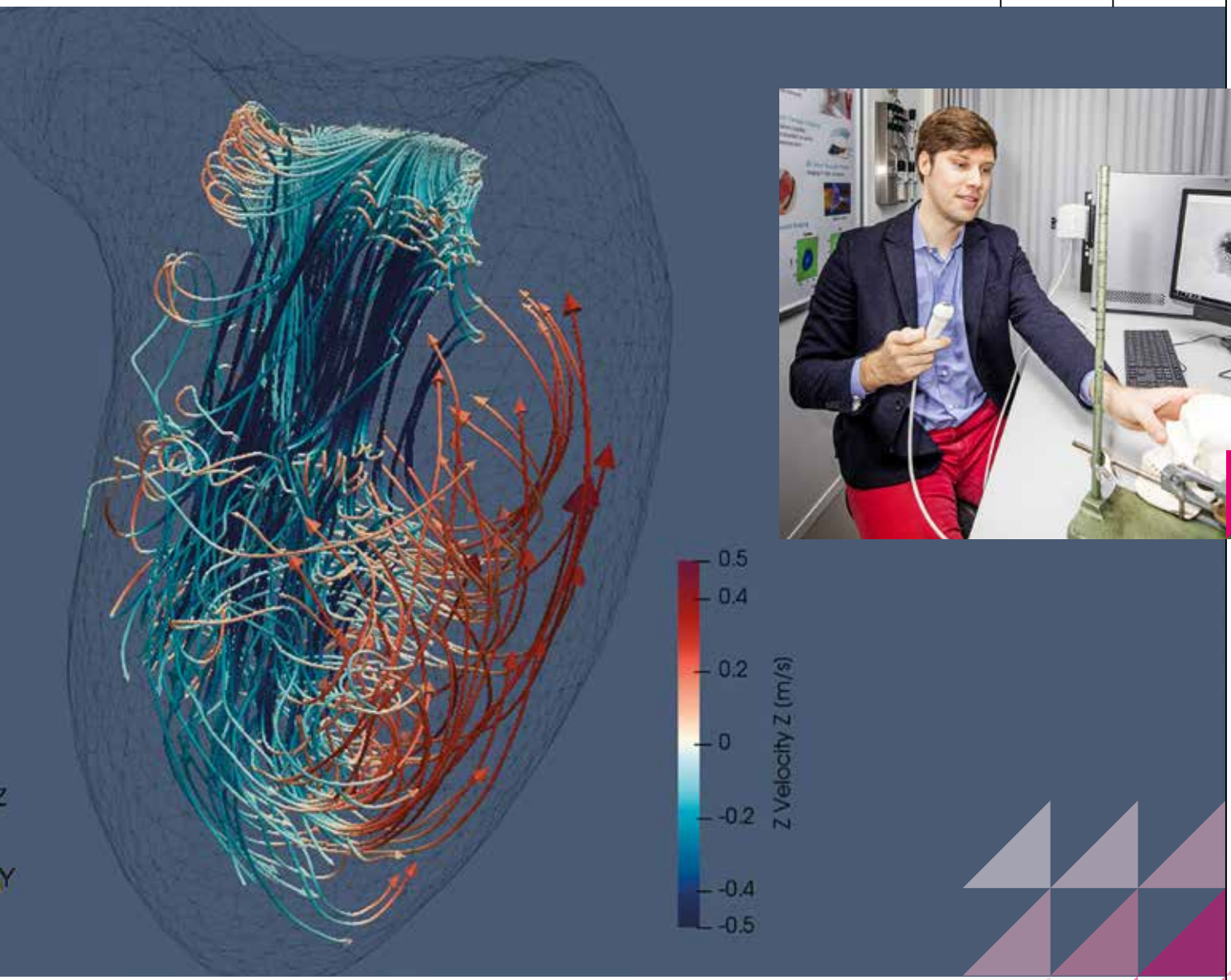
Ultrasound

Ultrasound is the most commonly used medical imaging technique. It is harmless, relatively cheap and, because it uses real-life images, it gives immediate diagnostic feedback. The technology is developing rapidly: new ultrafast imaging brings the functioning of the heart and brain directly into view, and special contrast agents make new diagnoses and treatments possible.

Technological developments

Three technological developments are expected to have an impact in this field. The first is ultrafast ultrasound imaging, involving thousands of images per second. This makes the blood flow in the heart and through organs and even the activation of brain parts directly visible (“functional ultrasound”).
The second focuses on the realization of new sensors, making ultrasound into a truly 3D modality. At the moment, almost all applications show a 2D visualization; this creates a limitation for treatment. In this program, 3D image reconstruction will be used, to improve diagnosis and treatment options in healthcare.

The third is the development of ultrasound contrast agents that target disease-specific markers and can transport drugs with them.



This program will offer diagnostic methods with excellent opportunities to tackle the major existing and evolving healthcare threats, such as heart failure, atherosclerosis and neurological disorders. The technological breakthroughs will also be directly clinically tested in the cardiology and neuroradiology departments at Erasmus MC. The expected results will represent a huge step forward for clinical practice, where doctors eagerly await the new possibilities these techniques offer.

Collaboration

Erasmus MC, TU Delft and LUMC are involved in this program, which is also very well linked to two Medical Delta living labs. The first is Medical Delta Instruments, focuses on the use of minimally invasive instruments. Ultrafast ultrasound imaging can be used during minimally invasive procedures for real-time tissue characterization – this is important, for example, in surgical procedures. The second is Medical Delta ResearchOR, which focusses on the use of protocols and measurement systems in the Operating Room. Ultrafast ultrasound imaging can be used for real-time monitoring during carotid, brain or cardiac surgery or procedures.

The expected results of this program will represent a huge step forward for clinical practice

Medical Delta Field and Living Labs:
between prototype and practice

The Medical Delta Living Labs form a crucial link in the healthcare innovation chain. They test companies' and healthcare institutions' promising technological healthcare solutions with healthcare professionals and patients in real-life environments. Practical questions are the foundation for the public-private projects the Living Labs take on. The interdisciplinary nature of the work is characteristic of the Living Labs' approach: health lecturers collaborate with technology lecturers from other universities of applied sciences. They conduct their research together with end users, healthcare institutions and companies, and through this collaboration, the Living Labs have a social and economic impact on the region. The Living Labs also provide a bridge to research carried out at Medical Delta's academic knowledge institutions.

Please find out more about the Medical Delta Field and Living Labs on our website:

Locations Field- and Living Labs

- Geriatric Rehabilitation@Home
- Integrative Medicine Technology
- Medical Delta Instruments
- Rehabilitation Technology
- Better In Better Out
- OnderzoeksOK
- VIT for Life
- Phenomix
- NeLL

Medical Delta Living Lab VIT for Life

Paying more attention to health and prevention will reduce the pressure on our healthcare system. Health apps and innovations that stimulate a healthy lifestyle and exercise do not reach all people with an increased risk of lifestyle-related complaints. Medical Delta Living Lab VIT for Life focuses on these groups and aims to make inaccessible apps or complicated technology user-friendly. In addition, it integrates these technologies into the broader range of interventions provided by doctors and physiotherapists.

At Medical Delta Living Lab VIT for Life, Rotterdam University of Applied Sciences, The Hague University of Applied Sciences, Stichting WMO Radar and Kinderfysiotherapie Regio Westland work together with patients and companies. The Living Lab also collaborates with universities affiliated with Medical Delta.

Medical Delta Living Lab Better In Better Out

The fitter someone enters a cancer treatment program, the higher their chance of a faster recovery. Medical Delta Living Lab Better In Better Out focuses on researching and developing e-health applications and technologies that improve the fitness of cancer patients.

At Medical Delta Living Lab Better In Better Out, The Hague University of Applied Sciences, Rotterdam University of Applied Sciences, HMC Anthoniushove and the University Cancer Center Leiden-The Hague work together with companies, healthcare professionals and patients on technological solutions for healthcare. The Living Lab also works on a project basis with researchers from academic knowledge institutions, including TU Delft, Maastricht University and Erasmus MC.

Medical Delta Living Lab Geriatric Rehabilitation@Home

E-health applications can significantly ease the pressure on geriatric rehabilitation and improve care. There is also a greater need for medical specialist rehabilitation. Medical Delta Living Lab Geriatric Rehabilitation@Home focuses on the development of e-health applications that promote home rehabilitation of the elderly. At Medical Delta Living Lab Geriatric Rehabilitation@Home, Inholland University of Applied Sciences, The Hague University of Applied Sciences, Rotterdam University of Applied Sciences, Stichting Omring and Pieter van Foreest work together with companies, care institutions, informal caregivers and elderly people. The Living Lab also works on a project basis with researchers from academic knowledge institutions.

Medical Delta Living Lab Integrative Medicine Technology

For some health issues, such as antibiotic resistance and pain complaints due to chronic diseases, regular medicine offers insufficient (good) solutions. Medical Delta Living Lab Integrative Medicine Technology is exploring non-pharmacological, integrated prevention and treatment approaches, such as the use of natural products, to make Integrative Medicine more available, accessible and acceptable in a responsible way. The University of Applied Sciences Leiden, University of Applied Sciences Rotterdam, NVAA and Cure + work in this Living Lab together with patients, healthcare professionals and companies. The Living Lab also works on a project basis with researchers from academic knowledge institutions.

Medical Delta Living Lab ResearchOR

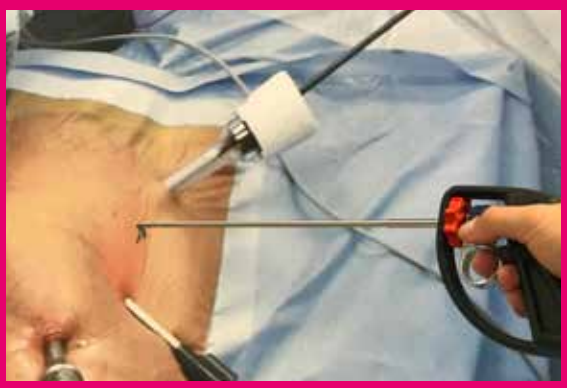
In the Medical Delta Living Lab ResearchOR, processes and systems are developed and validated to increase and guarantee efficiency and patient safety in the operative process. An operating room with measuring equipment and sensors is used for this. Reinier de Graaf Hospital and TU Delft are involved in this Living Lab.

Medical Delta Living Lab Rehabilitation Technology

Smart technology such as robotics, sensors, artificial intelligence and e-Health solutions offer opportunities for intensive rehabilitation. This can be done at home, in a rehabilitation center or at the physiotherapist. The Medical Delta Living Lab Rehabilitation Technology gives companies and other healthcare developers the opportunity to test their innovations together with end users and to develop them in practice. They can also take up questions from healthcare practice.
The University of Applied Sciences the Hague, TU Delft, LUMC, Erasmus MC, Sophia Rehabilitation Center, Rijndam Rehabilitation Center and the Rijnlands Rehabilitation Center collaborate in this Living Lab.

Medical Delta Fieldlab Phenomix

A good picture of one's current health can be created by measuring metabolic products such as amino acids, hormones, glucose and adrenaline. With the resulting 'metabolic profiles', doctors can make earlier diagnoses and personal treatment plans. In the Medical Delta Fieldlab Phenomix, companies, healthcare institutions and scientists work together on practical applications of metabolomics research. Leiden University and Erasmus MC participate in the Fieldlab together with various companies from the biotech and pharmaceutical industries. It is located at the Leiden Bio Science Park and is being established with an EFRO subsidy. InnovationQuarter, Medical Delta and others are involved in setting up and expanding the Fieldlab.



Living Lab Medical Delta Instruments

Minimally invasive medical instruments ensure smaller scars, less trauma, less blood loss, faster recovery and a lower risk of infection. The Living Lab Medical Delta Instruments connects technical and clinical Medical Delta researchers with companies and supports them in the development of high-quality prototypes of medical instruments.
TU Delft, Erasmus MC, LUMC, AMC, Reinier de Graaf Hospital and LIS (Leiden Instrument Makers School) collaborate in this Living Lab.

Medical Delta National eHealth Living Lab (NeLL)

E-health plays an important role in making healthcare future-proof. To make digital care part of regular care, Medical Delta Living Lab NeLL facilitates scientific research into e-Health solutions and their validation and testing. In addition, the Lab shares news, insights and knowledge.
Within this Living Lab, patients, caregivers, consumers, students, scientists, entrepreneurs, organizations and institutions work together on tomorrow's healthcare.

Medical Delta NIMIT: Novel Intruments for Minimally Invasive Techniques

Creating standardized methods to develop minimally invasive instruments

Prof. dr. Frank Willem Jansen
Gynaecology (LUMC/TUD)

Prof. dr. Gijs van Soest
Cardiology (EMC)

Prof. dr. Jenny Dankelman
BioMechanical Engineering (TUD/LUMC)

Instruments should be produced simpler and support sustainable surgery

In minimally invasive surgery, the surgeon operates through the small incisions. Compared to open surgery, minimally invasive surgery results in smaller scars, less trauma, less blood loss, faster recovery and a lower risk of infection.

In addition to the direct benefits for the patient, there are economic benefits too: shorter hospital stays and quicker recovery mean the patient can go back to work faster. Minimally invasive surgery relies on the minimally invasive instruments that are designed and developed in academia. Currently, many instruments being developed have unique designs and advanced functionalities. However, these instruments lack standardization, they are complex, expensive and difficult to manufacture. This creates hurdles for regulatory assessment and certification and delays innovation benefits for the patient. The Medical Delta NIMIT program aims to design minimally invasive instruments that enable a rapid innovation cycle based on wel characterized, documented process steps and standardized tests. This will eventually lead to quicker implementation in clinical practice. In order to achieve this, new design, manufacturing and assembly methods should be developed for minimally invasive instruments. The instruments produced should be simpler ad should support sustainable surgery.

Modular instruments

“As academic developers, we realized that we do not get far enough in the translational trajectory to transfer our technologies to clinical practice,” says Gijs van Soest, Associate Professor at the Department of Cardiology at Erasmus MC.

“It is a shame to throw away every part of a good technical device that still functions well, after having only been in the body for half a minute,” says Tim Horeman, Assistant Professor at the department of Biomechanical Engineering at TU Delft.

Circular design can help reduce this waste. The circular economy can be applied on three levels: reuse the instrument as a total assembly; reuse certain components or reuse the materials. The goal of this project is to develop a modular design approach for a variety of instruments for several purposes, for example the development of simple and smart hardware components with well-controlled properties that can also be reused for other applications.

Phantom models

The instruments must be tested following a set of regulations. In the Medical Delta program, phantom models will be developed. Phantoms are artificial structures representing human tissues, and they can be used to test medical instruments for function and usability. Such phantoms could also be used in place of some of the animal and clinical trials of the instruments. “It would be preferable if phantoms themselves were standardized and certified by regulatory bodies. This would contribute to the certification of medical instruments,” says John van den Dobbelsteen, Associate Professor at the department of Biomechanical Engineering at TU Delft.

When creating a new instrument, it is important to keep documenting the practical workflows of existing instruments and learn lessons from those devices. This should result in a standardized method for development.

It would be ideal to have a prototype lab where instruments can be made in small, reproducible series. “We don’t want to create and test instruments to have the perfect picture for a scientific paper, we want to test the instruments to be used in clinical practice,” says Van Soest.

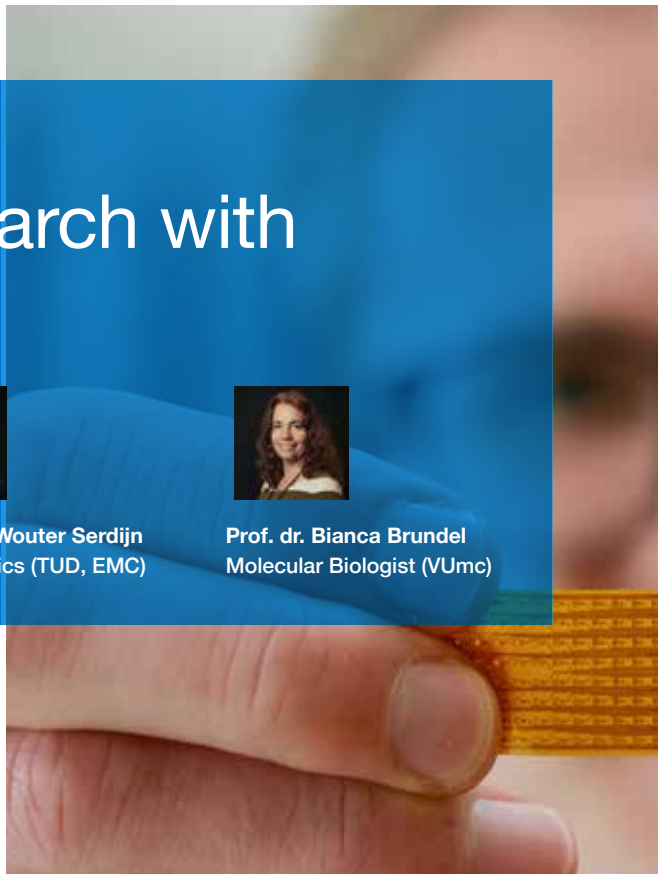
Collaboration

In this consortium, TU Delft and Erasmus MC provide the technical knowhow and labs with required equipment. LUMC and Erasmus MC provide the knowledge for safe application. Medical Delta Living Labs ResearchOR and Medical Delta Instruments are also connected to this consortium.

Because this program leads to standardized methods to develop instruments faster and better following regulations, the results can also be of value for other programs at Medical Delta.

Medical Delta Cardiac Arrhythmia Lab

Cardiac arrhythmia research with use of new techniques



Prof. dr. Natasja de Groot
Cardiologist-Electrophysiologist (EMC, TUD)

Prof. dr. ir. Alle-Jan van der Veen - Signal Processing (TUD)

Prof. dr. ir. Wouter Serdijn
Bioelectronics (TUD, EMC)

Prof. dr. Bianca Brundel
Molecular Biologist (VUmc)

The number of patients diagnosed with cardiac arrhythmia is rapidly increasing due to ageing, obesity, diabetes and elevated blood pressure. Cardiac arrhythmia is therefore the cardiovascular epidemic of the 21st century. Treatments are often not successful, but a new patient-specific therapy can improve existing treatments.

Cardiac arrhythmia is the cardiovascular epidemic of the 21st century. The number of patients diagnosed with cardiac arrhythmia is rapidly increasing due to ageing, obesity, diabetes and elevated blood pressure.

Providing a patient-specific therapy can improve treatment

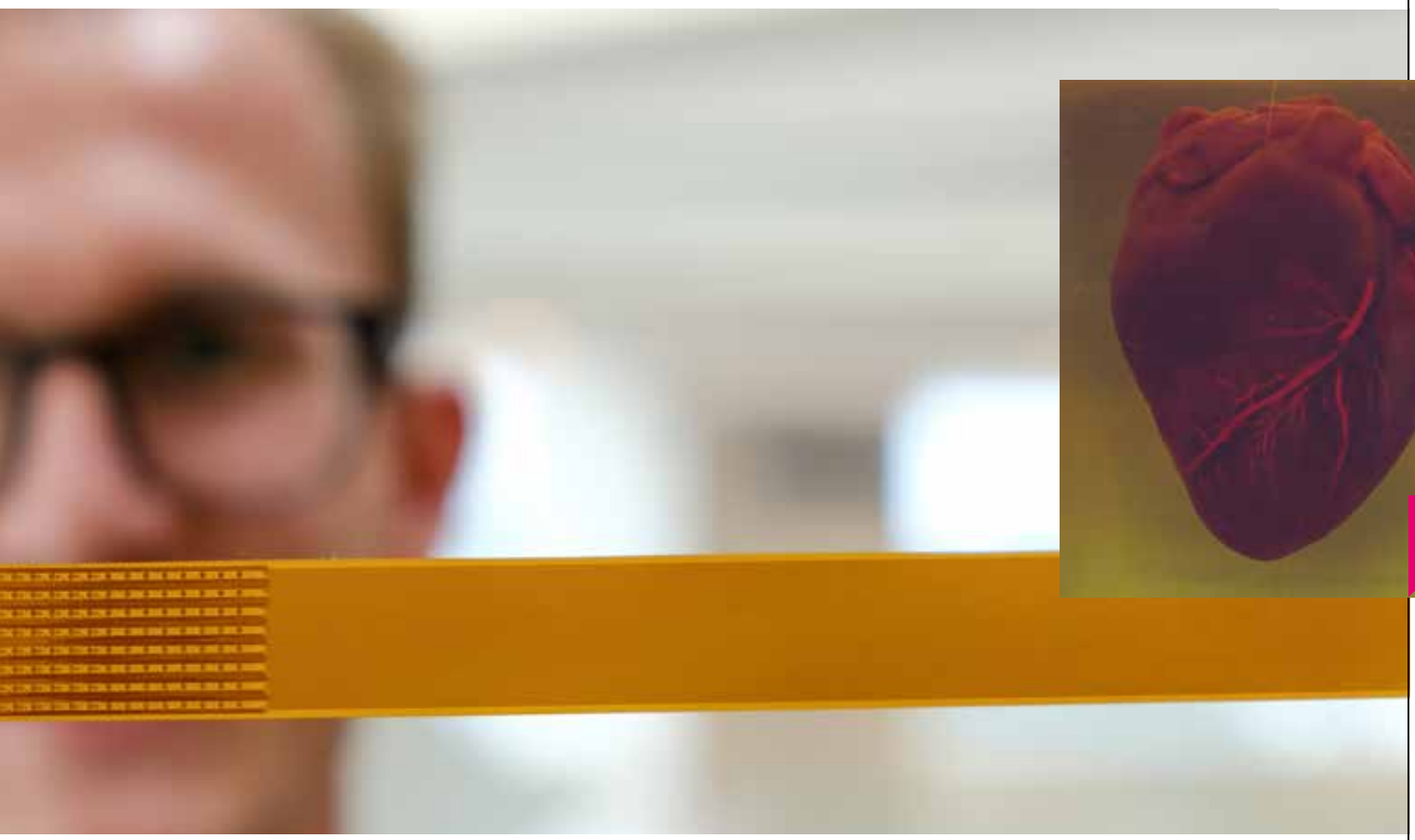
Atrium fibrillation is the most common arrhythmia. It is a progressive disease, which means that episodes of arrhythmia progress from short-lasting episodes to episodes which are continuously present and no longer terminate spontaneously. Atrium fibrillation may cause stroke and heart failure and is even associated with death.
Treatments are often not successful, but a new patient-specific therapy can improve existing treatments. This can be achieved by measuring the degree of electropathology ('staging the arrhythmia'). However, this is still not yet possible because there are no diagnostic tools to measure electropathology. It is therefore also not possible to recognize patients at risk of arrhythmia early. In addition, there are no therapies specifically targeting electropathology.

Treatment of Arrhythmia

Electrical signals recorded from young hearts usually have a simple morphology, as electrical waves propagate smoothly through cardiac tissue. Over the years, these electrical signals may become more complex (electropathology) due to damaged cardiac tissue. When the degree of electropathology exceeds a certain threshold, cardiac arrhythmia may occur. Treatment of cardiac arrhythmia is still often not successful, says Natasja de Groot, professor and cardiologist-electrophysiologist at Erasmus MC. Current treatment consists of either an 'electrical shock' to restore the normal heart rhythm, drugs or ablative therapy (eliminating the cardiac tissue that is causing arrhythmia). Unfortunately, these therapies have side-effects and are only moderately effective.

Unravel electropathology

The aim of the Medical Delta Cardiac Arrhythmia Lab is to reduce the cardiac arrhythmia burden by unravelling arrhythmia-related electropathology and designing and testing novel bio-electrical diagnostic



tools and therapies targeting electropathology. This enables staging of the cardiac arrhythmia and selection of the appropriate treatment in the individual patient, thereby improving therapy outcome.
A first step is to unravel electropathology by quantifying electrical parameters. For this purpose, a 192 electrode-array has been designed to record electrical signals directly from the surface of the heart during open heart surgery. Advance signal processing techniques are then used to comprehend electrical activation patterns during arrhythmia. Linking electrical signals with the structure of cardiac tissue is essential to unravel the mechanisms of arrhythmia. The future goal is to assess the degree of electropathology using non-invasive mapping techniques.

Arrhythmia-on-a-chip

To further unravel the mechanisms of arrhythmia, this consortium aims to design an arrhythmia-on-a-chip platform enabling the investigation of electrical conduction in relation to e.g. genetic defects.

Lowlands center for Bioelectric Medicine

The Lowlands center for Bioelectric Medicine, established by prof. Natasja de Groot and Dr. Yanick Taverne aims to restore a healthy, bio-electrical function of the heart by capturing, analyzing and modulation of an individual's bioelectronic signals.
The goals are to:

- create organ specific bioelectrical atlas by analyzing bio-electrical signaling governing organ (dys) function in a subset of diseases
- develop and test interface (diagnostic) technologies, including electrode-based interfaces for remotely monitoring bio-electrical function, implantable, shape adaptable electrode-based interfaces for monitoring of bioelectricity function of organs, and miniaturized electrode-based interfaces for integrated bioelectronic therapies
- establish therapeutic feasibility.

The scope of the Lowlands Center for Bioelectric Medicine is not confined to one organ but currently also extends to other organs, e.g. the brain, skin, intestines and bladder. Research facilities available in this lab include ex-vivo-heart-perfusion set up and biomimetic systems.

Collaboration

This program is a collaboration between biologists, engineers and medical doctors from Erasmus MC, LUMC and TU Delft. They combine their unique expertise on advanced signal recording and processing techniques, cardiac mapping tools and arrhythmia related molecular mechanics.

Medical NeuroDelta: Ambulant Neuromonitoring for Prevention and Treatment of Brain Disease

Neuromonitoring for prevention and treatment of brain disease

Prof. dr. Arn van den Maagdenberg
Geneticist (LUMC)

Prof. dr. Chris de Zeeuw
Neuroscience (EMC)

Prof. dr. ir. Wouter Serdijn
Bioelectronics (TUD/EMC)

High-frequency ultrasound would allow monitoring throughout the day in the home environment, which would be unique in the world

Brain disorders have a disastrous influence on people's lives, but they are notoriously hard to study and difficult to treat.
For example, migraine, which is characterized by repeated attacks of severe headache, is difficult to investigate in patients, because it is impossible to predict when an attack will strike.

When patients are asked to go to the hospital to investigate their brain disorder, they will often notice they do not get an attack. This happens because the hospital setting is so different from the patient's natural environment. "In order to better understand the disease, it is important that the patient's brain activity can be measured over a longer period of time in their home environment, preferably using a non-invasive method," says Arn van den Maagdenberg, professor of molecular and functional neurogenetics at LUMC.
The same holds for autism, a developmental disorder that starts in young children. "Autism is caused by a disturbed interaction between the cerebellum and cerebrum. People with autism have problems with social interaction and they show repetitive behavior. We need better means to monitor how the brain deteriorates in autism," says Chris de Zeeuw, professor and head of the Department of Neuroscience at Erasmus MC.

Observing patients in their home environment

In this Medical Neurodelta program, researchers focus primarily on autism and migraine – two disorders with widespread brain dysfunction. For both disorders, it is important to observe patients in their home environments to understand why disease worsens over time or how attacks begin. A non-invasive method would provide a much wider time window in which brain activity can be studied, giving doctors and scientists extremely valuable insights.

Wireless long-term neuromonitoring systems

The Medical Neurodelta program focuses on the development of wireless long-term neuromonitoring systems to register brain activity. Bio-electronics, acoustrodes and optrodes in combination with artificial intelligence and machine-learning will be applied for diagnosis and treatment.
The new system should not only monitor brain activity, but it should also modulate brain activity. Advances in light probes and ultra- sound, made at TUDelft, make this feasible. In Rotterdam, within CUBE, Medical Neurodelta researchers have already started to use high-frequency ultrasound to measure the activity in large parts of the brain; within the project, they will use low frequencies to stimulate specific brain areas to correct brain activity. According to professor De Zeeuw, ultrasound would also allow monitoring throughout the day in the home environment, which would be unique in the world. Compared with MRI, for example, this would be much easier – it would not be possible to place an MRI scanner in a patient's house.

Testing in mice

In the program, ways to monitor and modulate brain activity will be first tested in mice, paving the way for clinical applications in humans. Testing in mice is already being done, but these experiments are conducted in non-natural settings.
Professor De Zeeuw asks: "If you investigate autism with mice housed in isolation, how can you see the effects of an intervention?" In this new study, researchers will make use of their recently developed FlashTrack system, in which individual mice can move freely and can be easily identified within a group. Using this system, several mice can be put together and followed over time.

Collaboration

In this consortium, Erasmus MC, TU Delft and LUMC are collaborating. According to professor Van den Maagdenberg, the Medical Delta area is small enough that there is a regular crossover and large enough to incorporate different expertise and make real progressing. It is a unique opportunity to create added value.
In other projects within the overall Medical Neurodelta program, other brain diseases, such as epilepsy and brain dysfunction in infants, are also being investigated. The same technology can be applied to investigate these disorders.

Medical Delta: Improving Mobility with Technology

Improving mobility with technology

Prof. dr. ir. Jaap Harlaar
Clinical Biomechatronics (TUD/LUMC/EMC)

Prof. dr. Gerard Ribbers
Neurorehabilitation (EMC)

Prof. dr. Frans van der Helm - Biomechatronics & Bio-robotics (TUD/LUMC)

Prof. dr. Sita Bierma
General Practice (EMC)

Prof. dr. Rob Nelissen
Orthopaedics (LUMC/TUD)

Our society is aging. Motoric disabilities increase with age, which means there will be more and more people with restricted mobility. The Medical Delta Improving Mobility with Technology program focuses on the development of accurate diagnostics and treatments to improve mobility.

This program consists of two tracks: the rehabilitation track and the orthopaedics track, each with three themes.

Rehabilitation

The demand for care is expected to keep growing and to become increasingly complex. Stroke belongs to the five diseases with the highest annual care costs. As the society is aging, the number of stroke patients is expected to increase 34% between 2015 and 2035. The rehabilitation track focuses on improving effectiveness and efficiency of motor rehabilitation post stroke.
The way to move forward is to combine the expertise of TU Delft, Erasmus MC, and Erasmus University with Rijndam rehabilitation and Laurens geriatric rehabilitation on developing user-centered technology-based interventions. The sustainability of these innovations depends on factors such as complexity of settings and attitudes and beliefs of both clinicians and patients.

Orthopaedics: multiscale modelling

The second track focuses on orthopedics: the safety of arthroplasties, sports injuries and, in particular, osteoarthritis. Osteoarthritis is the leading cause of physical disability worldwide and involves the degeneration of joint cartilage. Working together, researchers from the Medical Delta combine their expertise in epidemiology, the biomechanics of gait, tissue and cell research, and dynamic imaging techniques. In this project, the researchers focus

on multiscale modelling, in which biomechanical computational models are made at all levels and combined to gain better insights into the effects of load on cartilage.

Precision diagnostics

Choosing the right therapy to improve patients' mobility requires knowledge of the etiology. This 'precision diagnostics' is a focus for both tracks. "We want to maximize the treatment effect by selecting the optimal option; we don't want to over-treat or under-treat the patient," says Jaap Harlaar, professor of Clinical Biomechatronics at TU Delft.

We want to maximize the treatment effect by selecting the optimal option

Collaboration

In this consortium, Erasmus MC, TU Delft and LUMC will collaborate closely. The Medical Delta Living Labs will also be involved in early prototype testing.

Medical Delta Institute of Fetal & Neonatal Care

Preventing morbidity and mortality for both mother and child

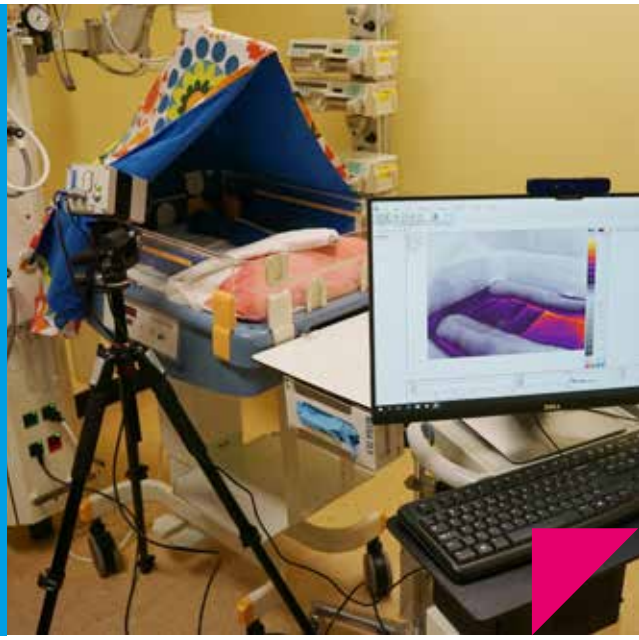
Dr. Alex Eggink
Obstetrics and Gynaecology (EMC)

Dr. Monique Haak
Obstetrical Ultrasound and the Fetal Heart Program (LUMC)

Prof. dr. Jenny Dankelman
BioMechanical Engineering (TUD/LUMC)

Prof. dr. Thomas Hankemeier
Analytical Biosciences (UL/EMC)

In the Netherlands, about 175.000 women give birth every year. In most cases, pregnancy and childbirth are uncomplicated and end with a healthy child and happy parents. Unfortunately, about 1300-1400 children die in the period aroud birth. The 100 days before conception and 1000 days thereafter are fundamental for the development of a child and also largely determine their future health.



The major causes of perinatal mortality are premature birth, congenital anomalies and fetal growth restriction. The aim of the Medical Delta Institute of Fetal and Neonatal Care is to prevent morbidity and mortality caused by complications during pregnancy, birth or the neonatal period for both mother and child. The program will focus on substantially decreasing the incidence of the three major complications that can occur during pregnancy and childbirth. The MOMETA program (monitoring and metabolomics of complicated pregnancies and neonates), one of the projects within this Medical Delta institute, will develop innovative techniques in maternal-fetal monitoring to provide a strong and healthy start for every child.
The program is divided into two parts.The first part will focus on developing new technological and medical solutions to monitor maternal and fetal heart rate.
To date, a pregnant woman is only admitted to a hospital when clear signals of illness are already present, which is often too late. Monitoring is done by a wired system, which is intrusive and limits patient mobility. In this program, a smart and wireless monitoring system will be developed to measure the heart rate of mother, fetus or neonate continuously. The system will ideally be combined with a Big Data analysis system and an automated early warning system to detect signs of clinical deterioration.

Metabolic monitoring for sepsis

The second part focuses on monitoring neonates and early diagnosis and prediction of neonatal sepsis (blood poisoning) using metabolomics.
At the moment, sepsis in the neonatal period is often diagnosed when the newborn is already critically ill. The early diagnosis of sepsis and early prediction of treatment outcome of sepsis would be very desirable. A monitoring device for sepsis will be developed focusing on discovering and validating metabolic biomarkers for the diagnosis of sepsis and prediction of treatment outcome.
The data from these two parts of the program will be combined in a Big Data analysis to support early prediction, decision making and intervention to prevent maternal, fetal and neonatal morbidity and mortality.

Collaboration

In the Medical Delta Institute of Fetal and Neonatal Care, a unique close collaboration is realized between the maternal fetal medicine specialist and neonatologist, supported by technological experts and engineers from TU Delft, Erasmus MC, LUMC and Leiden University. This unique collaboration of clinicians is a strength in this program. This institute is linked to the Medical Delta Living Lab Care Robotics.

A smart and wireless monitoring system will be developed to measure the heart rate of mother or neonate continuously

Healthy Society Hub

Life expectancy is increasing, the demand for healthcare is growing and healthcare costs are rising. Aging, loneliness and health differences are actual topics that require a new and integrated approach. Therefore, a broader approach to health, in which well-being, living conditions, psychological aspects or, for example, stress are taken into account becomes more important.

The goal of the Healthy Society Hub is to develop, evaluate and implement citizen-developed, personalized and digital health solutions to optimize health and well-being and reduce health inequalities

The Healthy Society Hub aims to improve health and well-being for all members of society. To create a powerful collaboration, the Hub includes interdisciplinary scientific research on prevention and health, participating citizens, personalized and digital health solutions, and bundles existing initiatives and solutions.

By keeping everyone healthy for a longer period in their life and giving people more control in their own environment, we want to contribute to accessible and affordable care.

Medical Delta and Healthy Society Hub

Medical Delta, with the associated universities, university medical centres and universities of applied sciences, together

with Leiden-Delft-Erasmus Universities (LDE), is looking for possibilities to expand the Healthy Society Hub from a joint perspective. Technological innovations and applications such as remote monitoring or health apps give people more control over their own health and provide healthcare professionals with the right tools to appropriately treat diseases at an early stage. Within Medical Delta, scientists from various disciplines work together with professionals from healthcare practices and the business community to develop these solutions. By doing so, they contribute to an inclusive healthy society.
Several of Medical Delta's Scientific Programs and Living Labs, directly contribute to the mission of the Healthy Society Hub.

Scientific Leader

Prof. dr. Andrea Evers

Scientific Coordinator

Dr. Sandra van Dijk

Medical Delta eHealth & selfmanagement for a healthy society

How eHealth is changing healthcare

Prof. dr. Andrea Evers
Health Psychology (UL/EUR/TUD)

Prof. dr. Niels Chavannes
General Practice and eHealth in disease management (LUMC)

Prof. dr. Mark Neerincx
Human-Centered Computing (TUD)

Dr. Valentijn Visch
Industrial Design, Design Aesthetics (TUD)

Dr. Rita van den Berg
Health-related physical fitness and lifestyle interventions (EMC)

Existing healthy lifestyle programs can be effective in the short term, but many people eventually relapse into their unhealthy behavioural patterns. A paradigm shift is needed in health behaviour - one that aspires to make healthy living attractive, immediately gratifying and convenient in the short term thereby consolidating healthy living in the long term.

It plays a key role in preventing chronic diseases and in maintaining a healthy lifestyle. The goal of this program is to create instructions on how to reach vulnerable groups and to create a customized integrated eHealth solution. An integrated program, such as the benefit for all program, rewards people for their healthy lifestyles. They get points for everything they do, including logging in to the app. Short-term success is not the main measure, it is the long term that counts. People can fall back, as long as they pick it up again. This integrated solution should also help people with multiple diseases by giving them one approach to use, instead of multiple apps.
Many people come into contact with eHealth while making an appointment with their dentist or doctor online, using a smartphone activity tracking app or taking heart rate measurements. eHealth is booming. eHealth is about patient empowerment and is considered the future of health and well-being in our digital society.

Vulnerable groups

“eHealth offers many solutions. However, there is a huge discrepancy between what is being developed and what is actually being used. Numbers indicate that the health gap between different socioeconomic groups is getting bigger. This is a large problem”, says Andrea Evers, professor in health psychology at Leiden University. The eHealth technologies being developed mainly benefit those who know how to handle them.
In this Medical Delta program, the development of eHealth self-management solutions that are accessible for vulnerable groups is key. Vulnerable groups are difficult to reach and consist of people with a lower socioeconomic position (SEP) or people

with multiple diseases or comorbid diagnoses. “Vulnerable groups do not have access to suitable solutions. It is important to learn more about how people can be motivated to adopt a healthy lifestyle. They need to be rewarded and encouraged in a different way; for example, a financial incentive is more important when targeting low SES groups”, says Evers

Data-driven prediction models

Data-driven prediction models using large data sets and machine learning will be used in this program to investigate what works best for whom, and why. Analysing and interpreting the data will enable personalized solutions to show which people benefit most from which type of intervention.

Collaboration

The consortium includes researchers at Leiden University, LUMC, TU Delft, Erasmus University and Erasmus MC working in collaboration. Researchers at these institutes excel in eHealth research, behavior change and smart technology solutions, and they are able to translate science into clinical applications. The consortium partners also actively participate in the Netherlands eHealth Living Lab (NeLL).

Short-term success is not the main measure, it is the long term that counts

Vital Delta: Medical Delta's journey towards vitality and health

Improving the vitality and health in the Delta region

Dr. AnneLoes van Staa
Lector Healthcare Transitions
(Rotterdam University of Applied Sciences)

A population that is physically, mentally and socially more vital and healthier; from young to old. That is what the program Vital Delta: Medical Delta's journey towards vitality and health strives for. The practice-oriented research program was set up by a consortium of the four universities of applied sciences within Medical Delta (Rotterdam University of Applied Sciences, The Hague University of Applied Sciences, Leiden University of Applied Sciences and Inholland University of Applied Sciences).

In the research program, citizens, students, clients, healthcare professionals and researchers work together with colleges, universities, healthcare institutions and companies. The interdisciplinary program improves the health and well-being of the population in the delta region of Leiden, The Hague and Rotterdam by promoting the development of innovative (technological) health solutions through practice-oriented research.

The eight-year program started in 2018 and focuses on four work packages:

Supported Vital focuses on the design, development and safe implementation of healthcare and welfare technology

Fysically Vital develops, evaluates and implements innovations to promote a healthy lifestyle among vulnerable target groups

Socially Vital stimulates and improves cooperation between professionals from the social and health domain in particular

Self Vital aims to let people take control of their own lives and health

Collaboration

The cooperation between healthcare, the social domain and technology is the starting point for each of these work packages. To ensure this, each work package is led by two lecturers from different universities of applied sciences and coordinated by a work package leader.

Vitale Delta receives a grant from the SIA Steering Body. In addition, Medical Delta and the four universities of applied sciences also contribute to the realization of the program.

Healthy Society Scientific Program (expected to start mid-2022)

Research into prevention and the promotion of a healthy lifestyle

Prof. dr. Andrea Evers
Health Psychology
(UL/TUD/EUR)

Prof. dr. ir. Maaike Kleinsmann
Design for Digital Transformation (TUD)

Prof. dr. Mattijs Numans
General Practice
(LUMC/Health Campus The Hague)

Dr. Judith Rietjens
Patient and Family Engagement in Medical Care (EMC)

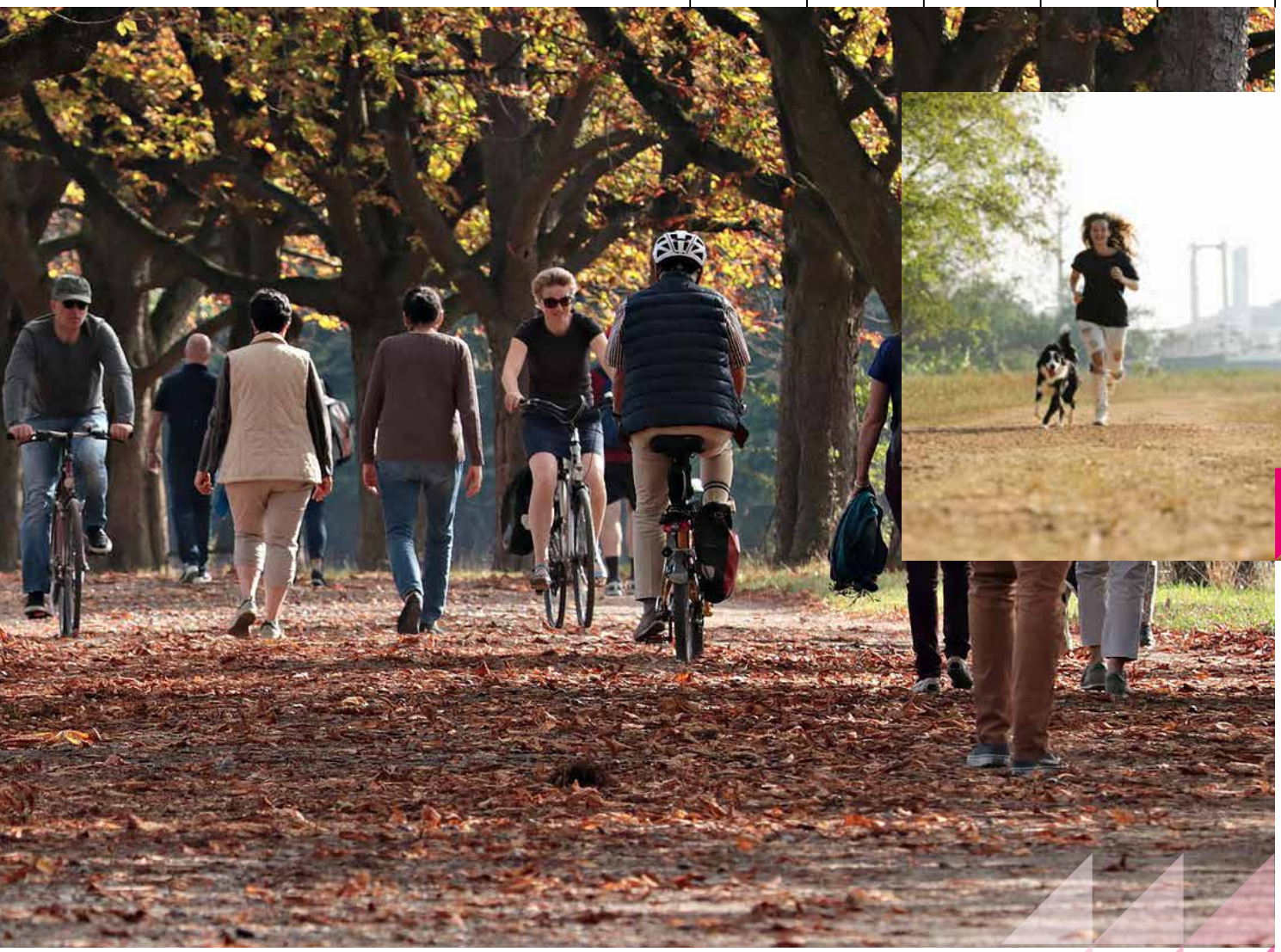
Prof. dr. Anna Petra Nieboer
Socio-Medical Sciences
(EUR)

The health care sector will face major challenges in the coming years. To relieve the care sector, the importance of prevention and a healthy lifestyle is increasing. This also increases the need for research into prevention and the promotion of a healthy lifestyle, for smart technology that connects with the home setting of citizens, and for preventing the risk of chronic diseases in order to reduce their economic and social impact. These developments come together in the Healthy Society scientific program.

The ageing population, loneliness and health inequalities are issues that require a new and integrated approach. There is increasing attention for a broader approach to health, in which well-being and factors such as living conditions, psychological complaints or, for example, stress are included. The Healthy Society scientific program aims to improve health and well-being in all sections of the population. Healthy Society does this with interdisciplinary scientific research into disease prevention and health, with the aid of citizen participation and with personalised and digital health solutions, with the focus on cardiovascular patients and their families.

Attention is also paid to the economic and social impact of the program and public-private partnerships with relevant regional and (inter)national stakeholders. The objective of the Healthy Society scientific program is the development, evaluation and implementation of citizen-based, personalised and digital health solutions to optimise health and well-being and reduce health inequalities. The scientific

There is increasing attention for a broader approach to health, in which well-being and factors such as living conditions, psychological complaints or stress are included



program focuses not only on changing the behaviour of individuals, but also that of their family members. It considers the role of the wider environmental context and the economic and social impact. In the program, various scientific disciplines from different academic institutions work together with social partners.

Influence of environment on health

Within the Healthy Society scientific program, projects will be selected for further research. For people with cardiovascular disease, lifestyle changes, such as quit smoking, increasing exercise or changing their diet, largely determine the course of the disease. The program wants to investigate how environmental factors can promote this. Within the program, two projects will be launched with the aim of

1. achieving sustainable behavioural change in cardiovascular patients and their family members,
2. to identify ways in which environmental factors can increase the effectiveness of lifestyle interventions in cardiovascular patients and their family members.

In the longer term, these projects aim to address a number of key challenges, such as:

- Contributing to more and happier years of life with a higher quality of life for citizens
- Contribute to reducing health inequalities between population groups, with special attention to citizens with low socio-economic position (SEP) and ethnic minorities
- Giving more attention to prevention, lifestyle and home care with the help of eHealth technology
- Creating unique datasets within Healthy Society Living Labs in the neighbourhoods within province of Zuid-Holland and connecting these datasets at every level with the help of AI technology

Collaboration

The consortium consists of researchers from Leiden University, LUMC, Health Campus The Hague, TU Delft, Erasmus University and Erasmus MC.

METABODELTA: Metabolomics for clinical advances in the Medical Delta

Growing old healthy by predicting and preventing diseases

Prof. dr. Thomas Hankemeier
Analytical biosciences (UL/EMC)

Prof. dr. Eline Slagboom
Molecular epidemiology (LUMC)

Prof. dr. Arfan Ikram
Epidemiology (EMC)

Prof. dr. Simon Mooijaart
Epidemiology (LUMC)

Most people want to know whether they are healthy and what they have to do to remain healthy as long as possible. Science has delivered many insights into how to live healthily and how to treat or prevent certain diseases. However, a lot is still unknown.

Dr. Mohsen Ghanbari
Molecular and Systems Epidemiology (EMC)

Dr. Daniel Bos
Imaging in Health Sciences (EMC)

Genes predict the risk of developing certain diseases in an individual. However, genes do not indicate if, and when, such a disease will develop. This is also determined by environmental factors such as nutrition and lifestyle.
Measuring the metabolites in the blood can tell you what is going on in the body. Metabolites provide information about someone's current health state. Metabolites are the result of the interplay between genes and these environmental factors. Metabolites are small chemical substances, like glucose or fats, that are products of the processes and reactions taking place within and between cells. Measuring metabolites therefore reveals information about such disturbances. Many of these metabolites are present in blood.

Metabolic profile

If many diseases can be early predicted with metabolomics, obtaining metabolic profiles for every person as a health monitoring approach becomes promising. The metabolic profile would give a warning before any symptoms appeared. "This kind of metabolic profile might be acquired in just a few years in a single drop of blood. In such way metabolomics can contribute to change healthcare in a fundamental manner," says Thomas Hankemeier, professor of Analytical BioSciences at Leiden University.
Measuring all the relevant metabolites is a challenge. Researchers are already able to measure thousands of metabolites in blood and urine samples using advanced analytical technologies, also called metabolomics. Metabolomics can be used to find a combination of metabolic biomarkers that predict complex diseases, such as dementia. It is even more interesting to investigate the underlying chemical processes causing the disruption in the metabolic equilibrium, to resolve or compensate the disruptions before the disease develops; early diagnosis is helpful in that case.

The METABODELTA: three themes

In the METABODELTA program, three themes will be addressed. The first – "From metabolomics for discovery to clinical practice" – is focused on the translation of metabolomics discoveries to clinical and point-of-care applications. For that, novel technologies for large-scale metabolomics will be developed and implemented. In parallel, a robust and clinical metabolomics analyzer will be developed. The aim of the project is to integrate the metabolomics analysis steps into a small analyzer that can be used as a point-of-care metabolomics analyzer. These technologies will allow monitoring of the metabolic health state for diagnosis and choice of the proper intervention.
The second theme is focused on using metabolomics to assess risk of mortality and vulnerability in geriatric patients and population based cohorts of elderly. Secondly to monitor the response of older individuals to lifestyle changes and to understand the main metabolic processes determining such heterogenous responses. Thirdly to use metabolomics assays to generate surrogate markers for metabolic disease risk factors and endpoints. Using the metabolome as monitoring a tool to improve the health of our ageing society would help to stimulate vitality, especially in those at risk.
And finally, the third theme focuses on the development of novel preventive intervention strategies for dementia by understanding the interplay between the microbiome, blood metabolome and vascular and neuropsychiatric pathology.

Collaboration

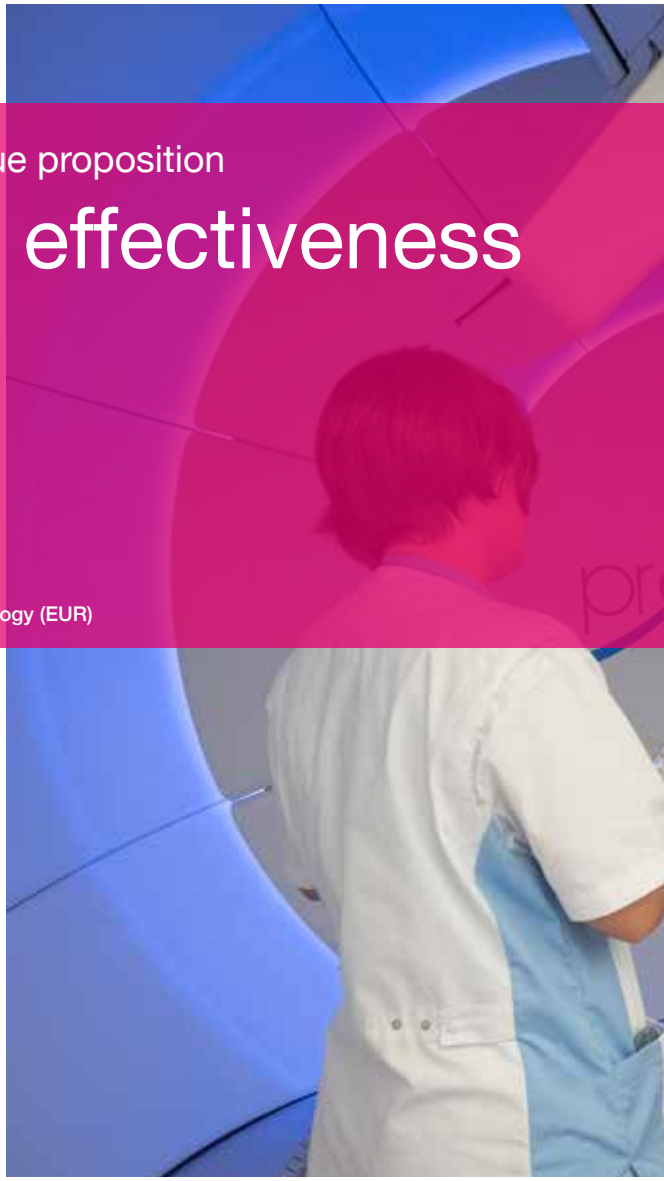
In METABODELTA, leaders in the development of metabolomics technology and clinical diagnosis join with leaders who have access to unique cohorts and other clinical studies, to apply metabolomics in population and clinical studies to study healthy ageing. METABODELTA will make metabolomics more accessible within the Medical Delta. "Together we are bringing the ideal of growing old healthily into closer reach," concludes Hankemeier. This program also aims to make the data obtained in its research comparable to metabolomics data acquired by other labs worldwide, to validate findings, implement others' findings into research being done in the Medical Delta, and ultimately, apply the data for the benefit of healthcare.

HollandPTC Medical Delta program on HTA value proposition

Determining the cost effectiveness of proton therapy

Prof. dr. Marco van Vulpen
Radiotherapy (EMC/LUMC/TUD)

Dr. Hedwig Blommestein
Health Policy & Management Health Technology (EUR)



Since healthcare costs are rising and resources are scarce, it is important to consider the societal impact in addition to the clinical impact of new technologies, such as proton therapy. It is essential for patients and society that scarce resources are spent as efficiently as possible. As proton therapy carries hight investment and operational costs, but may also provide high clinical value, a so-called Health Technology Assesment (HTA) is essential.

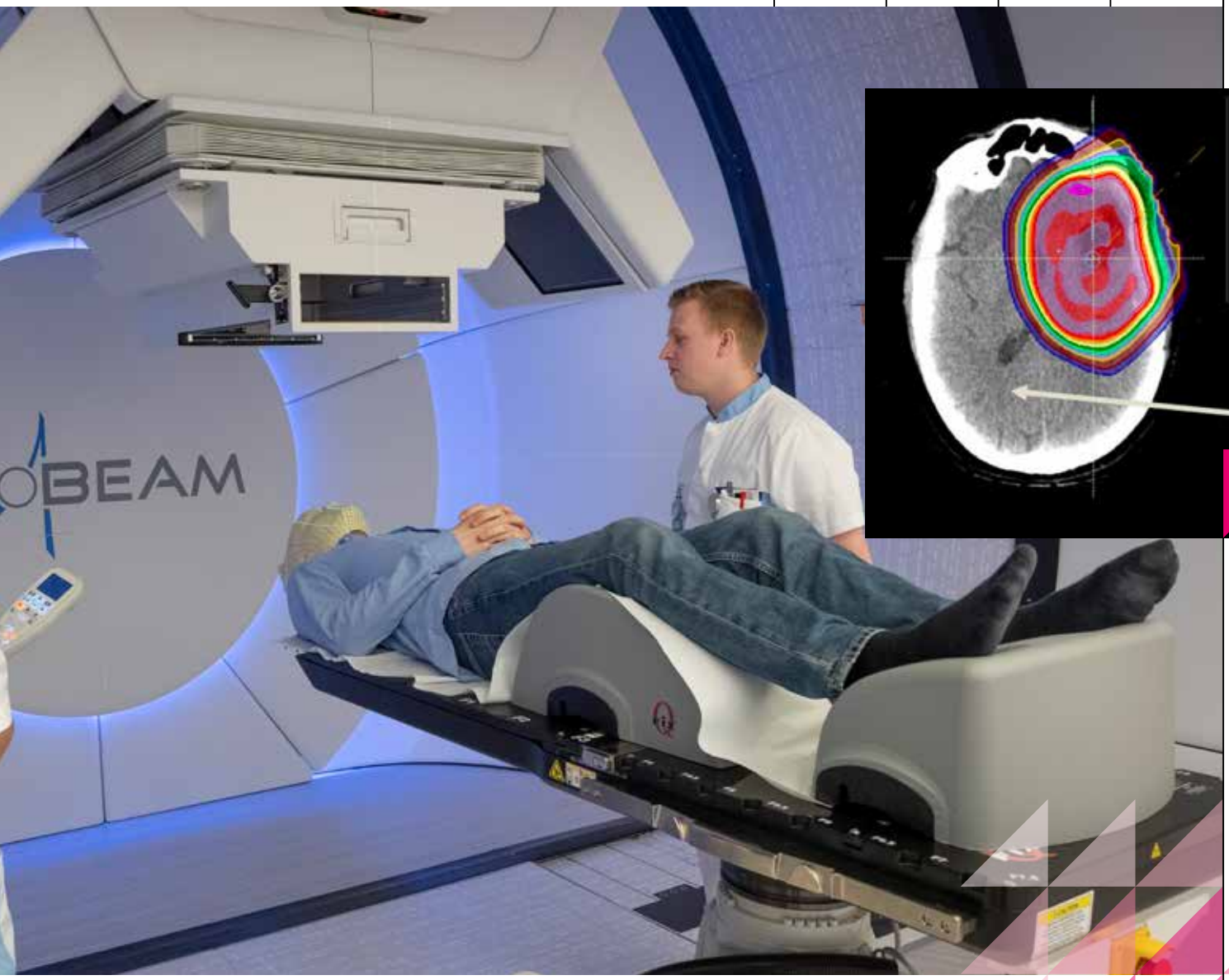
A HTA includes an economic evaluation to determine the cost- effectiveness of proton therapy compared to photon therapy. Furthermore, HTA also covers the logistical factors, the implication of technological advances and its impact on overall healthcare delivery costs.

Proton therapy

Radiation therapy is used in the treatment of cancer to kill cancer cells. The usual radiotherapy with photons works well enough for many patients, but sometimes the tumor is too close to vulnerable organs or is relatively insensitive to the usual radiation. In those cases, proton therapy can be an option.
Proton therapy is a new way to treat cancer. The program focuses on low-grade brain tumor and head and neck cancer. Proton therapy is different from traditionally used photon therapy, as it makes use of very local and precise dose deposition on tumors. This causes less damage to the surrounding normal tissue, resulting in fewer side effects. Proton therapy is a form of radiation that uses protons instead of photons. Protons are small, charged particles that are in the core of an atom. To irradiate a tumor, the protons are accelerated to more than half the speed of light. The proton beam is directed at the tumor. The speed of the protons can be adjusted in the accelerator in a way the protons only destroy the tumor tissue, and surrounding healthy tissue is damaged as little as possible.
However, it is more expensive than photon therapy and has high investment costs.

Two types of cancer

In this consortium, an HTA will be performed on proton therapy for the first time. The program initially focuses on two types of cancer. One is the low-grade brain tumor, which grows relatively slowly and often occurs in young people (30-45 years old). The other is head and neck cancer, which grows relatively fast and is more common among elderly people (60-75 years old). Currently, the patients involved in the assessment are being treated at HollandPTC and data collection has



started. HollandPTC, founded by Erasmus MC, LUMC and TU Delft, is a treatment center for proton therapy Including these two different kinds of cancer will give a broad overview of proton therapy for the HTA. This research will lead to a generic model that can be easily adjusted to map the cost-effectiveness and value of proton therapy for all other types of cancer, which will be very useful in the future.

Collaboration

Collaboration between the Erasmus University in Rotterdam, Leiden University and HollandPTC is realized in this program. One researcher will evaluate the cost structure of the proton center as well as the total cost of proton therapy from a societal perspective. Another researcher will be working on determining the value proposition of proton therapy for the two types of cancer, to eventually create a uniform model for decision making and cost- effectiveness analysis of proton therapy.

The program focuses on low-grade brain tumor and head and neck cancer

Medical Delta Regenerative Medicine 4D: Generating complex tissues with stem cells and printing technology

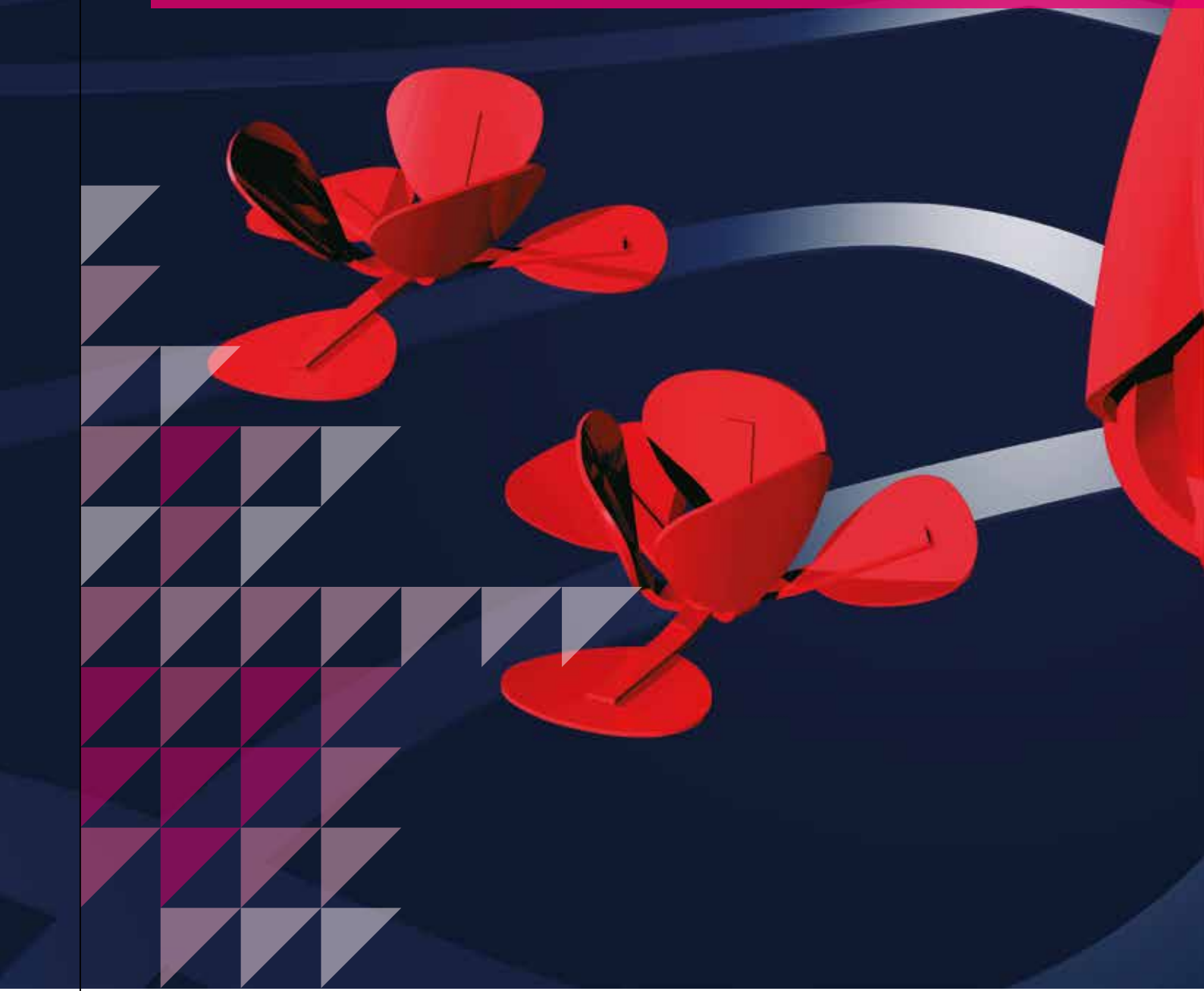
Generating complex tissues with stem cells and printing technology

Prof. dr. Gerjo van Osch
Orthopedics & Otorhino-laryngology (EMC/TUD)

Prof. dr. Amir Zadpoor
Biomechanical Engineering (TUD, LUMC)

Prof. dr. Rob Nelissen
Orthopaedics (LUMC/TUD)

Prof. dr. Luc van der Laan
Experimental Transplantation and Intestinal Surgery (EMC)



Regenerative medicine focuses on the development of new treatments to repair or regenerate diseased tissues and organs, such as cartilage, bone or liver, to restore function and improve patients' quality of life.

Prof. dr. Ingrid Meulenbelt
Molecular Biology of Osteoarthritis (LUMC)

The Regenerative Medicine Medical Delta program follows two tracks. The first focuses on reconstructing cartilage and bone defects, the second focuses on disease models.

Reconstruction: creating complex tissue constructs

4D printing is a new technology developed at TU Delft. The shape or the mechanical properties of an object can be adapted over time when stimulated by pH, light, temperature or other physical stimuli. This technique will be used to create complex tissue constructs to direct cell behavior. Using this advanced technology together with stem cell technology, the researchers are building a proof-of- principle cartilage-bone unit to repair defects with a biological implant.

Disease models: mimicking diseases

Disease models are used to mimic a disease as precisely as possible in a laboratory environment by putting together cells to construct complex tissues. In this program, induced pluripotent stem cells will be used. These are stem cells that can differentiate into all different cell types – for example, a cartilage cell or liver cell. In Medical Delta Regenerative Medicine 4D we will apply printing technology to improve disease models of cartilage and liver. This will enable us to better understand these diseases.

Future perspective

3D and 4D printing technologies offer possibilities to generate better implants used for the repair of failing tissues / organs (for example but not limited to cartilage, bone and liver). The methodology will also be applied to improve in vitro disease models that can be used to develop and test medication thereby speeding up the quest for new pharmacological treatments. Patients with osteoarthritis, a joint disease affecting cartilage and bone that leads to reduced mobility and pain, could benefit from these developments. It could also help patients with liver diseases, as the shortage of donor livers for transplantation has driven the field to look for alternative solutions including early interventions.

Collaboration

Regenerative medicine is a multidisciplinary field in which medicine, biology and engineering provide solutions jointly. The Medical Delta region is an ideal habitat in which to stimulate these developments. This program combines unique 4D-printing technology developed in Delft with strong knowledge on stem cells, hydrogels and disease models in Rotterdam and Leiden. This collaboration brings the developments in the individually strong research groups to a higher level.

Disease models are used to mimic a disease as precisely as possible

Medical Delta AI for Computational Life Sciences

Creating new opportunities for biomedical research

Prof. dr. ir. Boudewijn Lelieveldt - Biomedical Imaging (LUMC / TUD)

Prof. dr. ir. Marcel Reinders Bioinformatics (TUD / LUMC)

Prof. dr. Mario van der Stelt Molecular Physiology (UL)

Dr. Michel van de Velden Econometrics (EUR)

Prof. dr. Gerard van Westen Artificial Intelligence & Medicinal Chemistry (UL)

The possibilities to access the molecular data of cells and tissues are increasing, but this also creates new challenges. How can one find the information needed for research when there is such an enormous amount of data, for example?

The scientific program Medical Delta AI for Computational Life Sciences uses AI techniques to unlock biomedical data, discover new candidate drugs, detect special cell abnormalities or connections, and find useful information for research. This opens new doors for scientific research into the human body and in particular the development and effect of new medicines.

'Computational Life Sciences' combines computer science and life science. Using AI techniques, Computational Life Sciences helps researchers better understand biological mechanisms and make predictions about interactions between molecules and cells and with drugs. In this way, it helps scientists search more specifically for the molecules and genes that are of interest for a particular biological study. It helps them clarify hypotheses and better predict what medicines must contain in order to work properly. This creates new opportunities for, among other things, drug development that can be carried out faster, more specifically and better.

Medical Delta Professor and Scientific Leader Prof. Dr. Boudewijn Lelieveldt compares this to putting a new space telescope into operation. "If it suddenly becomes possible to see much further than one ever thought was possible, an astronomer has to think carefully about where to aim the telescope. Otherwise, he or she would get lost in the infinite possibilities. With the help of AI techniques, Computational Life Sciences helps us search for the molecules and genes that are interesting for specific biological research and drug development."

Leading scientists in the fields of bioinformatics, drug development, AI and computer science collaborate with pharmaceutical companies and with clinicians on the research projects within the program. In addition to the development and application of Computational Life Sciences with AI techniques in general, the program focuses on two lines of research: antibiotic resistance for tuberculosis and targeted medication for brain disorders.

Antibiotic resistance to tuberculosis

Tuberculosis is one of the deadliest infectious diseases in the world. Ten million people contract the disease every year, and 1.5 million of those people die (source: RIVM). A major problem in the fight against this disease is antibiotic resistance. Medical Delta AI for Computational Life Sciences wants to support research into antibiotic resistance with computer modelling and determine the effect of bacterial mutations by the use of algorithms, among other things. By gaining a better understanding of the mechanism of antibiotic resistance, the researchers hope to be able to search more specifically for ways to disrupt resistance and thus develop better candidate drugs.

Targeted medication for brain disorders

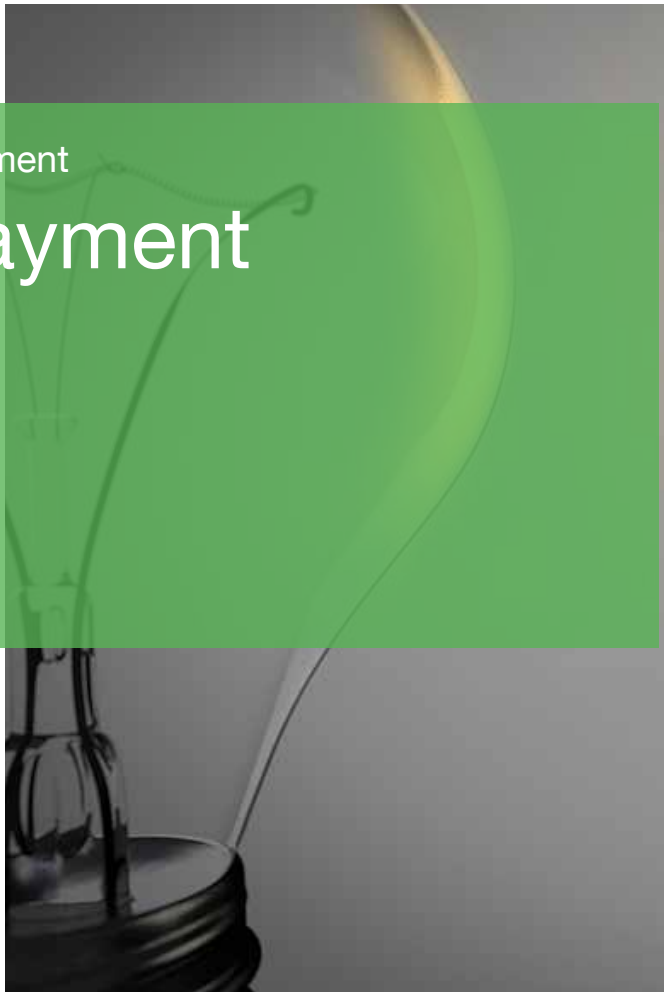
In the development of new medicines for brain disorders, it has proved difficult to translate data from laboratory animal research directly into the effects of medicines on humans. For example, the control of cells by genes differs between humans and mice. Medical Delta AI for Computational Life Sciences is looking for methods to convert research data correctly, so that the development phase of medicines runs faster and better.

Collaboration

In this program, scientists from Leiden University, LUMC, Erasmus University and TU Delft in the field of bioinformatics, drug development, AI and Computational Life Sciences work together with clinicians and pharmaceutical companies. Scientists from Erasmus MC are also involved in the program.

Medical Delta's Journey from Prototype to Payment

From prototype to payment



Prof. dr. Maureen Rutten
Economic Evaluation of Innovations for Health (EUR)

Prof. dr. Werner Brouwer
Health Economics (EUR)

Medical Delta aims to realize sustainable care with technological solutions. For an innovation to be sustainable, it is important to understand its full impact on society. This includes clinical, financial, organizational, and ethical factors, among others.

Moreover, innovations need to be safe, and their value should be proven. In 2014, the Dutch television program Radar was able to receive CE-certification for a pelvic floor mat using a tangerine bag. This semi-serious prank showed the need for stricter regulation of technologies and increased expectations regarding their proven value to society. In the Medical Delta program From Prototype to Payment, the societal perspective on innovation is positioned in parallel to the other scientific programs. The From Prototype to Payment program focuses on four pillars: 1) financial aspects, 2) health technology assessment, 3) governance and 4) organizational aspects. Each of these four pillars is elaborated on below in more detail.

From Prototype to Payment

The Medical Delta program 'From Prototype to Payment' considers these types of questions:

Financial aspects

What will be the financing model of a new technology? A device that will be used once inside the hospital will have a completely different business model than a device that will be used multiple times outside the hospital. Another question is who should buy the device? The hospital, insurance companies or the patients themselves? In this PhD project we aim to understand the important financial aspects influencing innovation from its development to its implementation in practice. By adopting the perspective from the innovators, we dive into their world and emphasize the financial struggles they encounter during the innovation process.

Health technology assessment

The development of new technologies should be guided by the assessment of its potential risks, costs, benefits and impact. A Health Technology Assessment (HTA) is a policy framework used to decide on market access and the reimbursement of new technologies. HTA provides the methods to assess efficacy, organizational consequences, financial questions and cost-effectiveness. Cost-effectiveness of a new technology is an essential part of the assessment. HTA looks at how much a certain technology costs and what added value it offers. It compares new technologies to technologies that are currently used. For instance, in the case of MRI scanners, it tries to understand whether it's worth investing in new ones that, despite being more advanced than current ones, cost a lot more.

By adopting a societal perspective in a such HTA framework, we include not only medical costs, but also costs outside of the healthcare system (e.g., costs for family, productivity costs).

Governance

What are the implications of the development of medical technologies for the governance of health care? How are (innovative) medical technologies governed at a national and an international level? With the expectation of new regulations, the development of novel methods for value assessment, and the introduction of various new players, responsibilities are changing. Conventional means of regulating these new technologies may not be feasible, nor sufficient to guarantee the quality, accessibility and affordability of medical technologies. In this PhD project, the governance of medical technology will be studied with a focus on the role of HTA bodies.

Organizational aspects

Organizational and professional consequences relate to the effects of implementing a new technology. Once brought into practice, technologies often generate unexpected, and even unintended, consequences. We thus need to ask, which new tasks will the technology create? Do we need to create new professional roles to take care of them? Will physicians delegate tasks to nurses? Will professionals trust new types of information provided, for instance, by data-driven technologies?
The PhD projects that are part of the From Prototype to Payment program can be combined to provide a full picture of the societal questions that need to be asked before, during and after technological innovation. Together, they can be integrated to inform decision-making at multiple levels of the health care system, from national reimbursement assessment to organizational decision making on how to optimize service delivery.

Collaboration

It is important to involve many stakeholders in this Medical Delta program, in order to provide a truly parallel answer to the other scientific programs. For instance, collaboration with the National Healthcare Institute (Zorginstituut Nederland) is essential for the governance aspects. Next to the Healthcare Institute, this program collaborates closely with innovators, healthcare professionals, healthcare insurers, patients and industry to understand the full societal impact of innovative technologies.

Young Medical Delta (YMD) is a platform for students, young researchers and young professionals who are at the starting point of their career in life sciences, health and technology.

Young Medical Delta connects students and young professionals who share a passion for medical technology and opens up new opportunities for them to explore. Young Medical Delta is partnering with associations from different universities, as well as the universities of applied sciences and PhD students from the different institutes that are connected to the Medical Delta. Through its connection with Medical Delta, Young Medical Delta is in contact with a large network of researchers who are working on the cutting-edge in their field.Young Medical Delta organizes its own events as well as events in collaboration with its partners. These events enable discussion and the discovery of recent research in the field of medical technology. One of such events is a yearly hackathon, where participants are motivated to find a solution to a problem that has been submitted from within the healthcare system. With the organization of symposia, Young Medical Delta presents ongoing research and allows for participants to network and find new collaboration opportunities.

Young Medical Delta Hackathon 2021

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Medical Delta Professors

Our Medical Delta professors are appointed to at least two of the five academic institutions represented within Medical Delta (TU Delft, Erasmus MC, Erasmus University Rotterdam, Leiden University and LUMC). The professors who receive this appointment are committed to interdisciplinary research in the field of health & technology.

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TU Delft & Universiteit Leiden

Prof. dr. ir. Nico de Jong
TU Delft & Erasmus MC

Inauguration Medical Delta Professors 2021

About Medical Delta

Medical Delta aims to realize sustainable healthcare with technological solutions. As a key player in the health and technology ecosystem, it aims to create an impact on people, care, knowledge and economy through interdisciplinary scientific research and practice-oriented Field and Living Labs. In doing so, Medical Delta helps make healthcare better, while keeping it accessible and affordable.

Medical Delta brings together three renowned universities, two university medical centers and four universities of applied sciences in the province of Zuid-Holland. Medical Delta started a major scientific program in 2019. In the coming years, over 350 scientists will work together in 16 different consortia on technological solutions for sustainable care. Companies, healthcare institutions, the province and major cities in the Delta are closely involved, including through Living Labs, where innovations with end users are tested in healthcare practice.

The objective for the period 2019-2023 is for the Medical Delta research programs to grow in size, achieve excellence and develop technological solutions for sustainable care.

Medical Delta was founded in 2006 by TU Delft, Leiden University, Erasmus University Rotterdam, LUMC and Erasmus MC. Since 2016, four universities of applied sciences have joined Medical Delta: The Hague University of Applied Sciences, InHolland University of Applied Sciences, Rotterdam University of Applied Sciences, Leiden University of Applied Sciences.
Medical Delta is managed by board members Frank Willem Janssen and David de Glint. The board is advised by the Scientific Council and the Societal Council. The Scientific Council is represented by Medical Delta professors, educational directors, lecturers and Young Medical Delta representatives. Medical Delta is facilitated by a small, effective agency.

David de Glint
Managing Director Medical Delta

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Chairman Medical Delta

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