

Medical Delta

Technological solutions for tomorrow's healthcare



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From prototype to payment

THE SOCIETAL PERSPECTIVE ON THE SCIENTIFIC PROGRAMS.

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Medical Delta: a new era

The average life expectancy in Europe is increasing continuously and fast: every week we gain a weekend. But the problem is that we're sick on Sunday. As more and more people require care, there are fewer and fewer people who can provide it.

We need to innovate our care system to accommodate the care our aging population is demanding. Citizens must remain active in society, professionally and socially – that's what keeps them healthy. Technology can play a major role in this. Over the last decade, the Medical Delta has brought together scientists, engineers, medical doctors, small and medium enterprises, large companies, universities of applied sciences, municipal and provincial governments, science funders and many others to address this issue.

Medical Delta is entering a new era. In this magazine, we introduce Medical Delta's 13 new scientific programs. Within these programs, academics are collaborating on technical solutions for sustainable health, from molecule to reimbursement. They exploit fundamental knowledge at the University of Leiden, LUMC, TU Delft, Erasmus University Rotterdam and Erasmus MC, they have doctors and engineers create solutions and collaborate with universities of applied sciences, then they have 'living labs' and care providers evaluate the solutions. And with the expert knowledge of law, social sciences and economics, the likelihood of these solutions being translated into the care system will be maximized.

Here are some examples of what we aim to achieve: within 10 years, we will have a better understanding of and better treatments for heart rhythm disorders; we will be better at predicting who will develop Alzheimer's disease or we will have more effective brain surgery techniques that cause less damage to the healthy brain; and we will have developed a technical and social structure that will make it possible for people with brain damage to live independently at home.

In this magazine, you will learn how Medical Delta is contributing to reinventing health care. I hope you enjoy it.

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Prof.dr.ir. Ton van der Steen

Chairman Medical Delta



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 South-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.

www.medicaldelta.nl



Medical Delta Diagnostics 3.0: Dementia & Stroke

Dementia and stroke: how deep learning algorithms make faster diagnoses



Prof. dr. Wiro Niessen
Biomedical Image Processing (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. Using images and data from large population studies and artificial intelligence techniques such as deep learning, they can estimate

if a person is at high risk of developing a disease. More accurate and faster diagnosis and prognosis can improve disease treatment and support steps towards disease prevention.

Stroke

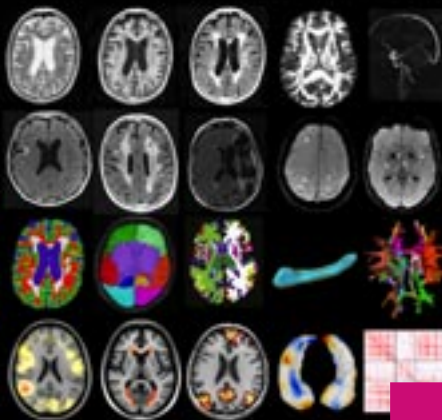
A stroke occurs when the blood flow to parts of the brain is cut off. This can happen due to a blood clot that blocks the blood flow or due to bleeding in the brain. These two different types of stroke require different treatments, and the right treatment must be selected.

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 quantitatively 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

Cancer Diagnostics 3.0



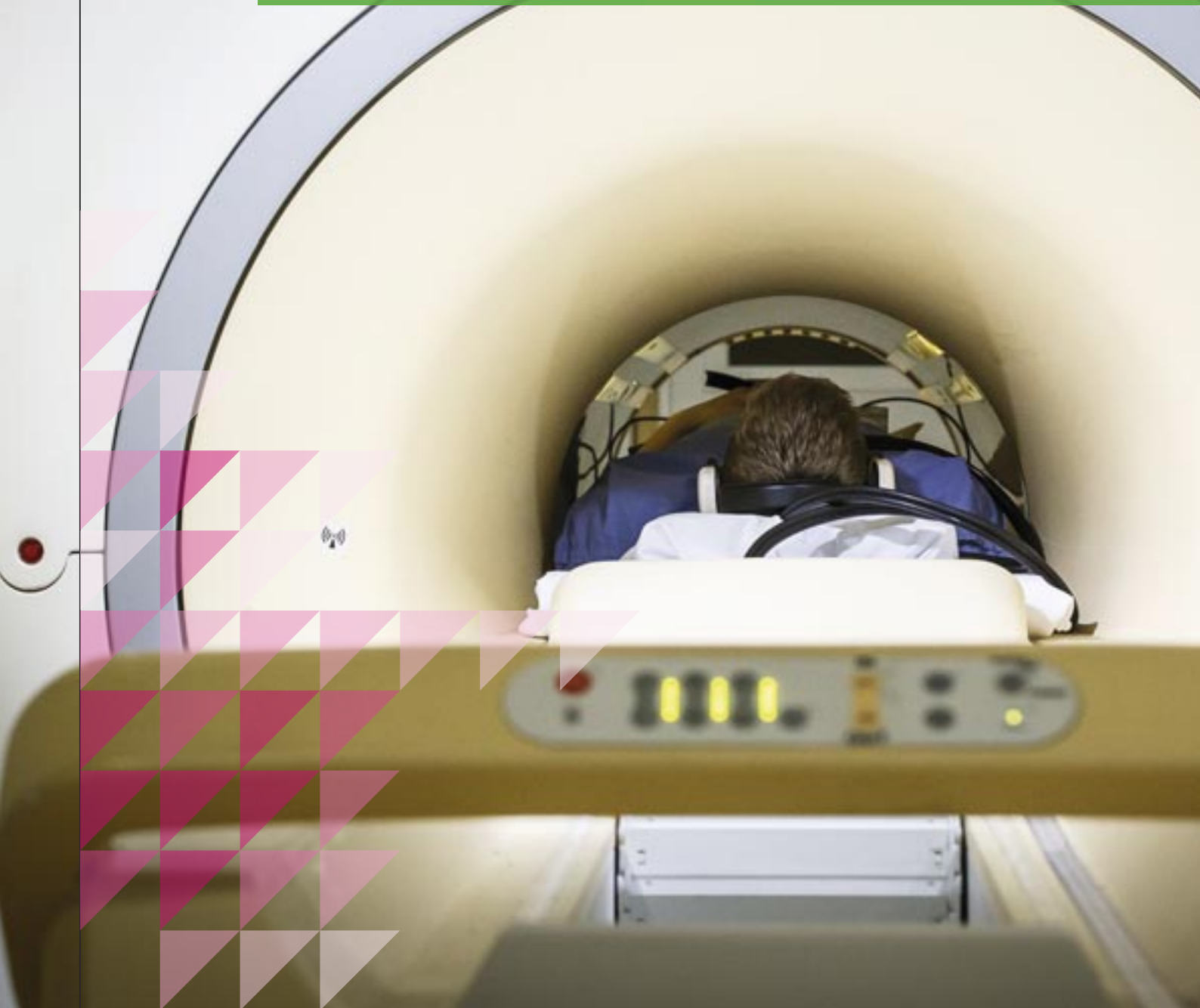
Prof. dr. ir. Matthias van Osch
Radiology (LUMC)



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



Prof. dr. Sjoerd Stallinga
Imaging 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 to better predict the course of the disease.

Creating non-invasive methods

At the moment, biopsies are taken to obtain information about the genetic and molecular characteristics of the tumor. Taking a biopsy is an invasive method that can sometimes be risky. Researchers from the Medical Delta Cancer Diagnostics 3.0 program believe analyzing tumors could be improved by extracting more information from MRI images.

Advanced MRI techniques

Within this program, which initially focusses on brain tumors, advanced MRI techniques will be used to gather relevant information about the tumor. The researchers will do this using standard 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 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 be 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 objective.”

Machine learning solutions are also in development in the field of digital pathology of biopsy material. Sjoerd Stallinga, professor of Computational Imaging at TU Delft: “Analysis and classification of tissue morphology is a very suitable task for modern deep learning methods.”

Machine learning techniques will help us to include more information from the MRI scan and to make diagnoses more objective

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 enable biopsy-free image-based diagnosis of cancers. The support this provides to personalized treatment selection and treatment monitoring 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



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Imaging Physics / Thoraxcentre (TUD/EMC)



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.

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

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.

Ultrasound

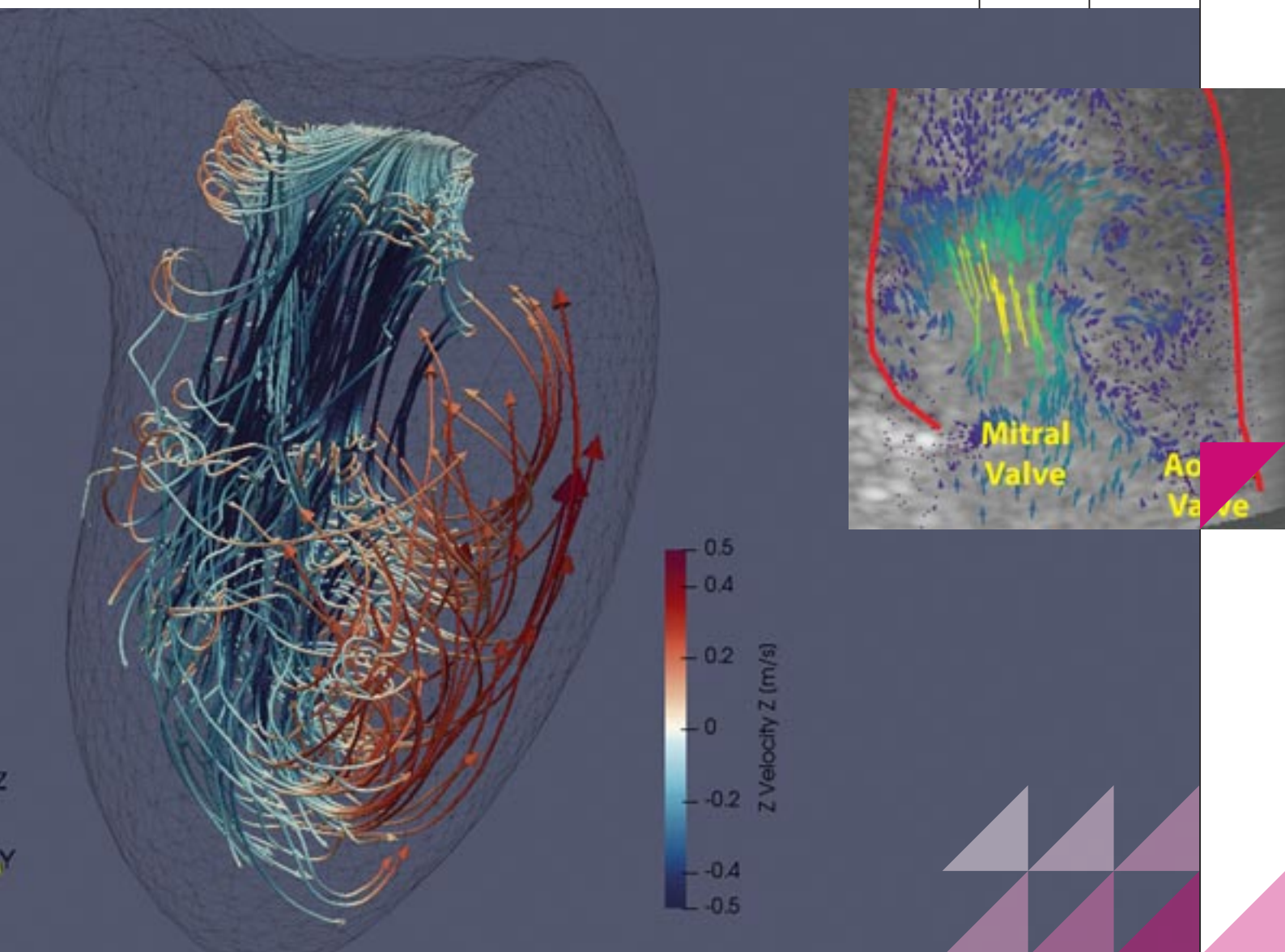
Ultrasound is the most commonly used medical imaging technique. It is harmless, relatively cheap and, because it uses real-life images, it gives immediate diagnostic feedback. The technology is developing rapidly: new ultrafast imaging brings the functioning of the heart and brain directly into view,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

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

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.

Medical Delta Living Labs

Creating real-life experimental environments

One important way in which the Medical Delta network seeks to encourage and accelerate innovation within the healthcare sector is by setting up 'Living Labs'. These provide experimental, real-life settings, either physical or digital, in which major stakeholders can develop and test new ideas in partnership with end-users. These ideas can then be implemented on a small scale, prior to full-scale launch. In this way, Living Labs deliver concrete, marketable innovations in the form of products, services, social initiatives, organizational solutions and so on.



Living Lab Rehabilitation Technology

In the Living Lab Rehabilitation Technology, innovations contributing to intensive home rehabilitation are developed to facilitate a faster transition from hospital to rehabilitation center to home environment. In this living lab innovations in robotics, sensor technology will ideally lead to increasing mobility and self-reliance of patients.

The Medical Delta Living Lab Rehabilitation Technology offers various testing and implementation facilities within the Rijndam Rehabilitation Center, Sophia Rehabilitation Center and Rijnlands Rehabilitation Center. These facilities enable users to develop, test and implement technological innovations in a realistic rehabilitation environment. The Living Lab contributes directly to the improvement of rehabilitation care and the strengthening of the business climate in the Medical Delta region.



Living Lab Care Robotics

Within the Living Lab Care Robotics, products are developed and validated in practice to allow people to live independently for a longer period, to improve self-reliance and quality of life. The focus is primarily on elderly people with cognitive or physical disabilities. An example of such a robotic product developed and tested in this living lab is a smart walker.

The Living Lab Care Robotics offers companies and other care developers the opportunity to test their innovations together with end users and to develop them further in practice. The Living Lab offers various real-life testing and implementation facilities at Pieter van Foreest, the LUMC and the Reinier de Graaf Hospital. These facilities enable users to develop, test and implement technological innovations in a realistic healthcare environment.

Living Lab ResearchOR

The Living Lab ResearchOR consists of a real-life operating room, in which processes and system are developed and validated to increase efficiency and guarantee patient safety in the surgical trajectory. The right measuring equipment and sensors are available in this ResearchOR living lab. The main focus is on minimal invasive instruments. Reinier de Graaf Hospital and TU Delft are involved in this Living Lab.



Living Lab Medical Delta Instruments

The Living Lab Medical Delta Instruments supports the development of high-quality prototypes, intended for pilots in patients. The focus is on instruments for minimally invasive interventions. The added value an instrument brings to a patient can be assessed in this Living Lab before any major investments are made in production resources and processes. The services from the Living Lab also include support throughout the certification process (technical files, clinical protocols), based on knowledge and expertise gained from various ongoing projects.

TU Delft, Erasmus MC, LUMC, AMC, Reinier de Graaf Hospital and LIS (Leiden Instrument makers School) collaborate in this Living Lab.



National eHealth Living Lab (NeLL)

National eHealth Living Lab (NeLL) was founded by the Leiden University Medical Center (LUMC) to develop eHealth applications in close collaboration with national and international stakeholders in healthcare and technology. Examples of digital applications for monitoring and promoting health are apps, sensors, wearables, robots and video communication tools. The applications are tested by a panel of healthcare users, healthcare providers, researchers, students and IT professionals. This structure allows the parties to inform and inspire each other to come up with new eHealth applications that are optimally tailored to the end user.

At the National eHealth Living Lab (NeLL), patients, healthcare providers, consumers, students, scientists, entrepreneurs, organizations and institutions work together to develop successful eHealth applications by sharing knowledge, contacts and experiences.

Medical Delta NIMIT: Novel Instruments for Minimally Invasive Techniques

Creating standardized methods to develop minimally invasive instruments



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



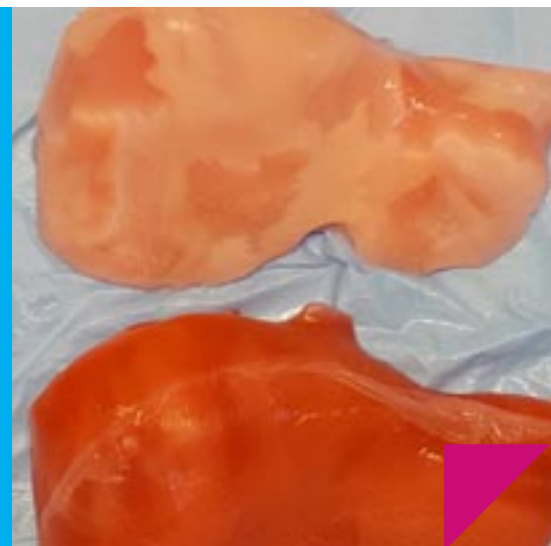
Dr. Gijs van Soest
Cardiology (EMC)



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.

Quicker implementation

“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. The Medical Delta NIMIT program aims to design minimally invasive instruments that enable a rapid innovation cycle based on well characterized, documented process steps and standardized tests. This will eventually lead to quicker implementation in clinical practice.

Modular instruments

In order to achieve this, new design, manufacturing and assembly methods should be developed for minimally invasive instruments. The instruments produced should be simpler and should support sustainable surgery. “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 Dobbelsesteen, 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

Medical Delta Cardiac Arrhythmia Lab



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



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



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.

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.

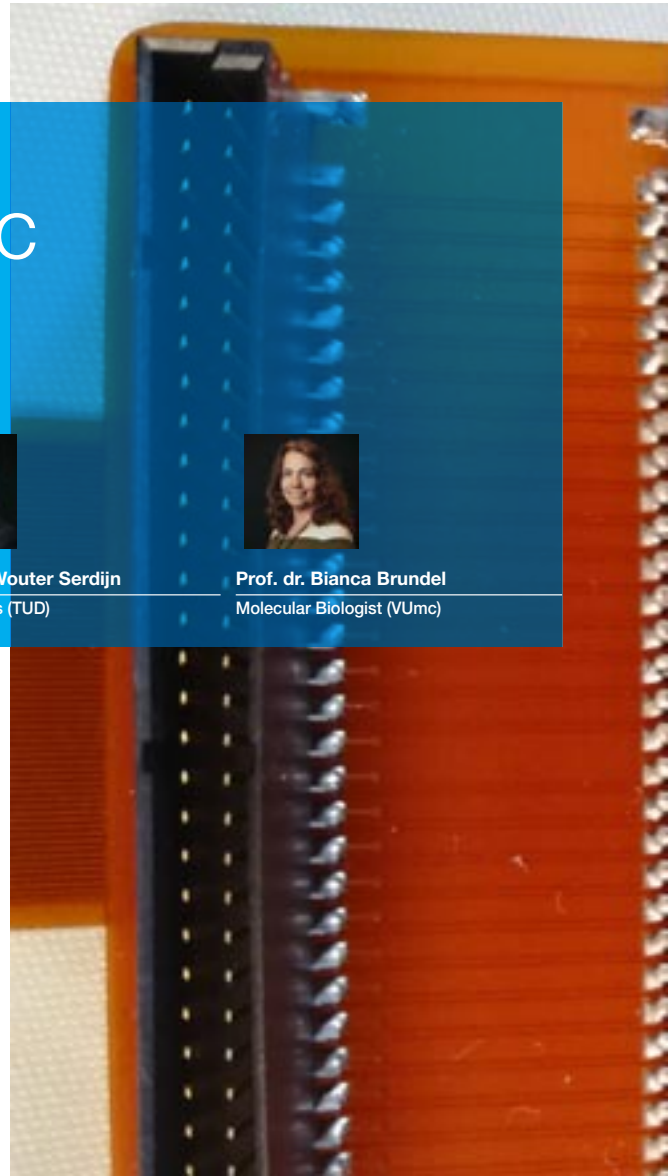
Providing a patient-specific therapy can improve treatment

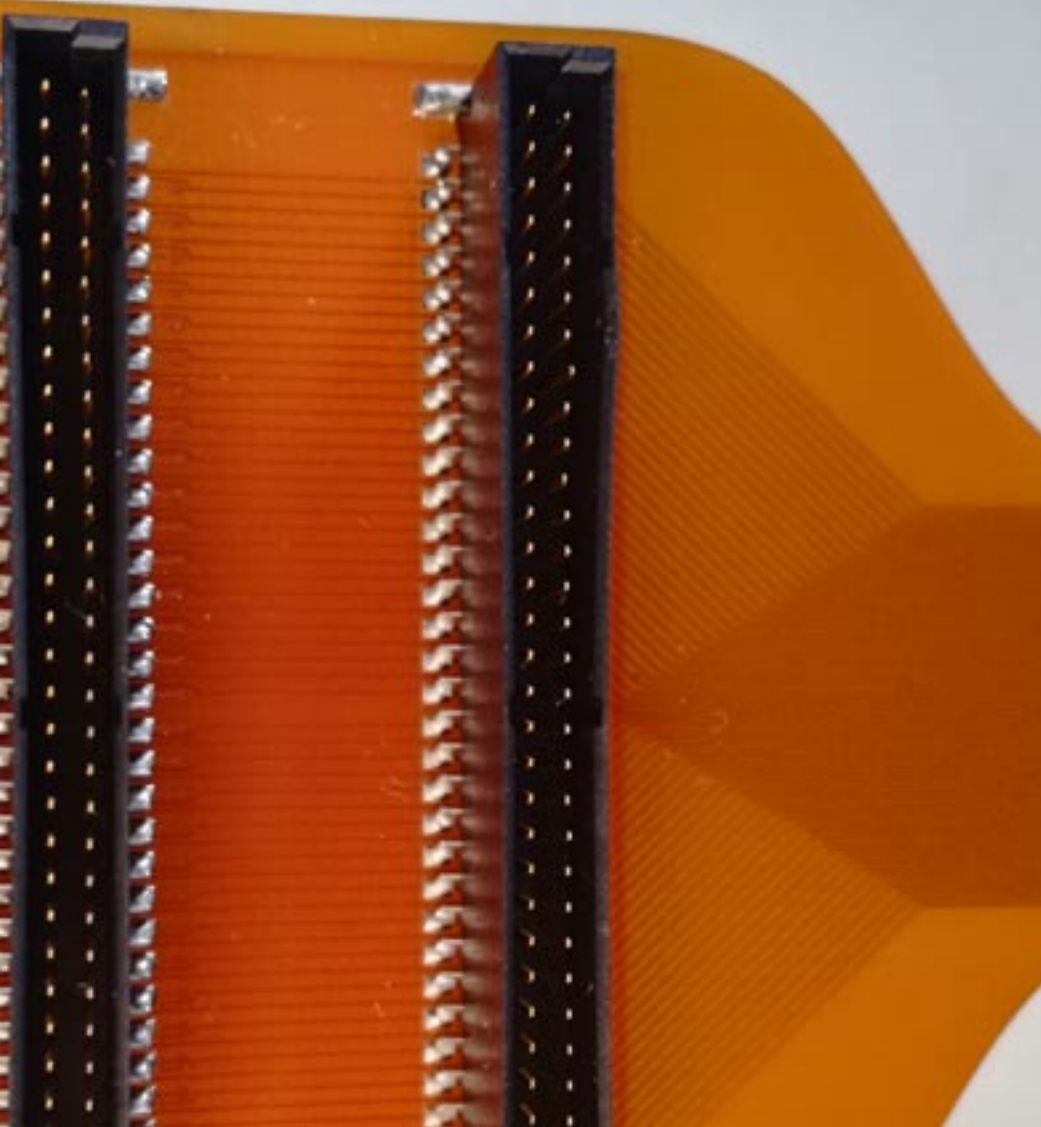
Atrium fibrillation may cause stroke and heart failure and is even associated with death. Electrical signals recorded from young hearts usually have a simple morphology, as electrical waves propagate smoothly through cardiac tissue. Over the years, these electrical signals may become more complex (electropathology) due to damaged cardiac tissue. When the degree of electropathology exceeds a certain threshold, cardiac arrhythmia may occur.

Treatment of Arrhythmia

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.

Treatment can be improved by providing a patient-specific therapy. 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.





Reduce the cardiac arrhythmia burden

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.

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

Medical NeuroDelta



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



Prof. dr. Chris de Zeeuw
Neuroscience (EMC)



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

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 ultrasound, made at TU Delft, 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.

The Medical Delta Improving Mobility with Technology

Improving mobility with technology



Prof. dr. ir. Jaap Harlaar
BioMechanical Engineering (TUD)



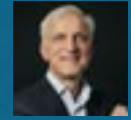
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BioMechanical Engineering
(TUD/LUMC)



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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: practice in a safe manner

The rehabilitation track focuses on outcome prediction, precision diagnostics and unsupervised training. The latter aims at maintaining balance in people who learn to walk again after a stroke. Rehabilitation techniques in the field of robotics are used for treatment.

“Therapy intensity is a major determinant for a positive outcome, but there is simply not enough individualized supervision by professionals to guide the patient”, says Jaap Harlaar, professor of Clinical Biomechanics at TU Delft. “The aim of our project is to let people practice more intensely in the rehab center and at home in a safe manner, by developing equipment they can use to practice unsupervised.”

Recently Heike Vallery, professor at TU Delft, demonstrated the feasibility of a new wearable balance assistance backpack to help people walk with more stability and to keep balance. Together with professor Ribbers from the rehabilitation center Rijndam, professor Vallery will develop this backpack and other wearables to incorporate safe gait training into clinical practice. Implementation in clinical practice will involve the Medical Delta living lab ‘rehabilitation technology’.

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 modeling, 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 Harlaar.

Collaboration

In this consortium, Erasmus MC, TU Delft and LUMC will collaborate closely. The living labs will also be involved in early prototype testing.

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

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)

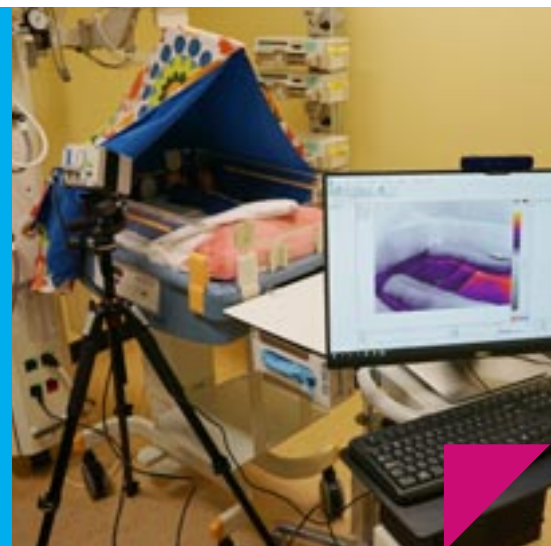


Prof. dr. Thomas Hankemeier

Analytical Biosciences (UL/EMC)



The 100 days before conception and 1000 days thereafter are fundamental for the development of a child and also largely determine their future health. 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 around birth. Stillbirth and death of a child during delivery or in the neonatal period is a dramatic event for parents. 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, with a 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.

Wireless heart rate monitoring

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 warning system to detect early 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

Medical Delta & Benefit for all: towards an inclusive e-Health selfmanagement ecosystem for healthy living

How eHealth is changing healthcare



Prof. dr. Andrea Evers
Health Psychology (UL)



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



Dr. Hans Bussman
Rehabilitation Medicine (EMC)



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

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. It plays a key role in preventing chronic diseases and in maintaining a healthy lifestyle. Existing healthy lifestyle programs can be effective in the short term, but many people eventually relapse into their unhealthy behavioral patterns. A paradigm shift is needed in health behavior – one that aspires to make healthy living attractive, immediately gratifying and convenient in the short term, thereby consolidating healthy living in the long term.

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, according to 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 status (SES) 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.

Integrated solution

The goal of the 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.

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

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. Analyzing 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 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.

All consortium partners actively participate in the Netherlands eHealth Living Lab (NeLL).

METABODELTA: Metabolomics for clinical advances in the Medical Delta

Metabolomics: growing old healthy by predicting and preventing diseases



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



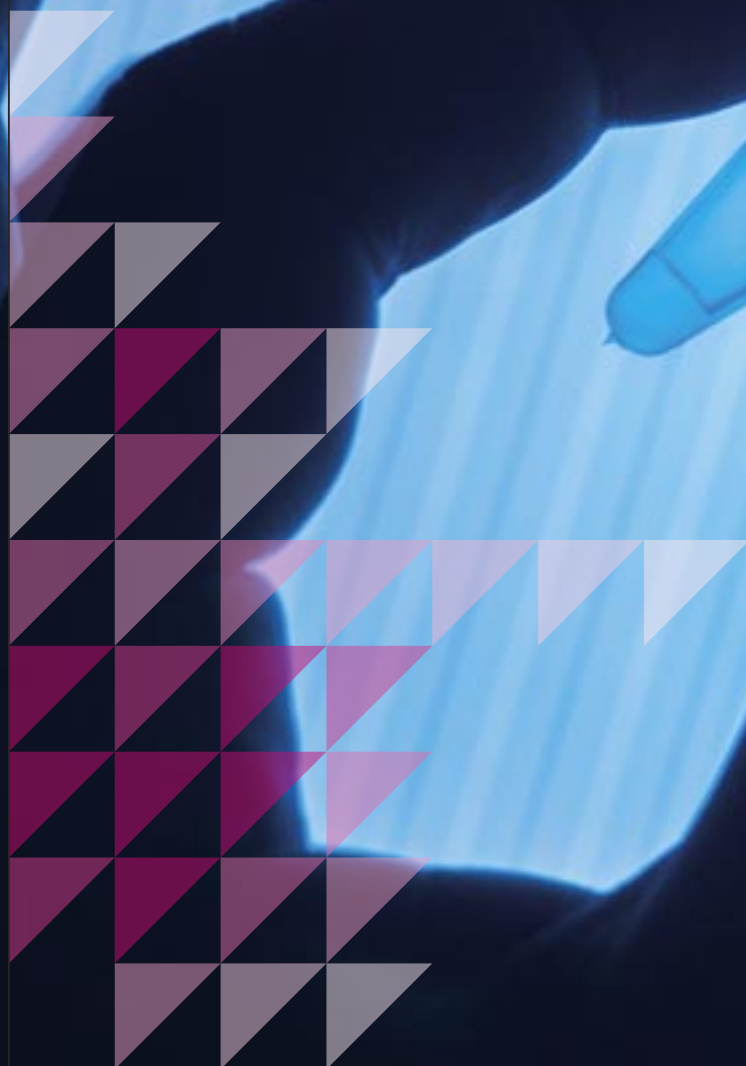
Prof. dr Eline Slagboom
Molecular epidemiology LUMC)



Prof. dr. Cock van Duijn
Epidemiology (EMC/UL)



Prof. dr. Arfan Ikram
Epidemiology (EMC)



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.



Prof. dr. Simon Mooijaart
Epidemiology (LUMC)



Prof. dr. Aad van der Lugt
Radiology (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.

Metabolites

Metabolites are the result of the interplay between genes and these environmental factors. Metabolites provide information about someone's current health state. 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, so measuring the metabolites in the blood can tell you what is going on in the body.

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.

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.

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 understand the main metabolic processes determining heterogeneous response of elderly people to interventions. Using the metabolome as monitoring a tool to improve the health of our ageing society would help to stimulate vitality. 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.

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.

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.

HollandPTC Medical Delta program on HTA value proposition

Determining the cost effectiveness of proton therapy



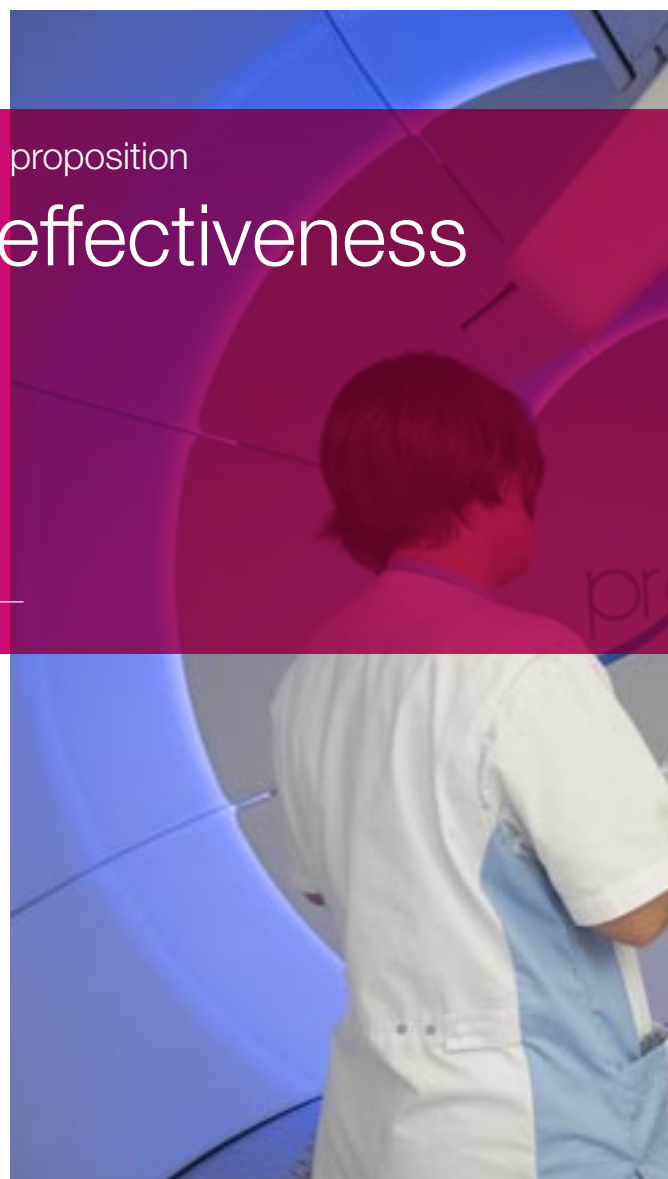
Prof. dr. Marco van Vulpen
Radiotherapy (EMC/LUMC/TUD)



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

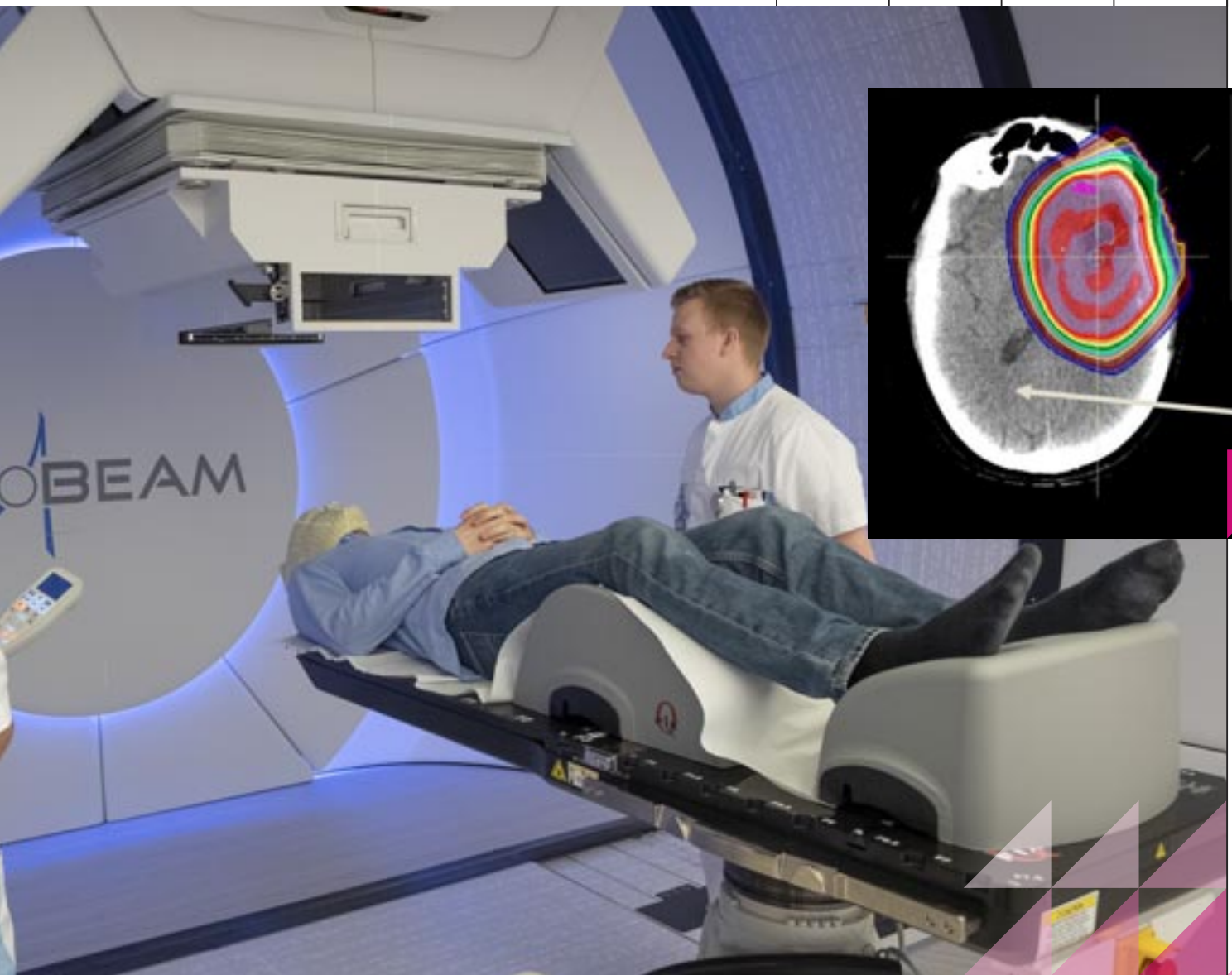
Proton therapy is a new way to treat cancer. HollandPTC, founded by Erasmus MC, LUMC and TU Delft, is a treatment center for proton therapy. Proton therapy is different from traditionally used photon therapy, as it makes use of very local and precise dose deposition on tumors. This causes less damage to the surrounding normal tissue, resulting in fewer side effects.

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 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.



Rising healthcare costs

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. A model to determine the cost effectiveness of proton therapy and to describe its value over photon therapy can be made using a Health Technology Assessment (HTA). This 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. It is essential for patients and society that scarce resources are spent as efficiently as possible. As proton therapy carries high investment and operational costs, but may also provide high clinical value, extensive HTA is essential.



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.

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.

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

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.

Medical Delta Regenerative Medicine 4D: Generating complex tissues with stem cell

Generating complex tissues with stem cells and printing



Prof.dr. Gerjo van Osch

Orthopedics & Otorhinolaryngology (EMC)



Prof. dr. Amir Zadpoor

Biomechanical Engineering (TUD)



Prof. dr. Rob Nelissen

Orthopaedics (LUMC/TUD)



Prof. dr. Luc van der Laan

Experimental Transplantation and Intestinal Surgery (EMC)

3D printing and printing technology

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.



For example, patients with osteoarthritis, a joint disease affecting cartilage and bone, that leads to reduced mobility and pain, could benefit from regenerative medicine. 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.

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. Flat objects can fold into 3D objects over time when stimulated by pH, light, temperature or cells – think of origami structures. 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.

The disease models will be used to better understand diseases. Using the models, medication can be screened, thereby speeding up the quest for new pharmacological treatments.

Future perspective

According to Gerjo van Osch, professor of Connective Tissue Regeneration in the Departments of Orthopaedics and Otorhinolaryngology at Erasmus MC, repairing defects or having biological implants instead of metal ones would be an improvement. However, this program aims to develop disease models in such a way that diseases can be treated at an early stage or even be prevented, so patients wouldn't need an implant at all.

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

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.

Medical Delta's Journey from Prototype to Payment

From prototype to payment



Prof. dr. Antoinette de Bont
Health Care Governance (EUR)



Prof. dr. Hans Severens
Health Policy & Management (EUR)

In the early 1960s, it appeared that thalidomide (Softenon), used as a sleeping pill and sedative for pregnant women, led to babies being born with malformed limbs. Because of this disaster, people realized that new drugs and technologies need to be regulated.

The idea that society must play a role in the development of technologies grew stronger and became the standard. New technologies are too important to leave to doctors and technicians; the development of new technologies should be guided by the assessment of its potential risks, costs, benefits and impact on society.

In the Medical Delta program 'From Prototype to Payment', this societal perspective is positioned in parallel to the 12 scientific programs.

Health Technology Assessment

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 ethical issues, organizational consequences and cost-effectiveness.

Ethical issues relate to doing good to all. Today, big data is used for early detection and diagnosis of

diseases. If we could better predict when someone would get sick, what would the consequences be? Would people want to know this? What would it mean for the insurance business? Would we continue to show solidarity with those who get sick?

Organizational consequences relate to the effects of implementing a new technology. Do we need to train technicians? Will physicians delegate tasks to nurses? What will be the financing model of the 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 would buy the device? The hospital, insurance companies or the patients themselves? Antoinette de Bont, professor Sociology of Innovation in Health Care at the Erasmus University Rotterdam, is considering these type of questions in this Medical Delta program.





The development of new technologies should be guided by the assessment of its potential risks, costs, benefits and impact

Added value

Cost-effectiveness of a new technology is an essential part of the assessment. De Bont comments: “We look at how much a certain technology costs and what added value it offers. New technologies will be compared to technologies that are currently used. An example would be MRI scanners. The scanners used today work well, but even better MRI scanners have been developed. They cost a lot more. Is it worth investing?”

Collaboration

It is important to involve many stakeholders in this Medical Delta program – as mentioned, new technologies are too important to leave to doctors and technicians. Collaboration with the National Health Care Institute (Zorginstituut Nederland) is essential. Next to care institutions, other decision makers, such as the Health and Youth Care Inspectorate and the Ministry of Health, Welfare and Sport, will be involved to develop the methods for evaluating health technologies.



VITALE DELTA

Vitale Delta is a consortium of the Universities of Applied Sciences Leiden, The Hague, Rotterdam and Inholland. This consortium, in cooperation with other partners, is committed to improve the vitality and health of people from young to old. Their work involves strengthening resilience and creating a healthy environment in the Delta region of Leiden, The Hague and Rotterdam.



Vitale Delta joins the strength and knowledge of multiple lecturers. They focus on vitality themes, such as health (care) technology, healthy living, integral health care, social care in the neighbourhood and selfmanagement support. The cooperation that exists within Medical Delta, universities of applied sciences and other knowledge partners (universities and UMCs) in the field of health care technology is being strengthened. Four work packages focus on substantive interaction, staff exchange, network expansion and increasing successful acquisition on the themes.

Vitality of (health care) professionals

One of the new lines of research that is being developed together with a number of partners in the program is Vital (health care) professionals. The quality of care is under pressure due to the rapidly changing (care) context that puts new demands on health care professionals and due to the increasing shortage on the labor market and the increasing workload. In the Rotterdam-Rijnmond region, regional strategic personnel planning shows a shortage of around 2150 care professionals in 2021. Vitale Delta wants to stimulate regional research in this area. This involves research into the sustainable employability of healthcare professionals by strengthening their vitality with the help of social and technological innovation.

www.vitaledelta.nl



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.



The YMD platform connects students in study associations at the LUMC Leiden, TU Delft and Erasmus MC Rotterdam, in the sectors of life sciences, health and technology. To promote the exchange of ideas and opportunities in the field of medical technology, we support and facilitate the study associations' activities. We offer students the opportunity to connect with other students and researchers in the Medical Delta. Via Facebook and LinkedIn, we aim to provide our followers interesting news in health and technology from within and outside the Medical Delta. In April every year, we organize a hackathon focused on health and technology. Healthcare workers, researchers, students, designers and programmers join forces to tackle a real-life problem. The winning team will represent South-Holland in the national finale and will be sponsored to further develop their solution.

For professionals: connect to the YMD talent pool

YMD connects companies and other institutions to the extensive talent pool in South-Holland. With a wealth of high-quality BSc, MSc, and Ph.D. programs in the field of health and technology, we represent over 8000 university students. Recently the students from South-Holland's universities of

applied sciences joined YOUNG Medical Delta. From April 2019, we aim to expand our network among these students. YMD connects students who are organizing an event with professionals who would like to share their idea, innovation, product or knowledge.

For students: Become part of the YMD network!

Would you like to join this growing network of students and young professionals with a passion for technical innovations in healthcare? Follow us on Facebook and LinkedIn to learn about conferences, company visits, competitions and career events in the health and technology sector. Are you looking for an internship or Ph.D. position? Keep an eye on our website's vacancy page. Medical Delta researchers in one of the 13 Research Programs could be looking for a student with your background and broad medical-technical interest.

About Medical Delta

Medical Delta brings together three renowned universities and two university medical centers with universities of applied sciences, governments, companies, healthcare institutions and other parties in South-Holland.

Its mission is to realise technological solutions for sustainable healthcare. Medical Delta thrives in a vital community in which health innovation has top priority. The activities take place in and around the university cities of Delft, Leiden and Rotterdam, all of which have a strong international reputation in life science and healthcare technology.

Medical Delta 2.0

The Scientific Program is central in the strategy note Medical Delta 2.0 Technological solutions for sustainable care 'From Molecule to Reimbursement'. In 2019, Medical Delta has started a large scientific program: over 250 scientists from three universities, two academic medical centers and four universities of applied science in the province of South Holland will collaborate in the coming years. In 12 different consortia they will work together at technological solutions for sustainable healthcare.

Companies, healthcare institutions, the province of South Holland and large cities in the delta are closely involved, for example through 'living labs', where innovations are tested with end users in (healthcare) practice.

The objective for the coming five years is that these research programs grow in size, achieve excellence and develop technological solutions for sustainable care. In this way, Medical Delta gives an enormous boost to the life sciences and health sector in the province South Holland and in the Netherlands as a whole.

Medical Delta is led by Ton van der Steen and Gertine van der Vliet. The board is advised by a Scientific Council and a Social Council and is accountable to the Supervisory Board. The Scientific Council includes Medical Delta professors, educational directors, lecturers and Young Medical Delta representatives. Medical Delta is facilitated by a small, effective agency.



Gertine van der Vliet Msc.
Managing Director Medical Delta



Prof.dr.ir. Ton van der Steen
Chairman Medical Delta