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#2

Magazine about Life Sciences, Health & Technology

we add

Magazine

medical delta
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Transforming healthcare for the next era

Medical Delta introduces 7 new professors!

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Magazine

Medical Delta is a network of life sciences, health and technology organisations. Based in the Netherlands but with a global reach, our aim is to bring together the rich body of knowledge and experience present in the region, and act as a catalyst for health innovation and cooperation

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medical delta

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Welcome to Medical Delta

Dear Reader,

Welcome to the latest issue of *We Add*, in which we bring you up to date on what's been happening at Medical Delta.

Time flies! For almost ten years now, we've been developing a unique network in the fields of life sciences, health and technology. It brings together academic researchers, commercial entrepreneurs and practical innovators – all with the aim of generating significant advances in human health.

In that time, a lot has happened, and we continue to go from strength to strength. On the academic side, we now have 18 professors affiliated to our network. Together we're offering now 5 joint Bachelor's and Master's programmes at universities in the region. On the commercial side, our activities facilitated the creation of many start-ups and assisted in the development of many exciting new products and services. In this issue, you'll meet our most recently appointed Medical Delta professors and read about our latest activities.

Looking to the future, we're developing activities in the field of healthcare Big Data, and are exploring relationships with local universities of applied sciences. We're also expanding our Living Labs testing environment, which considerably speeds up time to market. Further afield, we're expanding the international network through the recently launched EIT-Health with its Dutch-Belgium base in Rotterdam and we created an exchange programme for our senior researchers with the University of California and with entrepreneurs in Silicon Valley.

Are you active in healthcare or medical technology? Have you got a bright idea – whether practical or theoretical – that could lead to an improvement in human health? Would you like to take it further? Come and talk to us. Whether you're a student, an academic researcher, an entrepreneur, an engineer or a healthcare professional, we'd be pleased to meet you.

Meanwhile, I hope you'll find *We Add* an interesting read, and that it triggers some more bright ideas!

Roel Kamerling
Director Medical Delta

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Transforming healthcare for the next era

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When demand runs ahead of supply

The provision of healthcare has taken great strides forward over the past decades, positively affecting the lives of ever-greater swaths of the population. But as the power of medical science grows, the demand for medical care increases exponentially. To meet this demand, healthcare systems have, of necessity, resorted to mass production techniques. Solutions are applied on the basis of one-size-fits-all, patients are 'processed' in large institutions, and problems are often only addressed when they become visible. As the proportion of the population needing care grows bigger (due to ageing, for instance), there will be a temptation to go further, and faster, down this route. And yet, in terms of medical outcomes, it is far from ideal. We know that everyone reacts differently to treatments; that people get better more quickly if they are at home; and that prevention is many times better – and cheaper – than cure.

Time for a step change

Wouldn't it be great if we could treat people as individuals, offering them targeted, personalised treatments, helping them spend as little time as possible in hospital, having them receive most of their care at home? Wouldn't it be even better if we could prevent health problems arising in the first place? This vision of a new, people-centred healthcare would require a significant shift in approach. But we live in an age of innovation. Digital, miniaturised and mobile technologies in various configurations allow us to do more than ever before, with greater precision. Meanwhile, Big Data is enabling us to spot new patterns and relationships, triggering new medical insights. And remote monitoring is saving onerous journeys and yielding subtle, continuous views of a patient's condition. Such innovations also often lower costs.

Doing it together

No one can transform a healthcare system alone. To make the most of these new opportunities, we need to join up in different constellations of expertise, connecting across disciplines and organisations. But this won't just happen. Someone needs to make introductions and maintain momentum. At Medical Delta, we know that most specialists and entrepreneurs recognise the importance of cross-disciplinary research and collaboration. But in practice, they often struggle to find time to explore options and initiate cross-disciplinary projects.

Try it, you'll like it!

At Medical Delta, we help universities, regional governments, scientists and businesses to overcome disciplinary barriers and launch collaborations. Scientists and companies seek us out to help them find partners. We also reach out to them when we see interesting opportunities for interaction. And finally, we facilitate discussions between organisations that may never have considered cross-sector collaboration before.

Let serendipity reign!

The best ideas often come from unexpected connections and sudden insights. There's no logic in the way they occur: sometimes things are discovered by accident. That's why we at Medical Delta believe it's important to bring experts from various fields together in one place – and then 'stir well'.

Scientists, technologists, health professionals – and more

Medical Delta is always looking to promote partnerships between scientists, students, technologists, local governments and others, so that they can produce the best research and practical solutions. We set up meetings, conferences and seminars. Once a connection has been established, we provide practical assistance to get the project off the ground and ensure continuity through reliable funding. And when a project becomes a product or business, we can help with implementation, user-needs analysis, business development and evaluation. In this way, we ensure that such research is driven not only by what is possible, but above all by what is necessary.

Bringing the patient to the chip

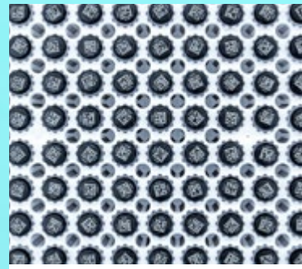
Prof.dr. Cock van Duijn

Different diseases, same genes
“When you study the human genome, it emerges that the majority of the most common disorders are the result of a large number of changes to the DNA that are in themselves harmless. These ultimately lead to common diseases, such as dementia and hypertension. The risk of a specific disease is determined by the sum of the number of genetic variants. However, no one had expected that there would be so many. In research into Alzheimer’s, we are already aware of around thirty genetic variants, but it will probably ultimately turn out to be hundreds. We are also finding that disorders are genetically correlated. For example, the genes that play a role in Alzheimer’s disease overlap with those for glaucoma, a disease in which the optic nerve deteriorates. The palette of glaucoma genes strongly overlaps with that of ALS. We are gaining an understanding of the genes that explain why diseases are clustered in a patient or family. The challenge is to translate this into the proteins and other molecules (metabolites) that relate to the expression of these genes and that can be used to develop drugs or serve as markers, indicating the start of the disease process.”

The lucky white ravens
“This is where the collaboration with Thomas Hankemeier from Leiden comes into its own. With his metabolomics facility, he can measure metabolites on a large scale across a broad range of concentrations. We are now measuring hundreds of substances in the blood of large groups of participants in epidemiological research. We are comparing people, who, based on their genetic profile, we know will go on to develop Alzheimer’s disease later in life. This allows us to identify the markers that predict the disease. They are the black ravens, or the unlucky ones. But we are perhaps even more interested in the white ravens: the group of people who are fortunate enough to have inherited a small number of variants related to the diseases from their parents. It is their metabolites that point the way towards the development of drugs.”

Brain on a chip
“These are the kind of moments when you think: this is too good to be true. For me, it happened at a meeting with Thomas Hankemeier and Rick Grobbee, from Utrecht, who is conducting research into cardiovascular diseases. Thomas was telling me about induced stem cells and his dream of converting them into cells that cover blood vessels. The idea is to create a ‘model organism on a chip’. This is how the idea of creating induced stem cells came about, converting them into brain cells and thereby creating a model of the brain on a chip. We now have various grants to translate the blood cells from ‘white ravens’ and ‘black ravens’ into a model of their brains on a chip. This will enable us to conduct large-scale research into what goes wrong in the brain of a black raven and what is so good about the metabolism in the brain of a white raven.”

Modelling complexity
“If you really want to tackle Alzheimer’s disease, you need to do it as early as possible, when the brain cells have not yet died off. We have secured various European grants and are now setting to work with the first prototypes, together with the industry. In particular, we are working on the interaction between the brain and the blood vessels. The ERGO study in Rotterdam suggests that this interaction is a key aspect in a large proportion of patients with Alzheimer’s disease in old age. There are still lots of improvements to be made. How effectively can you model the complexity of the brain and the blood-brain barrier? This is one of the first questions we intend to elaborate on in the Medical Delta.”



Storage of DNA, plasma, serum and urine in ErasmusMC Biobank.

Bio

Cock van Duijn graduated from the Agricultural University Wageningen in 1987 and gained a medical degree from the Erasmus University in 1992. She founded the MSc and PhD program in Genetic Epidemiology of Erasmus MC of which she is Scientific Director. She has been a member of the Royal Netherlands Academy of Arts and Sciences, since 2014.

Detecting the earliest signs

Prof.dr. Thomas Hankemeier

The tricky bit: a good readout

“Genes provide you with information about health risks. However, they do not tell you that you will definitely become ill, or, if you do, when that will happen. But when you look at metabolites – the interim and end products of metabolism – they give an indication of how well you really are at that moment! The tricky bit is to create a good read-out that measures all relevant metabolites that can predict the development of diseases in principle; it is then a case of making that affordable. After that, the data needs to be properly interpreted and then it is a question of suggesting therapies. This approach could even make it possible to identify potential diseases at a very early stage, when they are still reversible, enabling us to prevent disease.”

Blood samples from everyone in hospital

“We need to develop technology that can measure thousands of metabolites with the required level of precision. In other words, the relevant metabolites, which are associated with such processes as oxidative stress and inflammatory stress. These substances are transported by the blood. Currently, as an initial test case, we are able to make use of blood samples collected during studies in which people donated blood. However, I hope that we will be able to extend this to a large number of patients, for example by taking a blood sample from everyone admitted to hospital. It is already standard practice to take blood in this way, but the research conducted on it is very limited. This needs to be extended, so that we can use it – in addition to our previous knowledge – to learn how to detect a disease at an early stage.”

A body on a chip

“Currently, on a laboratory scale, we are able to measure hundreds of metabolites in around ten to twenty thousand samples every year. Building more laboratories would be ineficient. What is needed is new technology. That would bring us to the next step: from all those thousands of metabolites, you need to select biomarkers that provide information about people’s state of health. This then raises the question: is this purely about correlation or are there really causal relationships? How do you single out the causal markers? Part of the answer can be found in genetics – but there is another route. We want to be able to build systems on chips, which means using a person’s stem cells to grow several cells of a specific type, such as kidney or brain cells. The stem cells will also be used to grow blood vessels. We will then place these organ- and blood vessel cells on a chip, enabling us to explore how the body’s cells interact with each other and with the blood. In the near future, this will enable us to place the cells of people who we know to be at risk of a specific health issue onto a chip and conduct research on them. We will be able to see how the cells respond to specific substances that we administer via the blood vessels.”

“That will make it possible to refine therapies. On a chip of this kind, there are 96 units in which there is a piece of grown organ tissue and a piece of blood vessel. This therefore makes it possible to test a drug on 96 test subjects all that same time, or alternatively, to create 96 units with different cells from the same person and then to test the effect of various potential drugs on that single patient.”

Innovation should stay here!

“In many ways, you could say I am a fan of America. There, if they come up with a good idea, they put it into practice straightaway. In the US, starting a business goes much faster than in Europe. In the field of metabolomics, research in Europe is still ahead of the US, but there is now increasing investment in it there as well. My question is this: what can we do here and now in order to make these technological innovations happen here, rather than in the US? That is what I intend to fight for. For our organ-on-a-chip company, Mimetas, we have already achieved that here in Leiden. But collecting, conserving and monitoring patient material is not something that you can do in a company; that needs to be done in an academic setting. But it may be possible to achieve the technological innovations in a company. Whatever the case, I am determined to develop them here.”

Bio

Thomas Hankemeier received his PhD in analytical chemistry at the VU Amsterdam. From 1996 to 2004 he was Scientific Product Manager in the Department of Analytical Sciences at TNO. Since 2004 he has been full professor and head of the Division for Analytical Biosciences at the LACDR, Leiden University. He is also Scientific Director of the Netherlands Metabolomics Centre and co-founder of MIMETAS.

Building a cell from the bottom up

Prof.dr. Marileen Dogterom

Putting proteins in a droplet

“What we are researching is how the structures develop that make cell division possible. How the threads form that arrange the chromosomes in the cell nucleus and then pull them to two sides within the cell, enabling the cells to divide. We are attempting to bring together the proteins that form these threads and control this process, to see if we can initiate the process ourselves. We do it in a micro-droplet of water, floating in oil. In that droplet, we bring the proteins together, one by one. It then turns out that with an amazingly small number of proteins, you can build something like a ‘cellular division machine’. The addition of more proteins will rapidly intensify the complexity of the system, making it increasingly realistic.”

Towards a realistic synthetic cell

“Another way of studying cell division is to take a normal cell and ‘unclothe it’, by repeatedly removing one gene (and therefore one protein) from the DNA and then seeing if the cell can still divide. This is more like Craig Venter’s approach, who recently said in a paper that he had been able to trace the DNA of a bacterium back to several hundred genes. It would appear that this number is sufficient to enable the entire cell, including cell division, to function. But these include many genes whose function we do not fully understand. What is so great about this approach is that you build the system from the bottom up, which helps you to understand what the role of each individual protein is.”

“Currently, we are working with around ten proteins, but I think that this will need ultimately to increase by another factor of ten in order to be able to recreate an entire cell. Craig Venter is now working with several hundred genes. I think that, in five or ten years’ time, we will be able to build a realistic synthetic cell, with over a hundred genes, which can divide and maintain itself for several generations.”

A close-knit community

“Our research is part of a major international initiative. Here in Delft we are working with physicists and biochemists. We also collaborate with Groningen, AMOLF and VU University Amsterdam, Nijmegen and Wageningen. In Groningen, they are conducting research into cell metabolism; AMOLF and VU are exploring gene expression; Nijmegen’s focus is on the thermodynamics of the system and Wageningen is looking at genome engineering. As for real cells, we are working closely with Anna Akhmanova’s group in Utrecht; they are manipulating the same proteins in living cells that we are adding to our micro-droplets. We are also collaborating closely in this field with Leiden and Rotterdam, and within Medical Delta we have a complete close-knit single molecule and cellular biophysics research community, with Thomas Schmidt in Leiden and Claire Wyman in Rotterdam.”

The route, not the destination

“Both of these research lines, synthetic cells and cellular biophysics research, will increasingly grow closer together in the years ahead. It is difficult to predict what impact this will have, but it will definitely result in a much more fundamental understanding of the cell – which is already of significant interest for the medical community. With the synthetic cell, we will soon have a testing system (which I like to compare with a flight simulator), in which we can add or manipulate all kinds of proteins in order to measure their effect. But you need to realise that achieving that ‘thing’ is not really the main aim. On the route towards that, we are learning to understand living systems at a much deeper level. That fundamental understanding can teach us so much.”

Bio

Marileen Dogterom was trained as a theoretical physicist at the University of Groningen. After finishing her thesis in Paris and Princeton, and a post doc position at Bell Labs, she became head of department at the FOM Institute AMOLF in Amsterdam. In 2000 she took up a professorship at Leiden University. She has been professor at TU Delft and Chair of the Department of Bionanoscience since 2014.

Looking at DNA repair

Prof.dr. Claire Wyman

‘Feel’ the proteins working

“When I arrived here in Rotterdam about 20 years ago, the fields of physics and biology were just starting to converge. A new kind of science was being developed. I started working on tools to manipulate and study individual biomolecules with researchers at TU Delft. My neighbour in Delft, Cees Dekker, was developing new nanobiology tools in his lab. His instruments could hold and stretch individual molecules. He and Nynke Dekker were already working with DNA. The physical properties they could measure told us a lot about how DNA works. We studied what happens during the repair process of DNA breaks, which can cause cancer and other medical problems. In the cell nucleus, breaks are repaired by teams of different proteins, one of the key ones being RAD51. When this protein binds to a DNA strand to do its repair work, the strand changes shape, length and stiffness – all things we can measure. Nynke’s group developed an instrument to measure twist changes in DNA and the forces involved. Through these instruments, you can ‘feel’ the proteins working!”

Modify to make it faster

“I’m currently working with Martin Depken, a theoretician at TU Delft, on the behaviour of the protein BRCA2. This is a very large and very fascinating protein; first, it detects a DNA break and then leads RAD51 proteins to the site to fix it. In Rotterdam, we developed certain microscopy methods with the Optical Imaging Center and image analysis tools to actually follow BRCA2 in the nucleus of live cells. We can observe a single molecule: how it diffuses in the nucleus and how long it stays in a particular place where it may – or may not – do its job. Together with the theoreticians, we want to develop a mathematical model of this process. In a subsequent phase, we aim to modify the protein to force it to stay in a specific spot for a longer or shorter time and see how this affects DNA repair. If we make the process go ten times faster, it might make no difference; but if we can make it go ten times slower, that could be a big deal. Such changes could determine whether or not a person gets cancer, or responds to a certain treatment.”

“Research into BRCA2 is especially promising because a lot is already known about the variations that exist in human populations. But we still know very little about how these variations correlate with particular diseases. Perhaps we can correlate these known mutations with biophysical data on BRCA2 behaviour. These variants would then have prognostic value to better predict cancer risks, and to improve cancer treatment. We already know, for instance, that certain cancer treatments are very effective in people who have a specific BRCA2 mutation.”

Too good can be dangerous

“People often ask me: ‘Can’t you simply make a highly effective variant of BRCA2 or RAD51 and use that as therapy?’ That’s a very good question, but you have to consider that things that are highly effective can be dangerous too. A healthy cell can repair DNA damage perfectly fine without help. But when that system fails, we want to know what went wrong. Was there not enough protein? Not in the right place? Et cetera. We can produce or isolate different versions of RAD51 that do their job very well. But when you put them into a nucleus, they may hang around for too long and get in the way. Like the cranes that were outside my office window for several years building that new hospital; they were very useful for driving in the foundation pilings but had to get out of the way when construction started. In other words, you can have something very promising in a test tube, but you have to understand the biochemical balance in a living cell. That’s why we work so closely with cell biologists and use various animal models.”

Bio

Claire Wyman received her PhD in Molecular Biology from The University of California at Berkeley in 1990. In 1996, she joined the Department of Cell Biology and Genetics at the Erasmus MC. In 2005, she was appointed Associate Professor in the Department of Radiation Oncology at Erasmus MC. She has been Professor of Molecular Radiation Biology since August 2008.

‘To really get things moving…’

Prof.dr. Corrie Marijnen

Building a bridge

“Medical professionals, are always working on improving healthcare for their patients. Innovation with a focus on the individual patient is very important to realize this. For me, collaborating with TU Delft poses a unique opportunity to integrate healthcare needs with technical innovation. Starting by looking around the EEMCS faculty: Electrical Engineering, Mathematics and Computer Science. I see it as my role to build a bridge between what Leiden needs and what TU Delft has to offer.”

“My specialist field is radiotherapy: using radiation to treat cancer. This treatment tends to cause side effects to our patients. In recent years, I have taken an interest in proton therapy, a major step forward in the treatment of patients with certain types of cancer. It enables a significant reduction of side effects, whilst tumour control is the same as with conventional radiation. As a consequence, the quality of life will be better in cancer survivors.

Within the Medical Delta consortium currently one of the most modern facilities for proton therapy is being built in Delft, facilitating both optimal patient care and innovative research.”

Analysis tailored to the patient

“The question is: ‘Who is eligible for this therapy?’. The best way to find out would be to conduct double-blind studies, but that is very difficult for both ethical and technical reasons. Instead, we will create two treatment plans for every patient: one based on proton therapy and the other based on conventional radiotherapy. Based on the calculated radiation dose, you can estimate the likelihood of damage to the organs in close proximity to the tumour, which is something we want to minimise as much as possible.”

“We now aim to systematically record the most up-to-date information about the individual patient. We are setting up a model in which every patient will complete questionnaires, so we know exactly what the therapy has achieved and whether damage has been caused. The information will be immediately used in iterative process: the data from each patient treated will provide input for the model and contribute to the quality of the subsequent decision.

In the LUMC, we have developed a method called Adaptive Conjoint Analysis (ACA), which uses a computer program to find out the patient’s preferences. However, it works on the basis of aggregated data from large numbers of patients. That is far too crude. What you really need is an tailored analysis of costs and benefits based on the individual patient characteristics.”

Call in expertise from Delft

“Some studies show that certain patients have a preference for a lower chance of cure, in order to avoid severe side effects. Elderly patients sometimes prefer a less radical approach, whereas young parents opt for the therapy that offers the greatest chance of cure (potentially with a lot of side effects). This shows that doctors shouldn’t decide for their patients, shared decision making is absolutely required. For example, in patients with a tumour in the head & neck region, radiation may cause damage to the saliva glands, or to the muscles involved in swallowing. Currently, the care providers decide how the radiation dose is distributed and what organs are most at risk. But it is possible that a patient would prefer to avoid certain side effects rather than others. He or she could find a dry mouth much more of a problem than issues with swallowing. This information needs to be taken into account in the treatment planning system. That will involve the processing of a lot of complicated data, which is why it is time to call in the expertise at TU Delft.”

“I not only intend to look at EEMCS; Many projects at Industrial Design Engineering could be useful for patients as well. We can no doubt also learn from Technology, Policy and Management about issues such as optimising our logistical processes. I see it as my role to say: this is something that could certainly be useful to us. Or perhaps to pose a question for which we still don’t have an answer, but that matches the expertise at TU Delft.”

“This assignment comes with certain responsibilities. It challenges me to look at things that we have been wanting to change for years and really get things moving now. In my view, that is what the Medical Delta is meant for.”

Bio

Corrie Marijnen started her training as Radation Oncologist at LUMC in 1994 and received her registration in 1999. In 2002, she completed her thesis on Rectal Cancer and became a member of staff. From 2004 to 2008, she worked at the Department of Radiotherapy in the Netherlands Cancer Institute. She returned to Leiden as Chair of the Department of Radiotherapy and has been involved in the HollandPTC initiative, for the past few years as Medical Director together with Jean-Philippe Pignol.

Destroying tumour cells with nanoparticles

Prof.dr. Jean-Philippe Pignol

Simple, fast, painless

“Thanks to early detection techniques such as mammography, colonoscopy and PSA screening, cancer is being diagnosed at earlier stages than ever before and we’ve seen real progress in cancer treatments. I specialise in breast cancer, and sixty per cent of women who get breast cancer are diagnosed at an early stage, which means that the cancer is still confined to the breast and has not spread to the lymph nodes in the armpit or to other organs. The current standard treatment is to remove the lump, and give radiation treatment to treat any microscopic cancer cells that remain in the breast to prevent recurrence. Normally, radiation treatments are administered five days a week over several weeks. This is highly disruptive to the patient’s normal life, and the treatment itself has painful side effects. The aim of our research is to develop a treatment that is simple, efficient, fast, painless, and that preserves the breast with the best cosmetic outcome possible.”

Radioactive seeds

“For about 30 years, men with prostate cancer have been treated using a special technique in which radioactive seeds are inserted into the tumour in a single, one-time procedure. The procedure takes only around an hour to complete, and the radiation treatment is slowly released while the patient is at home or at work as normal. I have developed the same technique for women with breast cancer to take place after the lumpectomy, which is a limited surgical procedure to remove the bulk of the tumour. With PBSI (Permanent Breast Seed Implant), we insert radioactive seeds the size of a grain of rice into the breast. The results are really good. It’s better and safer than any other technique to date and there are practically no side effects. This procedure also takes around an hour and after that the patient can go home and lead a normal life.”

And then we heat them..

“Now, the plan is to take the same idea but with nanoparticles of approximately thirty nanometres, which will consist of a radioactive core within a shell of highly magnetic metal. This shell makes it possible to see the nanoparticles using magnetic resonance imaging, or MRI. So we can see in real time where the radiation goes, and which direction it is moving in. In addition, the magnetic shell enables us to use oscillating magnetic fields to produce heat for cancer ablation. Within a couple of weeks, once the radioactivity has been fully released, the nanoparticles become inactive and disappear.”

Best of both worlds

“Thanks to Medical Delta, I am now working with Antonia Denkova and Kristina Djanashvili from TU Delft to develop the nanoparticles. At Erasmus MC, Prof. Gerard van Rhoon and I are also working with the University of Eindhoven to optimise a technique using heated radio frequencies to destroy tumour tissue. This research is being supported by Elekta – a major player in the field of radiotherapy. Elekta is interested because it believes that this is the future of brachytherapy.”

“For me, working in the Netherlands is really wonderful. We have a combination of the best of North America and the best of Europe. In the US, people are very good at making things happen. And so are Dutch people, who created a whole country out of the sea bed! But here you also find more refined European values, like good cooperation and a clear sense of the big picture. After eighteen months here, I am truly amazed how bright and open-minded the researchers at Erasmus, Delft and Leiden are! Medical Delta also attracts big companies that trust the quality of the work done here – it really is a mark of quality when you say something was done in the Netherlands.”

Bio

Jean-Philippe Pignol is a specialist in radiation oncology with a PhD in nuclear physics. In 2000, he joined the University of Toronto and became a full professor in 2008 of the Departments of Radiation Oncology, Medical Biophysics and at the Institute of Medical Sciences. Since August 2014, he has been Professor and Chair of the department of Radiation Oncology at Erasmus MC Cancer Institute in Rotterdam, with a co-appointment at TU Delft.

‘That’s what I need!’

Prof.dr. Rob Nelissen

Doctor and engineer

“In an academic hospital, you can come up with all kinds of great ideas – but then you need someone to put them into practice. What’s great is that engineers and doctors have different ways of thinking – and it is all about interaction. Someone at Delft will come up with a device on the drawing board that looks absolutely great, and everything has been calculated with the utmost precision. But it’s then up to a doctor to make sure it actually works in a living patient. That’s why you need to have doctors working with the engineers. For my part, I feel I am a bit of both, which is pretty characteristic for orthopaedic surgeons, I think. They enjoy working with their hands. My days in the operating theatre are the most relaxed days of the week. But I also enjoy academic work!”

An adenovirus to remove tissue

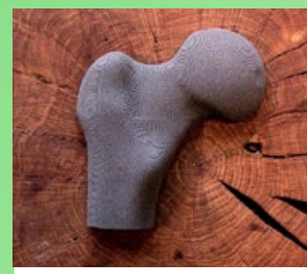
“The best example of this interaction is, of course, our joint approach to prostheses in older patients that have become loose. In such cases, operating is not a good idea because of the risk. Non-invasive therapies are more advisable. In order to reattach the prosthesis (usually an artificial hip), we use cement that we spray between the bone and the prosthesis. But before that, the tough ‘interphase tissue’ that has grown in between them needs to be removed. Rob Hoeben, from the LUMC, had contact with a British company that was working on gene therapy. In collaboration with them, we developed a method which involved treating the tissue using a genetically manipulated adenovirus (the virus that causes sore throats). An additional gene had been added to the virus that initiates cell death, breaking down the tissue. Here in Leiden, we were the first to use gene therapy in this way. Twelve patients were involved. The early results were reasonable, but the British company wanted its money, and we did not have it. As a result, we had to come up with an alternative solution.”

“We looked at such options as water jets and laser’s. But one day I was talking to a urologist, Rob Pelger of the LUMC. He was working on a catheter for kidneys – and I thought: I need something like that! I want to use it to get inside and deal with the tissue. They are now working on the device at TU Delft. It may be possible to remove the tissue mechanically using the catheter, but we could also use it in combination with gene therapy, which would enable us to apply the virus in a much more targeted way. So that it reaches where it really needs to be. This is something we are still in the process of considering.”

Ideal surgeons

“What I would like to do is compare this approach using gene therapy with the current methods we use. But it’s difficult to do this based on people’s perception of pain, which can be very subjective. You also need to measure whether the prosthesis has shifted. Normal x-ray does not offer the accuracy needed for that. This all brings me back to some great collaboration with TU Delft: we have developed RSA, Roentgen Stereometric Analysis. It measures the migration of the prosthesis to an accuracy of 0.01 mm and rotation to an accuracy of 0.1 degrees. It’sreally fantastic. It means you don’t need large groups of patients for research but can work with small groups to demonstrate an effect. That makes the research more interesting for companies that want to market new implants. The result is therefore better products – and more PhD students for us, of course.”

“Surgeons and engineers need to come together. This is why we – Leiden, Delft and the Erasmus MC – launched the Bachelor’s degree programme in Clinical Technology in September 2014. It is a three-year programme that prepares students for the Master’s degree programme in Biomedical Engineering or ... for Medicine. In this way, we get doctors who are semi-engineers. They could end up becoming the ideal surgeons.”



Integrating Human Technology

Bio

Rob Nelissen graduated in Medicine in 1985 at Leiden University. In 1994 he became a consultant orthopaedic surgeon at Leiden University Medical Center. He received his PhD in 1995. Five years later he became the Director of the residency programme and in 2005 he was appointed Professor of Experimental Orthopaedics and later became Professor of Orthopaedics in 2008. In 2006 he was appointed Chair of the Department of Orthopaedics. He is founder of the Dutch Arthoplasty Register and currently he is the President of the Netherlands Orthopaedic Association.

The Sophia Rehabilitation SmartLab is developing workable applications for medical rehabilitation. It provides excellent developing and testing facilities for companies, using actual rehabilitation patients.

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, organisational solutions and so on.

The partners in Medical Delta – businesses, knowledge institutions, healthcare providers and regional governments – are currently working to establish a system of joint Living Labs. These will focus on a number of key themes, including clinical technology, rehabilitation, independent living, and healthy lifestyle and prevention. Our region already has a number of well-established and newer labs with excellent growth potential. They could benefit greatly from collaboration and from sharing best practices. The Medical Delta partners are therefore providing expertise, facilities and manpower to help them develop a professional approach that will make them leaders both in the Netherlands and Europe as a whole. A new website presenting these labs is to be launched in the summer of 2016.

For more information about the Medical Delta Living Labs, please contact Rian Rijnsburger at rian.rijnsburger@medicaldelta.nl

Medical Delta Business Partnerships: typically Dutch

'Medical Delta is not only an academic party,' says Dr Colja Laane, appointed as a Business Partnership Manager for Medical Delta on 1 April. 'We want to be the grease in the wheels of the golden triangle of government, knowledge institutes and industry.'

In order to create links with the latter target group, Medical Delta is inviting companies to become Business Partners. 'Approximately 35 companies have already done just that, says Laane'. 'And there are dozens more on our wish list.' As Business Partners, companies receive access to an unprecedented network of knowledge and entrepreneurship. 'Companies that are looking to develop a new market will find a good foothold and a great deal of experience and expertise with us.

The necessary initiatives for supporting and fostering entrepreneurs, such as InnovationQuarter, the regional development agency for South Holland, already exist both in the region and in the Netherlands at large. Dr Laane says: 'We're not going to do what is already being done. This is why we're now exploring what companies want. The Business Partnership must have added value.' "Come to us and tell us what is needed," is Laane's message for the business community in the Medical Delta region.

For this reason, Laane is looking into whether the old instrument of public-private PhD projects can be resurrected. 'We also see that companies often don't make use of available resources, such as the TKI bonus. We can help them to not miss out on that additional 25-cent subsidy per euro investment.' Medical Delta also wants to provide space for matchmaking between start-ups and venture capitalists.

The Netherlands has substantial experience with public-private partnerships, which are often entered into apprehensively in other countries. 'Whether you call it unproductive dialogue, or a golden triangle, we now know how to approach this type of partnership and interesting things come of them.' And this is what Medical Delta wishes to contribute to as much as possible.

EIT Health:
bold words, great ambitions

'It's really very simple,' says Menno Kok, Director of the Belgian-Dutch Health branch of the European Institute of Innovation & Technology (EIT Health). 'The EIT does in Europe what Medical Delta does in South Holland and the surrounding area.' Kok should know because, until 1 March 2016, he was Director of the Medical Delta organisation. Every so often, he still uses the *we* form when talking about his previous employer, but his new *we* is all of Europe.

More than 130 companies, the academic elite of Europe and 2 billion euros: everything about EIT Health seems overwhelmingly large. Kok goes on to qualify this impression: 'The 2 billion is 25% EU subsidies and 75% our own funds. Participating in EIT Health is not about money, but rather about a common strategy for innovation in the healthcare domain and for sustainable partnerships. In the lead'up to launching the EIT, we parted ways with certain companies that expected to receive sums of easy subsidy money.'

The entire subsidy goes towards substantive activities; the partners themselves must cough up all the overheads and organisational costs. EIT Health is composed of seven centres, one of which lies in the heart of Medical Delta. 'These centres are, above all, a meeting place for young companies that come seeking advice or coaching, or to get to know EIT and other players in the healthcare domain.' 'We don't want EIT Health to be some anonymous organisation.'

EIT Health runs three types of programme ('Campus', 'Accelerator' and 'Innovation Projects', see http://eithealth.eu) in particular to stimulate collaboration between various parties, subject to a joint strategy and mutual openness. Partners learn from each other the best way of introducing innovations to the market; they help each other and share their knowledge in the spirit of 'open innovation'. The Medical Delta partners, as co-founders of the EIT, have the most direct access to the subsidies, with the fewest restrictions. Kok says: 'At the same time, the EIT model is unique in that it is freely accessible to anyone in Europe, whether you're a partner or not. This enables us to reach thousands of SMEs.'

The overarching objective of EIT Health is to make healthcare sustainable. 'Bold words, great ambitions,' Kok says. The role of education is crucial here, ideally it should go without saying that knowledge amassed during a PhD project, for example, should then be transformed into innovations. An innovation-oriented mind-set in education is one of the business community's greatest desires and a task for the universities.'

In his new position, Kok travels all over Europe. 'Despite all our modern means of communication, physically sitting down together is still the best.' The people he encounters believe in the opportunities the EIT offers. 'They don't want to talk endlessly, but roll up their sleeves and get down to work.' It's also no coincidence that the Belgian-Dutch department of EIT Health is based iin Rotterdam, city famous for it's energy and practical resourcefulness.

YOUNG Medical Delta:
building a new network

At the beginning of March 2016, seven students and PhD candidates launched a committee of a new initiative: YOUNG Medical Delta. In doing so they took on the challenge of helping a new generation experience the collaboration between science, the business community and education on the one hand, and between the disciplines of the life sciences, health and technology on the other. Since then, a great deal has come the committee's way.

In March, Roel Kamerling, Director of the Medical Delta organisation, said that YOUNG Medical Delta would be a boost for Medical Delta as a whole. In order to get the job done, the committee members were appointed a year previously in order to shape its activities with a degree of autonomy. 'It's a wonderful thing to be part of,' says Carla van Alem MSc, a PhD candidate at the Leiden University Medical Center and chair of the new committee.

'Everyone in the committee is highly motivated and working extremely quickly. We have already made enormous strides in the right direction'. YOUNG Medical Delta is now busy recruiting members. Its Facebook page had 100 likes within 12 hours of launching ('Wow, great everyone!' responded Kamerling enthusiastically on the page). Van Alem says: 'Our task is to lay the foundations for this initiative. Committees that come after us will hopefully reap the rewards of our efforts.' Her role as chair is already costing Van Alem more time than originally anticipated. 'But perhaps my expectations were a little naive.'

The committee is being approached from all sides to mobilise the young members of Medical Delta for network meetings and/or career days. 'I didn't think we would have this much on our plate,' Van Alem says. 'We're now working on recruiting members and creating an online registration form so that shortly we'll be able to provide members with targeted information, including through newsletters.'

In the coming months, YOUNG Medical Delta will participate in various events and, in late 2016, will organise its own first event. 'We're still brainstorming what that will be.' Other matters still on the to-do list include expanding to include entrepreneurs who are starting out and setting up an internship database. Van Alem hopes that the initiative will create significant added value for Medical Delta. 'Keep your eye on us!'

Our 18 Medical Delta professors

Prof.dr. Jenny Dankelman
TU Delft - Biomechanical Engineering
LUMC - Gynaecology

Prof.dr. Marileen Dogterom
TU Delft - Bionanoscience
Leiden University - Physics

Prof.dr. Cock van Duijn
Erasmus MC - Epidemology
Leiden University - LACDR

Prof.dr.ir. Richard Goossens
TU Delft - Industrial Design
Erasmus MC - Physical Ergonomics

Prof.dr. Thomas Hankemeier
Leiden University - LACDR
Erasmus MC - Epidemology

Prof.dr. Frans van der Helm
TU Delft - Biomechanical Engineering
LUMC - Medicine

Prof.dr. Frank Willem Jansen
LUMC - Gynaecology
TU Delft - Biomechanical Engineering

Prof.dr.ir. Nico de Jong
Erasmus MC - Thorax Centre BME
TU Delft - Imaging Science & Technology

Prof.dr.ir. Boudewijn Lelieveldt
LUMC - Biomedical Imaging
TU Delft - Multimedia signal processing

Prof.dr. Corrie Marijnen
LUMC - Radiotherapy
TU Delft - Bioinformatics

Prof.dr. Rob Nelissen
LUMC - Orthopaedics
TU Delft - Biomechanical Engineering

Prof.dr. Wiro Niessen
Erasmus MC - Biomedical Imaging
TU Delft - Imaging Science & Technology

Prof.dr. Jean Philippe Pignol
Erasmus MC - Radiotherapy
TU Delft - Applied Physics

Prof.dr.ir. Ton van der Steen
Erasmus MC - Biomedical Engineering, Transducers and intravascular techniques
TU Delft - Applied Sciences

Prof.dr. Hans Tanke
LUMC - Molecular Cell Biology
Leiden University - NeCEN
TU Delft - Bionanoscience

Prof.dr.ir. Edward Valstar
TU Delft - Biomechanical Engineering
LUMC - Orthopaedics

Prof.dr.ir. Lucas van Vliet
TU Delft - Imaging Science & Technology
Leiden University - Science

Prof.dr. Claire Wyman
Erasmus MC - Radiation Oncology
TU Delft - Bionanoscience

Medical Delta is formed by the following partners:

Universiteit Leiden · Leids Universitair Medisch Centrum · TU Delft · Erasmus MC · Erasmus Universiteit Rotterdam · Gemeente Delft · Gemeente Rotterdam · Leiden · Provincie Zuid Holland · inholland hogeschool · Hogeschool Rotterdam · hogeschool Leiden · De Haagse Hogeschool

medical delta
we add

Colophon
Medical Delta
Lorentzweg 1
2628 CJ Delft
The Netherlands

www.medicaldelta.nl

Editor in Chief
Sari Makkonen

Editors
Andy Baxter
Marcel Hulspas
DBAR

Photography
Vincent Basler
Bram Says

Design
Walvis & Mosmans









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