Engineering the future of biomedicine for health

Two leading Dutch institutions are joining forces to create the country's first technical university medical centre to TRANSFORM HEALTH.

A patient undergoes orthopaedic surgery for the insertion of origami-folded implants, which expand to fit her skeleton perfectly, reducing discomfort and optimizing the surgical procedure. During rehabilitation she is monitored by motion-capture imaging techniques to visualize load on her new joint and ensure her freedom of movement. Meanwhile, in another ward, a patient is discharged to return to his daily routine. In his body, he is carrying a device the size of a blood cell that will search for early signs of cancerous spread, or the development of plaques in his arteries.

These visions of healthcare are among many being explored by engineers at Delft University of Technology (TU Delft), and scientists at Erasmus University Medical Center (Erasmus MC) in the Netherlands.

Their management teams are jointly planning to bridge the boundaries between biomedical sciences, medicine, technology, engineering, design and ethics by creating a technical university medical centre.

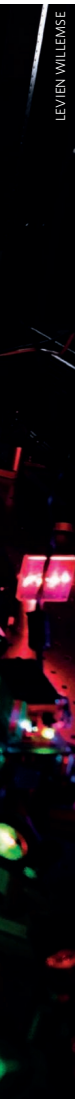
"WE WILL FACILITATE A 'PROACTIVE' RATHER THAN 'REACTIVE' APPROACH."

By joining forces, they will address medical challenges using cutting-edge engineering techniques and technologies to create, for example, nanoscale devices that monitor disease or cellular-scale models of organs for drug development. Researchers will focus on tailoring treatments and creating coherent, digitalized patient records that feed into artificial intelligence (AI) models to inform future therapies and improve clinical outcomes. Roland Kanaar, head of the Department of Molecular Genetics at Erasmus MC, says of this development: "It is time to break down the boundaries between disciplines and work together closely to create innovative solutions for the future of healthcare."

A long-held alliance

Erasmus MC and TU Delft have a collaborative history. With the Erasmus University Rotterdam, they have run BA and MA educational programmes in nanobiology since 2012; a second education programme in clinical technology began in 2014, which also includes the Leiden University Medical Center and Leiden University. Both have proven immensely popular with students, who will become a new generation of 'hybrid' health professionals: scientists with biomedical knowledge and skills in patient care, supported by technological prowess — an ability to look on biology with an engineer's eyes.

"The skills our students gain are incredibly valuable for their future careers," says Claire Wyman, molecular biologist at Erasmus MC and director of the nanobiology programme. "A blend of maths, physics and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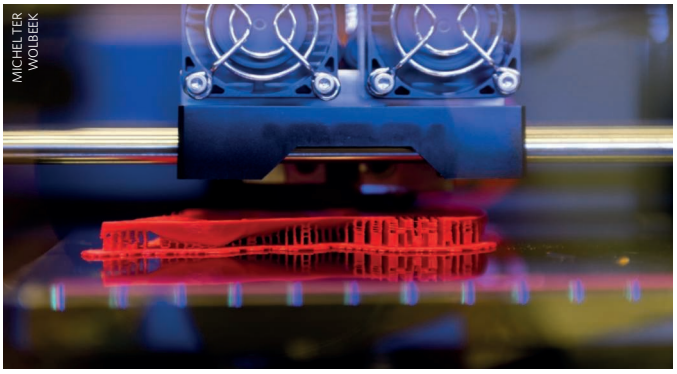
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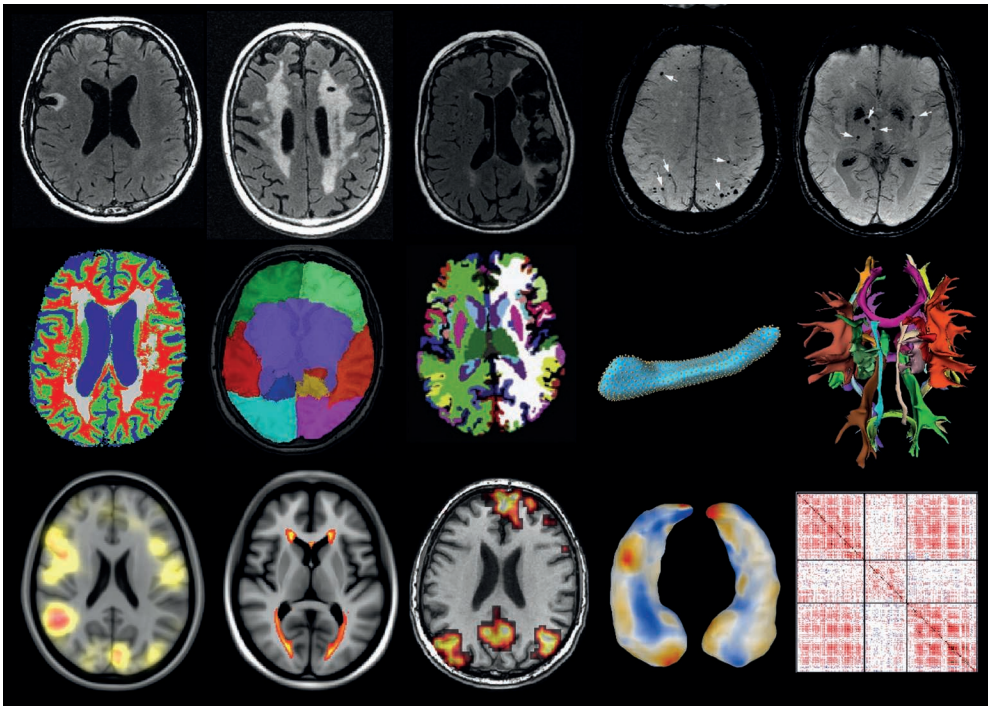

Left: A custom-built high-throughput screening microscope for single cell biology. **Centre top:** Printing a liver. **Right:** Claire Wyman leads the nanobiology programme. **Bottom:** Brain MRIs from the Rotterdam Scan Study give insights into changes in normal ageing and disease.

medical understanding that can make a real difference to patient care." On the nanobiology course, students split their time between the hospital at Erasmus MC and the campus at TU Delft. "They are exposed to two very different working environments and are therefore comfortable in both," she adds.

"We need professionals who can bridge the knowledge and conceptual gaps between subjects," says Jaap Harlaar, clinical biomechanics expert at TU Delft and director of the clinical technology programme. He says that the collaboration will enhance the success of the existing cooperation among the three universities and two academic medical centres, building upon the initiative of Medical Delta. "It makes sense to harness this potential and combine forces."

Four initial research programmes will lead the convergence, stemming from projects that already involve researchers from the institutions. The Syn Cells for Health(care) programme will improve understanding of the cellular processes inherent in serious diseases, using synthetic cells to monitor the body. My Digital Twin will develop comprehensive digitalized records for every patient, and gather data to model disease risks across the population. Researchers on the Deep Imaging programme will improve on existing image technologies, developing new tracers, smart devices and analytical platforms. Finally, scientists will create smart instruments and devices to limit the impact of chronic illness and mobility disorders for the Augmenting Humans programme. Over time, new research priorities will emerge and the centre will work flexibly and quickly to integrate them.

Reporter cells and mini-brains

The Syn Cells for Health(care) programme aims to improve understanding of communication within and between cells, and develop synthetic cells that may one day track and catch diseases in their earliest stages.

Wyman's research focuses on cancer and she hopes that the convergence will enable her department to work alongside engineers to design new ways to monitor real-time molecular processes and cellular interactions. First, however, her team must work out what cellular changes to look for — for example, precursory changes that would warn of metastasis in cancer. They would then design and introduce a sentinel cell with reporter capabilities that could enter the body and search for these signs. "Imagine if we could trace potentially metastatic cancer cells before the damage is done?" says Wyman.

Another scientist hoping to advance his research through working with technical specialists is Erasmus MC's developmental biologist, Joost Gribnau. Part of his research is focused on creating organoids – simplified versions of organs, such as the kidney or brain, which are grown on microfluidic chips with electronic sensors, meaning that interactions between cells can be carefully observed. A brain organoid, for example, can be created using induced pluripotent stem cells (iPSCs), derived from ▸

TU Delft Erasmus MC University Medical Center Rotterdam Cradle

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Left: Jaap Harlaar uses technology to improve physical rehabilitation. **Right:** Richard Goossens and Régine Steegers-Theunissen explore an immersive data visualization that creates a common language for their different disciplines.

skin cells, which differentiate into neurons to create working models of different brain conditions.

Gribnau has a keen interest in Rett syndrome, a rare neurological disease that largely affects girls, resulting in extreme autism, developmental difficulties, and mobility issues. "Brain organoids provide beautiful opportunities to study neural diseases such as Rett in detail, including the potential to trial new drugs," says Gribnau. "With the right technology, using a robot to generate the iPSCs from patient cells, for example, we could greatly speed up this discovery process."

Seeing double

Halting diseases before they take hold in the body, or indeed before any symptoms manifest, would transform the costs and effectiveness of healthcare, as well as the clear benefits for patients. Searching for early warning signs will be a key part of the My Digital Twin and Deep Imaging programmes, which will harness the power of machine and deep learning algorithms to generate predictive models for different diseases and clinical outcomes. A key goal will be the advancement of high-resolution, high-throughput imaging technologies, which could provide detailed information about tumours and neurodegenerative diseases, for example.

"We must take a holistic approach to integrated healthcare, particularly as we are faced with an ageing population," says Wiro Niessen, biomedical imaging specialist at Erasmus MC and TU Delft. "We will facilitate a 'proactive' rather than 'reactive' approach to health and healthcare." The new medical centre will ensure robust data collection, data sharing and integrated analyses so that doctors and researchers can evaluate health status and risks for individuals over time. The data collected will also help predict outcomes for the treatment of future patients.

The My Digital Twin concept will collate details about individuals – including consultation notes, blood test and imaging results — giving doctors a quick, simple way of accessing past and present data about their patient's health and wellbeing. Researchers will also use these data, in anonymized form, in large population-wide studies of specific diseases, using AI algorithms to predict future risks and potential health-related challenges.

Applied imaging techniques will also feature strongly in the Augmenting Humans programme. Researchers will incorporate AI techniques into clinical decision-making and treatment processes. "Introduction of technology to remotely and non-invasively monitor at the bedside will improve outcome for patients," says Diederik Gommers, head of Intensive Care at Erasmus MC.

Smart instruments will play a big part in improving the success of both medical procedures and rehabilitation. "Patients will recover quicker if surgeons can use very thin instruments with advanced functionality at the tip for minimally invasive treatments," says Jenny Dankelman, a biomechanical engineer at TU Delft. Harlaar sees scope for smart instruments in his field of physical rehabilitation, too. "From improving existing motion-capture imaging to investigate movement and loading on joints, to designing prosthetics for the future," he says, "there are huge benefits in combining cross-disciplinary expertise."

"THERE ARE HUGE BENEFITS IN COMBINING CROSS-DISCIPLINARY EXPERTISE."

Throughout the convergence and beyond, both institutions will take utmost care over all ethical and privacy concerns, and will ensure that patient safety and security remains key to all decision-making regarding new technologies and strategies. A strong health data infrastructure will be vital to ensure the resulting large datasets can be analysed and stored effectively.

The management teams at both institutions believe that merging branches of the physical sciences, engineering and design with life sciences, medicine and ethics will fuel pioneering innovations for the benefit of patients and those working in the healthcare industry. "The state-of-the-art infrastructure at both institutions will provide excellent breeding grounds for new ideas and exciting future projects," says Lucas van Vliet, Dean of the Faculty of Applied Sciences at TU Delft.

The benefits of the Erasmus MC – TU Delft convergence initiative are wide reaching, from generating employment and maintaining a vibrant presence in the local community, to national shifts in the quality of healthcare and access to the latest precision medicine. Ultimately, the convergence will fuel the emerging knowledge economy, and both TU Delft and Erasmus MC hope they will soon be showing that, when engineers meet biomedical scientists, everyone benefits. ■