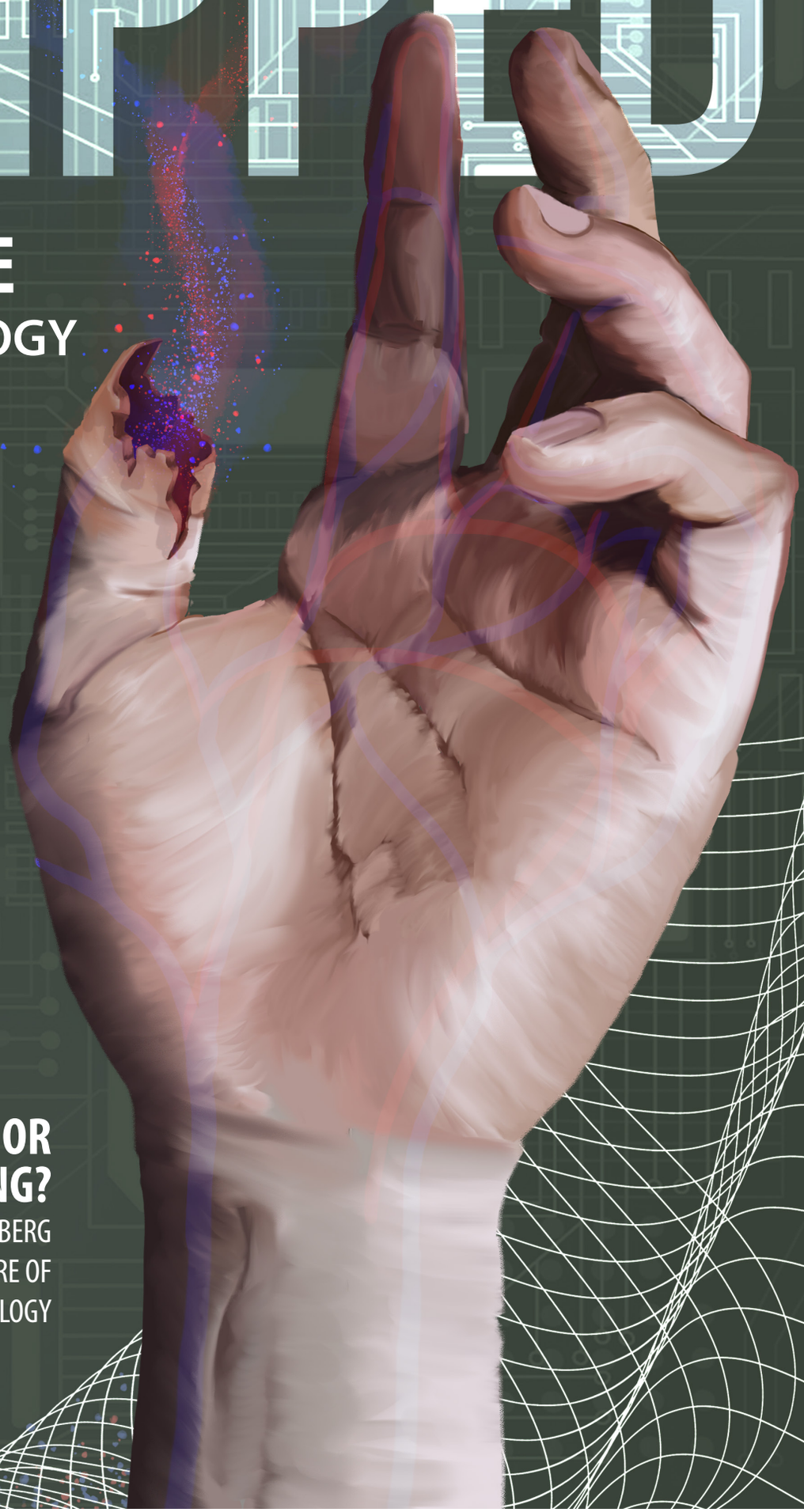
CHIPPED

SPECIAL ISSUE
NANOTECHNOLOGY
IN HEALTHCARE



SIZE MATTERS
AN ESSAY ON THE MEDICAL INNOVATIONS OF TODAY

IT TAKES GUTS
THE BREAKTHROUGH OF NANOTECHNOLOGY WITHIN ORGAN DONATION

DANGEROUS OR PROMISING?
WE SPEAK TO DR. ALBERT VAN DEN BERG TO FIND HIS OPINION ON THE FUTURE OF NANOTECHNOLOGY

NANOTECHNOLOGY
IN HEALTHCARE

FROM THE EDITORS

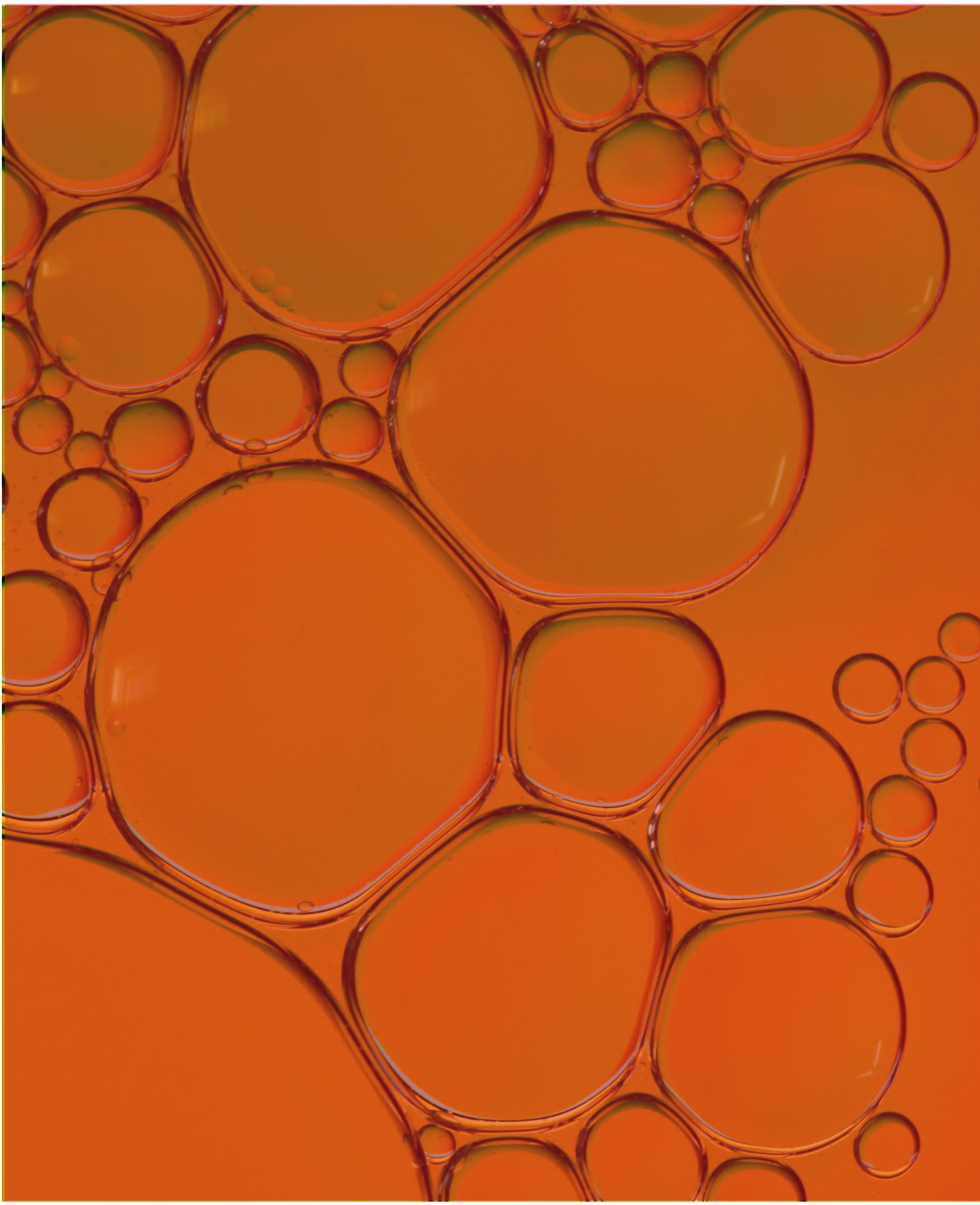
The current times are challenging for the healthcare sector. The pandemic is changing our lives and healthcare is being pressured like never before. During these times, it is clear that new health-related developments are more fundamental than ever. In this magazine, the technologies that are discussed can help healthcare during these times. An interesting aspect of these technologies is that they make use of nanotechnology with the aim to make care more precise. For example, a nano pill that is able to detect cancer cells, and the development of artificial organs could be made easier due to this nano pill. A vaccine patch that makes it possible to vaccinate more people in less time. Or nanotechnology that is able to prevent the rejection of donated organs. All these new upcoming technologies on the horizon look promising for our current healthcare system.

In this magazine, the possible future of healthcare will be discussed by giving information about these new upcoming health technologies. Thereby, we will provide you with the tools to formulate your own opinion about it, by providing information and related ethical concerns. Furthermore, we will give an insight into a variety of technologies through interviews with different researchers. Also, we added a collection of articles about the different healthcare-related technologies, followed by informative images that explain the innovation in a simple yet coherent way.

Enjoy reading our magazine! Hopefully, after flipping over the last page, you have formed your own opinion regarding the use of nanotechnology in healthcare.

The editors,

Sophie Horlings, Ellen Hu, Jord Loohuis and Maaike Pouwels



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SIZE MATTERS

WHEN SMALL BECOMES BIG

In today's global societies, healthcare plays a more important role than ever before. Stable trends of increasing life expectancies and long-term changes in lifestyles, just to name a few reasons, provide new challenges to worldwide healthcare providers. The emergence of new diseases and health hazards requires healthcare providers to alter existing treatment methods and to develop new treatment approaches. Besides that, healthcare aims to improve existing treatment approaches to increase their efficiency and benefits. In order to reach these goals, the use of technology in healthcare became indispensable and constituted a revolutionary change. One far-reaching example of such powerful and complex technological innovations is the development of nanotechnology and its implementation in medical management.

WHAT IS NANOTECHNOLOGY?

Nanotechnology is defined as the study of extremely small things. These technologies are so small that they are imperceptible to the naked eye, and even with optical microscopes they are still hardly visible. In fact, nanotechnology refers to the manipulations of particles that are smaller than 100 nanometres (which equals 100 millionth of a millimeter!), such as atoms and molecules. Since it is difficult to imagine the size of nanotechnology, it can be compared with a human hair, which still is many hundred times thicker than a nano-object. The technologies involve designing, developing and producing devices within that size range. One thing to focus on could be the fitness industry: our smartphones most likely have a program that counts the steps we take, which can also be otherwise accomplished with a fitness tracker that can be worn around your wrist. However, all these devices could soon be replaced by wearable sensors that act as advanced fitness trackers and which are embedded into textiles such as t-shirts. These technologies could offer a greater number of health tracking features, higher accuracy and increased user comfort. Other nanotechnologies include pills that are able to detect cancer by simply swallowing them, pills that deliver medications and patches that deliver vaccines without any pain. These are just a few examples of the revolutionary nanotechnology branch.

THE VALUE OF NANOTECHNOLOGY

Nanotechnology revolutionizes and benefits all kinds of parts of society. It is implemented within the energy sector, food technologies, the communication sector and the industrial branch. But, what makes it so valuable is the fact that everyone, including yourself or your loved ones, might soon benefit from nanotechnologies which potentially change your life.

An especially interesting and influential sector where nanotechnology plays a huge role is healthcare. In this area, it holds enormous potential, just like a sandstorm: grains of sand that you barely can see transforming into something big and powerful. Nanotechnology is going to be just that for healthcare.

> "It is very clear that the **future of medicine** lies within the field of **Nanotechnology**.
>
> - (Quantumrun*, n.d)

POTENTIAL OF NANOTECHNOLOGY IN HEALTHCARE

There are various ways of how the great potential of nanotechnology can be used. Possible applications are seen in many different areas: diagnosing diseases, improving drug delivery, revolutionizing vaccines and new forms of treatments. Technologies that have been unthinkable just a few years ago and seem like science fiction, might become reality and permanently change healthcare. Let's take a closer look into the crystal ball and see what the future may hold.

DIAGNOSTICS

Nanotechnology, in particular nanoparticles are currently in research to develop new ways to detect diseases, with two main benefits: speed and sensitivity. Rapid testing through nanotechnologies may allow the diagnosis and start of the necessary treatment within just one session at the doctor, instead of long waiting for test results from the lab. Furthermore, higher sensitivity through these methods could allow earlier diagnoses than with current techniques. So that not only the treatment can be started earlier but also more damage to the patient's health can be prevented. Most of the current diagnostic research with nanoparticles is focussed on detecting types of cancer, however, diagnostic approaches are developed for other diseases as well, such as COVID-19.

** research and consulting agency for future trends*

DRUG DELIVERY

Another area that is awaiting a major revolution through nanotechnology is drug delivery. Current drug delivery works mainly orally or through injections, however, it does not allow for a specific local use of the drug. Drug delivery systems based on nanotechnology are seen as a game changer. They can be used to deliver drugs for a specific area without attacking other healthy parts of the body, which is especially valuable for cancer treatments. But there is even more to it. Nano drug delivery systems can also be used to elongate the lifespan of certain drugs, that other ways stay active for only short amounts of time, such as stavudine and zidovudine that are used for HIV treatment.

> “Guided by our extreme euphoria, we often forget to pay attention to the small, but important details.”

VACCINES

Nanotechnology can also provide alternatives to injectable vaccines that require administration by medical professionals and start a new era of immunisation. Especially in poor countries, healthcare professionals are scarce and treatment expensive. The need for constant refrigeration of normal vaccines makes delivery difficult and consequently more expensive. Scientists are therefore working on different nanotechnologies to solve those issues and might even allow you to vaccinate yourself at home. Research is mainly focused on two main domains: delivering vaccines via aerosols and vaccine patches.

OTHER AREAS OF USE

Nanotechnology might already seem quite impressive but there is more. It also offers many advancements for surgeries, implant technology and organ donations. It can find use in numerous surgical applications, implants can be coated with nanoparticles to improve biocompatibility or the organ donation process can be enhanced by nanoimmunotherapy. So as you see, nanotechnology has an enormous potential to drastically change healthcare in a groundbreaking way.

LIMITATIONS OF NANOTECHNOLOGY

Until now it surely became obvious to you that nanotechnology can be a powerful tool in healthcare. However, all that glitters is not gold. We also need to consider the downsides and possible risks that come with nanotechnology, especially in healthcare. In this context, ethical issues are particularly interesting.

IS NANOTECHNOLOGY EVEN SAFE?

Obviously, no one can implement a product without extensive researching and testing, to ensure a safe product. However, we already know examples of less complex fields, where dangerous materials or technologies made it to the market and were used confidently. Just think of exploding phone batteries. Another example is asbestos that was built into houses for a long time but turned out to be highly toxic and resulted in many people dying of its consequences. Who can assure that there are no similar problems with nanotechnology, that have not been researched yet? Some experts assume that nanotechnological particles may be threatening to our health, and stress that this definitely needs to be researched further.

ARE WE OVERLY CONFIDENT?

It is unquestionable that we already achieved great things with nanotechnology. However, we must be careful that we do not get overly confident about it. Of course, these new technologies open doors for impressive achievements, that we would not have considered as possible only a few years ago. But this can also be dangerous! Guided by our extreme euphoria, we often forget to pay attention to the small, but important details. We become blind to mistakes and imperfections, which leads to a massive impairment of the product's safety. Nanotechnological innovations can only improve our life if they are developed carefully. Developers need to pay attention to every detail, from every single nanoparticle up to the broader context of the final product.

WE CANNOT FORESEE THE CONSEQUENCES

Nanotechnology is a rather new field of technology and it is developing fast. Sometimes even so fast that we cannot keep up with it anymore. For a small moment you did not pay attention, and suddenly there are twice as many new innovations on the market as they were before. At least it can feel like that sometimes. Because of this fast development, it is impossible to predict the next step. "But what's wrong with this, isn't it that what is so exciting about it?", you might think. And while that might partly be true, it is also alarming. There is little time to reflect on ethical issues and other problems, which can have dramatic consequences.

PROBLEMS IN SOCIETY

In our current world, we already struggle with demographic change. People get older and older, and so does society in general. In many western countries, the number of elderly increases continuously. While it is great for us that we have more time with our grandparents, this also leads to several challenges in society. The elderly often depend on the support of younger people. The higher the number of the elderly gets, the more difficult it will be to provide this support. But what does this have to do with nanotechnology? Well, nanotechnology in healthcare can cure diseases that were incurable until now. And this is great! But it also means that our society keeps getting older, and caring for the elderly gets harder and harder. So what is it about in the end? Are we really improving quality of life with nanotechnology or do we only want to show off with our new capabilities in technology? Is it about improving healthcare, or do we just want to feel like we live in our favourite science fiction movie?

WHAT DOES THIS MEAN FOR THE FUTURE OF NANOTECHNOLOGY?

The future of nanotechnology is an uncertain thing. Like mentioned before, nanotechnology in healthcare influences almost every sector you can imagine. Along with the development of nanotechnology in healthcare, all other nanotechnology developments also run at high speed. This creates a complicated future for nanotechnology.

WHO WILL BENEFIT?

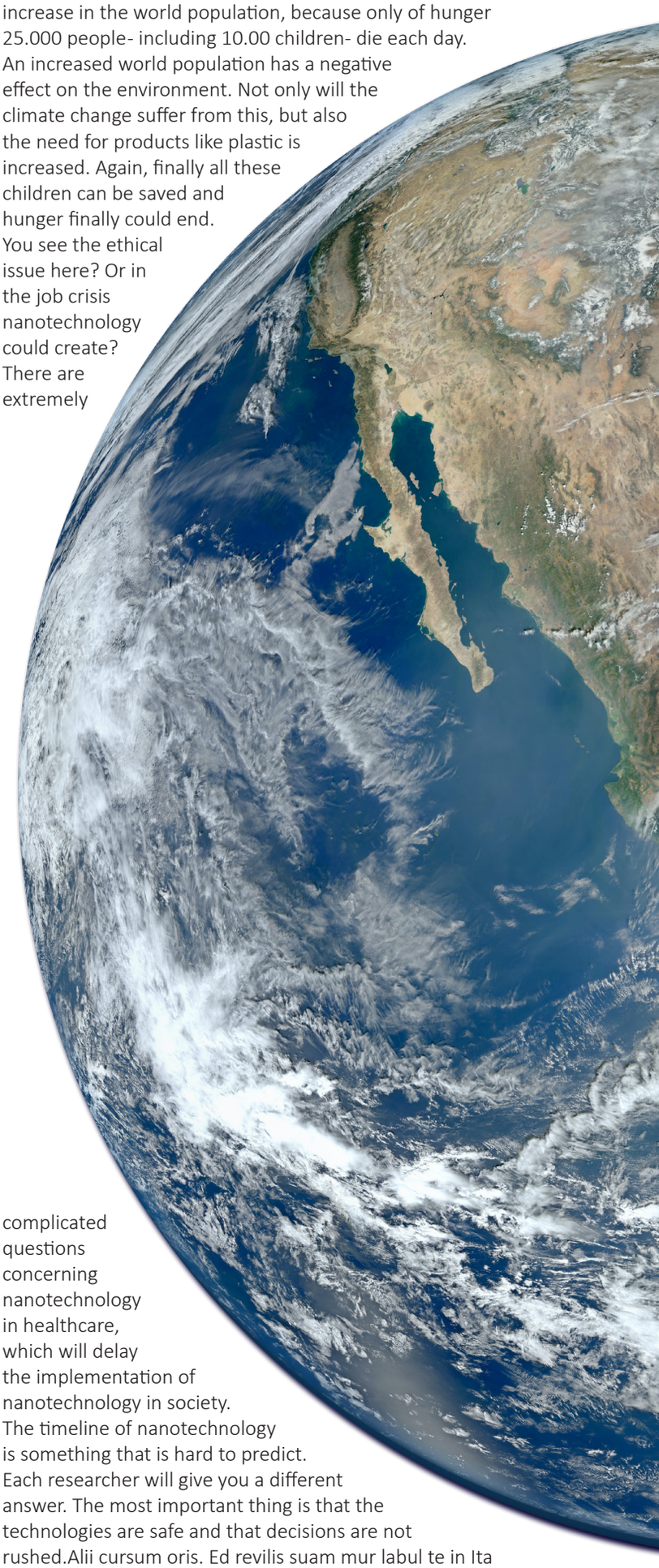
Previously, you have seen that nanotechnology can save lives and can make lives more comfortable. This is a benefit to all people currently on medication, but also to people that are scared of getting, for example, cancer. The people currently on or in need of medication include all diabetes patients, patients with sick organs, patients with HIV or aids, people in hunger and this list continues. We can say that almost every inhabitant of this world could benefit physically from nanotechnology. Besides the inhabitants, the governments could benefit a lot. With the population not being sick, their lives will change. They will be able to work and no longer need a payment from the government. The treatment prices could go down, because people are no longer in need of long term treatment performed by staff. This results in people having less concerns about paying treatments, which could boost the economy. Boosting the economy influences a lot of sectors, but a fact is that the government gets more taxes. With these taxes things like climate change, creating work, improving infrastructure, loneliness campaigns and tons of other examples can be put into action.

WHO WILL SUFFER?

This is a complex question. Like you could read above, nanotechnology in healthcare could change everything. The departments in hospitals, for example oncology, will be decreased in size. This makes a lot of people lose their jobs. Nanotechnology will replace current treatments. This means that the current market in medicine will be put upside down. Nowadays billions of euros and tons of jobs are created due to this market. Furthermore, nanotechnology has the benefit of limiting the side-effects of drugs. This, again, reduces the reliability of people on the pharmaceutical market. The fact that side effects are influenced does not only concern jobs in healthcare. A few side effects are dry skin or impaired hearing of vision. This influences jobs outside of healthcare as well, as these problems might occur less. To conclude the answer to this question, people will lose their jobs. The new question is, will it be possible for the government to create enough new jobs?

APPLICATION AND TIMELINE

As you might have seen before, the challenge for the implementation of nanotechnology in society is in finding a healthy balance. An example of a situation, next to the job crisis, where balance is needed is the growth in the world population. Nanotechnology can improve the amount of food in the world. This could, next to HIV treatment, save lives in third world countries. This results in an enormous increase in the world population, because only of hunger 25.000 people- including 10.00 children- die each day. An increased world population has a negative effect on the environment. Not only will the climate change suffer from this, but also the need for products like plastic is increased. Again, finally all these children can be saved and hunger finally could end. You see the ethical issue here? Or in the job crisis nanotechnology could create? There are extremely complicated questions concerning nanotechnology in healthcare, which will delay the implementation of nanotechnology in society. The timeline of nanotechnology is something that is hard to predict. Each researcher will give you a different answer. The most important thing is that the technologies are safe and that decisions are not rushed.Alii cursum oris. Ed revilis suam mur labul te in Ita

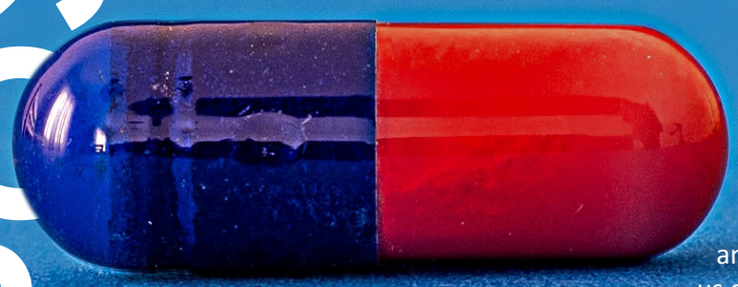


SO, WHY DOES SIZE MATTER?

Nanotechnology is a complex topic with many different facets. It is growing fast, and new innovations are introduced every day. People constantly have new ideas about how to improve healthcare using tiny nanoparticles.However, one cannot only focus on the benefits, the downsides also need to be considered and eliminated. But there is no one-size-fits-all solution, every case needs to be evaluated individually. Although there are some ethical concerns that can arise, these can be tackled with meticulous development. We need to stay down-to-earth and spend enough time to develop each new innovation. Ethical questions need to be answered, and solutions need to be found to tackle current uncertainties. After all, nanotechnology should improve people's lives, and not make it harder or even lead to suffering. These are basic requirements for a successful and safe utilisation of nanotechnology. And with consideration of those, nanotechnology can revolutionize healthcare dramatically and change all our lives for the better. Until now, many technologies have already been developed, which improved healthcare effectively but there is much more to come. Soon from now, we might be able to heal diseases which we still consider as incurable today. Through early detecting and diagnosing we could prevent many people from suffering. Nanotechnologies might be incredibly small but their power to revolutionize our healthcare lies in their size.

THE POSSIBILITIES

in the size of your average brown bean



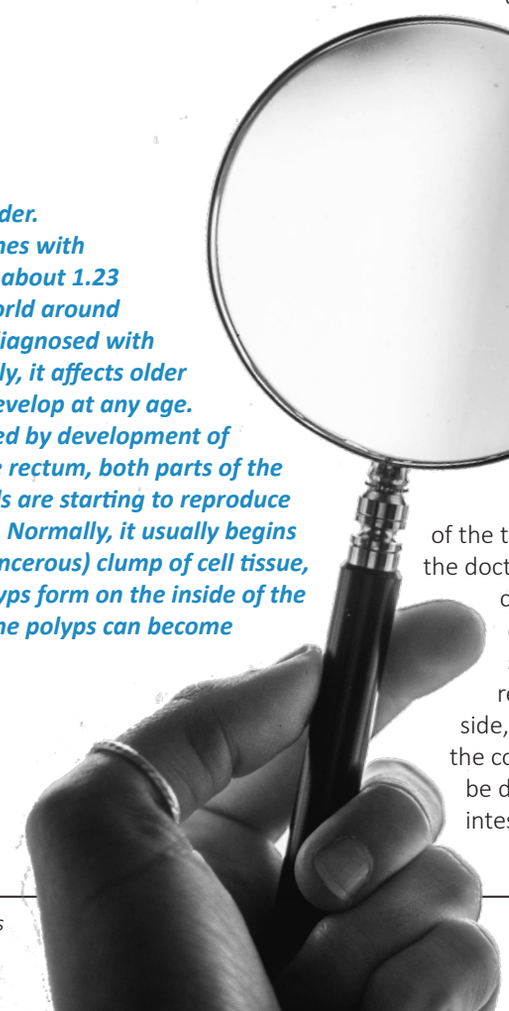
In 1966, writer Harry Kleiner and director Richard Fleischer took us on a submarine mission through the human body. In their American science-fiction movie Fantastic Voyage, a submarine crew shrunk to microscopic size in order to venture into the body of a scientist to perform an actual brain surgery. Although this story is purely fiction, science and technology are nowadays making great strides in this direction. Especially the future of healthcare; technology is shaping in front of our own eyes and becomes more intelligent, powerful and complex. With these revolutionary developments it turns out that some issues in healthcare perhaps don't need to be approached 'grandly' as we may have previously thought. Possibly, some problems can be tackled on a more 'modest' scale? Recently, with the arrival of nanotechnology pills, a 'journal through the body' becomes a step closer to our reality.

THE EARLIER, THE BETTER

Colorectal cancer poses an increasing health hazard to populations all over the world, being the third most common form of cancer with the second-highest mortality rate. This results in approximately 900.000 deaths worldwide each year. A remarkable fact, since an early diagnosis of this disease gives a patient a 90% five-year survival rate. The chance of survival also depends on how advanced the cancer is, the person's overall health and whether or not all the cancer cells can be removed with surgery.
Luckily, there are many treatments available to control the growth when colon cancer is found in time. A few examples include radiation therapy, surgery and drug treatments, such as chemotherapy. Symptoms include changes in bowel habits, rectal bleeding or blood in the stool, abdominal discomfort and unexplained weight loss. Sadly, colon cancer often gives symptomes at a later stage of the development. Once the cancers have spread widely and are no longer curable, the focus of the treatment will shift to improving the quality of life and symptoms. The characteristics of this disease makes screening more fundamental than other types of cancer. Early detection is crucial to reduce the number of yearly deaths.

TAKING A CLOSER LOOK

In order to make early detection more common, everyone in the Netherlands between the ages of 55 and 75 is invited once every five years for a bowel examination. Nowadays, the most common method used for an early screening of colorectal cancer is colonoscopy. In advance of the colonoscopy, patients are asked to submit a sample of their stool. With a test sample, the amount of blood in the stool is measured. A larger amount of blood can indicate possible colon cancer. When there are alarming results, the patient is referred to a colonoscopy for further investigation.
Although the name of the procedure might sound fancy, the actual procedure is easy to understand. During colonoscopy, a colonoscope is used to examine the large intestine for any abnormalities. A colonoscope is a flexible, long, tubular instrument. The tube is around ½-inch in diameter. At the end of the tube there is a small video camera that allows the doctor to view the inside of the colon. The tube can be controlled and is able to reach the end of the large intestine. Before the procedure, sedative will be given to make the patient relaxed. The patient will be asked to lie on the left side, this makes insertion of the tube easier. Next, the colonoscope is inserted into the rectum and can be directed by the doctor till the end of the large intestine. If needed, a biopsy can be taken during



Hopefully, we all grow older. Unfortunately, aging comes with many challenges. Yearly, about 1.23 million patients in the world around the age of 50 are being diagnosed with colorectal cancer. Typically, it affects older adults, though it could develop at any age. Colorectal cancer is caused by development of cancer in the colon or the rectum, both parts of the large intestine where cells are starting to reproduce and grow uncontrollably. Normally, it usually begins as a small benign (noncancerous) clump of cell tissue, called a polyp. These polyps form on the inside of the colon. Over some time, the polyps can become colon cancers.

the colonoscopy. The whole procedure lasts about 30 till 60 minutes.
Unfortunately, there are some downsides. Firstly, the stool sample method receives quite some criticism because it gives a high percentage of false-positive results. Secondly, many patients are asked to undergo the colonoscopy, which often is an experience that is perceived as embarrassing and uncomfortable. Thirdly, during a colonoscopy an actual abnormality is only found in a small percentage of the patients. And lastly, even with the strong advice to undergo a colonoscopy, people reconsider it because of the costs. The price of performing a colonoscopy is estimated around $800 to a whopping $4000. All these unpleasant experiences result in a low level of screening attendance.

In comparison to the standard colonoscopy, the Pillcam offers a non-invasive alternative screening method.

A PICTURE IS WORTH 1000 WORDS

Hopefully, for our next generation, a more patient friendly method shines on the horizon. With the help of nanomedicine, the University of Twente is working on a nanopill. That pill comes in the size of an average brown bean, called the Pillcam. In comparison to the standard colonoscopy, the Pillcam offers a non-invasive alternative screening method.
The main idea behind this Pillcam project is to develop an ingestible smart diagnostic pill. A feature of the pill is that it is equipped with a camera that will take thousands of pictures of the bowel, which will form a video. After being swallowed, the Pillcam travels through the body and eventually ends up in your intestines.
During the screening process, the patient wears a recorder on the waist which measures and stores the data wirelessly. The images are saved which enables an expert to look for abnormalities after the pill has passed through the bowel. After approximately 8 hours the pill will leave the bowel and can be flushed through the toilet. If cancer-specific DNA is detected, the doctor will contact the patient and conduct a follow-up screening in which the abnormal cells can be removed.

CAN A NANOPILL A DAY KEEP THE DOCTOR AWAY?

The Pillcam, a promising revolutionary piece of technology that brings about a new way to perform endoscopy. However, the Pillcam also has its ups and downs too. A more explicit advantage it has compared to colonoscopy is that it does not require a cable (or long tube) to support it. Whether it is for powering or transferring information. This makes the Pillcam much less invasive and less embarrassing for the patient to perform an endoscopy. The need for anesthesia will also no longer be necessary. Hopefully for the patient, the idea of conducting an endoscopy becomes less terrifying or traumatic.
Accompanied by that, the price of a Pillcam ($500) is significantly less than a colonoscopy ($800 to $4000). The difference in price makes endoscopy more accessible and more widespread. This could tackle a main problem with colorectal cancer, (too) late diagnosis. The 5-year survival rate of a patient with stage III colorectal cancer is 71%, while someone with stage IV, just a stage above, has a survival rate of 14%. With the Pillcam, an early diagnosis is more feasible, which could increase the survival rate of patients with colorectal cancer.

Like a coin, there are two sides to this technology. A side that should not be blind-sided, the disadvantages that this technology brings. A focus group was held regarding the Pillcam, there were two main concerns that surrounded the Pillcam. One of them is privacy, a matter of who has access to your results. The pictures of your colon might not seem like sensitive information. However, when the internet was still young, your browsing history was not considered as sensitive information too. But from such data, a profile of you can be made with your preferences and history and you may be at risk of identity theft. Another disadvantage of this technology is what happens after the Pillcam is used. Since the Pillcam is made from different materials, such as the battery and the metal parts in it, it is not suitable to be flushed again. In addition, it may be reusable. However, collecting it may be very troublesome. So the environmental aftermath of this piece of technology is also speculated.

Equally important, what happens if something goes wrong while having the endoscopy with the help of the Pillcam? The chances of the Pillcam being stuck is 0.5%. Let's say if 200 people, equivalent to about 3 full capacity busses, get an endoscopy using the Pillcam, it's likely that at least one of them will need to have the pill surgically removed.

As time goes on, technology will be more and more advanced. The Pillcam might be equipped with more sophisticated pieces of technology, maybe even performing more than just an endoscopy. And maybe one day, as dreamt by Harry Kleiner and Richard Fleishcer, we might possess the technology to shrink down and perform the endoscopy ourselves at one point.

PILLCAM VS COLONOSCOPY

Diagnosing colorectal cancer

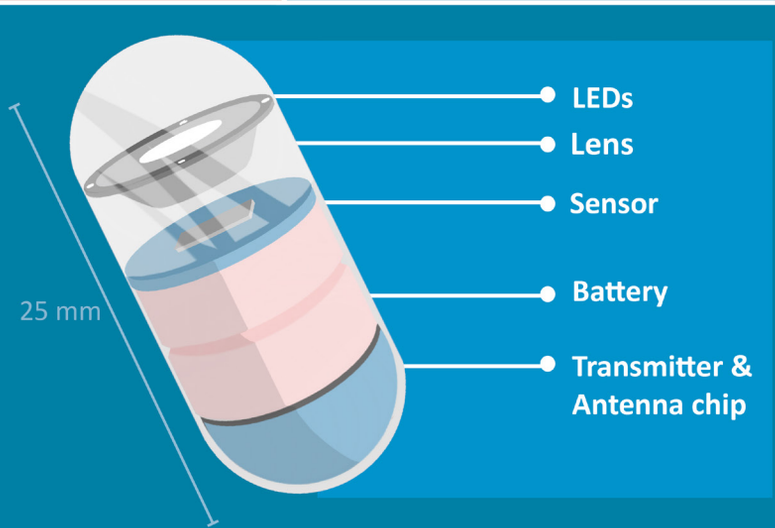
Colorectal cancer: Abnormal cell growth in colon or rectum

1.23M cases/year

Currently the **2nd deadliest** cancer

Late detection leads to drastic **decline in survival** chances

COMPONENTS



PRO'S & CON'S

+

- Cost efficient
- Comfort
- User friendly
- No sedatives
- No hospital stay

−

- Environmental concerns
- Privacy concerns
- 0.5% chance of getting stuck
- May interfere with internal electronics
- Less inclusive results

PROCEDURE

Colonoscopy

1. A **sedative** is given to relax the patient
2. **Camera** is inserted through the rectum to **scan for abnormalities**
3. Possibility for a **biopsy**
4. **Hospital stay** required until the sadative has worn off

Pillcam

1. The recorder is connected to the Pillcam
2. The pill is **swallowed**
3. The patient can continue his/her day with the recorder on a waistband
4. Thousands of **pictures** are taken in the bowel
5. After 8 hours the pill is excreted by the bowel

INTERVIEW

LAB ON A CHIP?

Mariana Carcia-Corral Islas

David Choy Buentello

Bachelor	Biomedical engineering at the University of Monterrey, Mexico
Master	Biomedical engineering at the University of Twente, Netherlands

In her masters, Mariana's project was more based on biology so that she could see the interaction between the brain and the gut on a micro scale using a platform that is only in the range of microns. Mariana's task was to develop this platform and design it and fabricate it. Her other objective was to obtain the cells that are neurons that are derived from the brain and forwarded to the gut, and then see how they behave together.

Bachelor	Biology and minor in Chemistry at the Sacred Heart University, CT
Master	Neuroscience University of Hartford America
Currently	PhD in Technology at Monterrey University, Mexico

After doing his MSc, David worked at the Pennsylvania State University to research neurodegenerative diseases like alzeheimer and parkinson. Currently he uses that background information to study how different tissue cultures can grow better, by help of microfluidics.

In the Interview with Mariana Garcia-Corral Islas and David Choy Buentello, which are both researchers at the University of Twente, we seek to understand how an entire lab can be compromised into a tiny device, the Lab on a Chip. The Lab on a Chip can help to speed up diagnosis and treatment options in the medical field without being too invasive. In chemotherapy we could investigate if it is working without many side effects before testing it at the humans itself!

WHAT ARE YOU WORKING ON AT THE MOMENT?

David: I am currently doing a semester here at the University of Twente while also writing my PhD thesis at the University of Monterrey. My work primarily derives from using primary cells obtained from animal studies in animal species. But currently I'm working at the Applied STEM Cell Technology Department, where I'm using stem cells in order to create organoids by using human neurons. Organoids are little versions of organs within these microchips.

Mariana: Yeah, I am also or I was also doing my master's thesis assignment at the Applied STEM Cell Technologies Lab that I just finished!

AND WHAT ARE THE FINDINGS OF THE PROJECT?

Mariana: So basically we ended up with a little chip. Within this chip we could stretch cells. Then these cells could travel through small compartments to meet other cells.

WHAT CAN THOSE FINDINGS BE USED FOR LATER?

Mariana: This can be used to understand the disease, or to try to find new cures, or to develop a very personalized medicine. You can even get cells from a patient that has a specific disease, put them inside the chip and then try to see if this patient is responding well or not, for example, to chemotherapy.

David: Also are there connections between different organs like the brain and the gut, unfortunately one can't really study it inside a human or inside an animal because you can't put a microscope inside the body without being very invasive further is uncomfortable and might get different results. So what you do, is you try to use cells. But the only problem is that you cannot try to put them together in a petri dish. As they are naturally competing for resources. So it's very hard to keep two different cell populations together in a petri dish. What Marianna did, is she created a platform that actually can have two different types of cells combined in the same platform and then interacting with each other. But more importantly, these platforms allow us to actually study the different interactions they have in a very precise fashion. So we actually see how certain connections are being formed or how certain molecules are being transmitted from one cell population to the other.

ARE THERE ANY ADVANTAGES WHEN YOU COMPARE THIS TECHNOLOGY TO EXISTING TESTING METHODS?

Mariana: Current drugs have to go through several animal trials before humans testing is allowed. With the lab on the Chip we only need to use two platforms. One trail on animals and one trail on this new platform that has human cells. Additionally is it complex enough to resemble an organ! This allows researchers to explore side effects in an elaborate way. This can be done using those created organs. For instance, for the vaccine for covid, you could try to see if the vaccine has the negative side effects on one of the microfluidic platforms, let's say the lung.The lungs are well established because in the platform you even can exert the inspiration and expiration! This is groundbreaking, because some side effects don't show on cells that are just cultured without anything happening on them.

WHAT ARE THE CURRENT CHALLENGES?

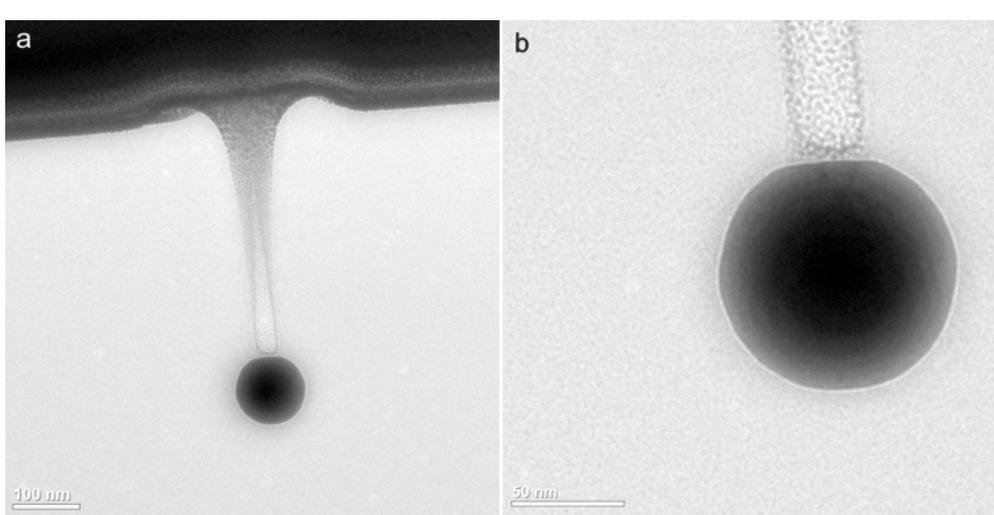
David: The only problem in working with stem cells is that stem cells are derived from patients. These cells still take a long time to grow. It takes about 30 days to actually have something that's mature enough to show any signs of the actual organ. So still it would take time. But the technology becoming common practice will not be a lifetime away. So within 20 to 30 years, something big would be available to most people!

WHAT IS THE END GOAL OF YOUR PROJECT?

David: So the ultimate goal in our project is to diagnose faster and have faster treatment options. This is pretty much what we wanted to achieve. Further does this technology makes nearly all animal testing redundent! So millions of animals' lives can be spared!

IS THERE ANYTHING ELSE YOU WOULD LIKE TO POINT OUT?

David: Yes! We try to speak in layman's terms, we hope it is understandable, but there's still a big barrier between science and the rest of the world. And the thing that we talk about that seems very fantastical and overpowering, but they take a little time to develop. It is just something that sounds like: "oh, maybe we can get cancer right away". But it's one of the things we're working on slowly. People have done great things and great advances. But then there's something that can make that process a little bit slower. So we do not want to give the impression that we are nearly at the end of the road but are taking steps on a road we just recently discovered!



IT TAKES GUTS

to be an organ donor

You probably have watched an episode of Grey's Anatomy where at the last crucial minute, an identical twin showed up braindead. Or have you ever seen one of those action scenes where a doctor runs towards a helicopter that contains a needed organ exactly in the right second? Unfortunately, this luck is not realistic. The organ donation processes nowadays do not bring much luck. However, several technologies bring light to this situation. Organ donation has a brighter future than ever before: nanotechnology. Nanotechnology can become anyone's braindead identical twin.

Imagine you are in the situation of somebody on the sickbed in Grey's Anatomy. "These are typical signs of heart failure." your doctor says. And so, the drama begins. You have to visit the hospital many times for different tests and the results show that indeed your heart is failing to do its job. Ordinary medicine will not work and your best option is organ transplantation. Although this process has a high success rate, there is a large problem: in the Netherlands, the waiting list for this kind of transplant is abysmal. On average, 50 to 100 people are awaiting a heart transplant. This could mean that you will only be able to receive a healthy heart after four years! Four years filled with uncertainties, low energy and a lot of pills and medication.

YOU SHOULD THINK TWICE

When it is finally time to have surgery because there was a donor, there are still many risks. First of all, it's possible that you do not make it out of the surgery alive or that you die directly afterwards. This, most people know. However, the first five years after the transplant are also full of insecurities. Only 75 to 80 percent of all heart transplants survive the five years after their surgery. This is because of organ rejection. Organ rejection occurs when your immune system sees the donated organ as 'foreign' and 'dangerous' and attempts to fight those cells. This process is always kept in mind, but never foreseen.

With organ rejection, there is currently one way of treatment that is commonly used. This is the use of immunosuppressant drugs, combined with antibiotics. This medicine suppresses the actions that the immune system would take against the transplanted organ. However, this also suppresses the immune system in other parts of the body. As you can imagine, this is a very dangerous process because having a weakened immune system makes you much more susceptible to other diseases. This will remain a problem for the rest of your life, as you will not be able to stop taking immunosuppressants after an organ transplant.

As of now, we can say that organ donation is not optimized yet: there are too little organs for the patients who need a new organ, the waiting time is too long, you will have to take immunosuppressants and antibiotics on a daily basis and there still is a relatively big chance that you will not survive the first five years.

THE EXTREMELY SMALL

There is a solution to this problem: a new nanotechnology. As with any emerging technology, people doubt its ease of use at first.There are many uncertainties and complexities within new technologies. Because of this, I will explain how the technology works and describe the amazing things it could do for the future.

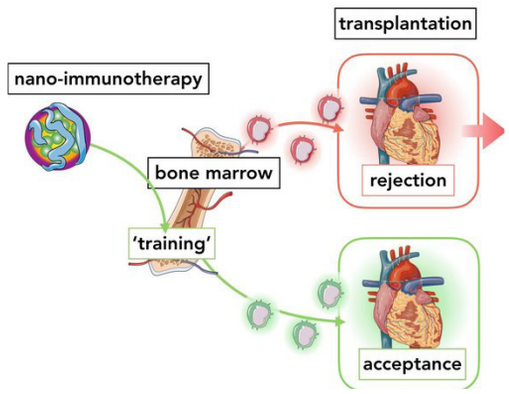
What is interesting to note is that when this technology will be widely used, **there is a lower need for organ donors**. The nano immunotherapy ensures that organs will be accepted in the body and therefore **rules out rejection completely**.

Nanotechnology is a technology or a way of working on a nano level. That is, on the small level of nanometres. It is very detailed and can provide medical solutions in certain parts of the body, without affecting other parts. Professor Willem Mulder from the Technical University of Eindhoven has developed a new nano immunotherapy with which patients will not need their medication anymore. The therapy specifically programs the right cells of the immune system in the bone marrow, even before the immune response against the donor tissue has started. During the procedure, non-relevant parts of the immune system remain untouched and healthy. The 'reprogramming' is done through training of cells in the bone marrow. This new innovation, combined with a higher number of organ donors, could do amazing things in the future.

MONTHS TO WAIT BEFORE ORGAN TRANSPLANTATION

In 2019, 1,271 people were on the waiting list for a healthy organ. The average waiting list is approximately 2.5 years. The longer people have to wait, the smaller the chance that the surgery will actually take effect as the patient's state has worsened. The need for organ donors , therefore, is big. For people that are awaiting an organ, it is very important that you make your choice known in the donor register. It only takes you two minutes, but could give patients the opportunity to extend their lives with much more than just two minutes.

What is interesting to note is that when this technology will be widely used, there is a lower need for organ donors. The nano immunotherapy ensures that organs will be accepted in the body and therefore rules out rejection completely. This means that less people will need new organs after they had an unsuccessful transplant, as there will not be any unsuccessful transplants anymore (at least not due to organ rejection).



Visual: Willem Mulder

This technology has a potential to change the game. We can 'outsmart' our bodies in order to prolong our lives. But we also have to be careful. We will be taking a piece of technology in our body. This calls for a lot of personal ethical reflection. To what extent can we outsmart our bodies? Image you have been waiting for years and the doctors finally found you a donor organ. The match is not 100%- because you don't have an identical twin – so there will be a rejection towards the transplanted organ. You have two options. One is a lifelong medication paired with a lifelong impaired immune system, with all its consequences. Option two is to take one nanotechnology pill, that will make your body accept the organ as if it is your own. Although this seems like a promising solution, it is one that you need to think through thoroughly before using this nanotechnology. The ethical aspect of the new technology could get in the way of its development.
Nanoparticles offer hope for patients who have to take strong medications after an organ transplant. Nanoparticles are not classified as an actual drug nor as an actual technology, which might raise doubts. However, other people, that we could call early adopters, might be willing to use nanotechnology in organ donation and would choose this option over the classic treatment. Even though nanotechnology has been around for at least five years, it is still being investigated and further researched.
This clearly creates a divide between the people who feel limitations towards emerging technologies and people who feel comfortable supporting the 'untraditional' options.

WHAT NEXT?

In conclusion, there are two main improvements which could optimize the process of organ transplantation. First of all, the system around organ transplantation can be improved by convincing more people to become a donor. This way there will be more organs available for transplantation which will improve the current situation. The other option is nanotechnology. Nanotechnology could be the answer to the problems of organ transplantation. By training the immune system to accept the transplanted organs, there is a more efficient use of the donated organs, as less organs will be rejected. Therefore, more people will have a working organ after the initial five years after surgery which causes a decrease of people who need organ transplants for a second time. Without nanotechnology, there is a 25 percent chance that your organ is rejected in the first five years and that you will need another organ.

Thus, when organ rejection does not take place, there will be a decreasing number of people on the waiting list paired with a shorter waiting time for people who are waiting for an organ transplant. This is a very positive preview of what the future holds for us when we are going to use nanotechnology. The transplantations will be optimal and more people will be saved. Although this therapy is encouraging, there is some future research that needs to be done. This technology

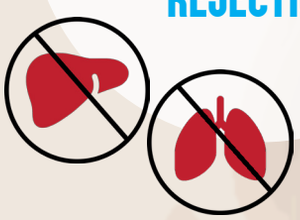
The ethical aspect of the new technology could get in the way of its development.

is only tested on animals so far and there are not yet any side effects known. Thus future research should enhance nanotechnology by improving the technology in such a way that possible risks are minimized. There will come side effects and risks with this therapy and it is important to know what these are to be able to prevent them and to ensure that patients can make a well-educated choice on whether or not to use this immunotherapy. When more is known about the therapy, it could have the potential to save thousands of lives. That new organ that is brought in from the helicopter at exactly the right moment could prove to be very useful and effective.

COMBATTING ORGAN REJECTION

THE ISSUE

Within the process of organ donation, we face a large problem: **ORGAN REJECTION**.

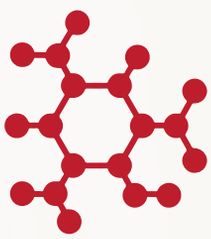


CURRENT SOLUTIONS

MEDICATION

- lifelong medication
- suppresses immune reaction

NANOTECHNOLOGY



- one-time treatment
- training of immune system

HOW IT WORKS

1. 
Immune system fights donated organ

2. 
Nanotechnology trains immune system

3. 
Organ is accepted

4. 
No more medication needed

WHY CHOOSE NANOTECHNOLOGY?

STRENGTH OF THE IMMUNE SYSTEM				
STATE OF THE ORGAN				
WHAT DOES IT MEAN?	The organ is healthy, there was no transplant.	The organ is transplanted without medication, the organ is rejected.	The organ is transplanted and accepted, but immuno suppressant drugs will be necessary.	The organ is transplanted and treated with nanotechnology. It has been accepted.

A SMALL THERAPY WITH LARGE EFFECTS.

IN CON

ALBERT VAN DEN BERG

Prof.dr.ir. A. van den Berg is a professor of sensor systems for biomedical and environmental applications at the University of Twente.

Albert van den Berg received his MSc in applied physics in 1983, and his PhD in 1988 both at the University of Twente, Enschede, Netherlands. In 2000 he was appointed as full professor on Miniaturized Systems for (Bio)Chemical Analysis in the faculty of Electrical Engineering and part of the MESA+ Institute for Nanotechnology. He published over 450 peer reviewed publications in Science, Nature, PNAS, NanoLetters etc, and from his group more than 10 spin-off companies started. In 2018 he became (co)director of MESA+ institute for Nanotechnology. As a qualified researcher in the field of nanotechnology, it was only appropriate to gain some insights into the topic of nanotechnology in healthcare from him and to present his thoughts for the future of nanotechnology.

IVERSATION WITH...

When asked what is so fascinating about nanotechnology, dr. van den Berg expressed that it is amazing what one can do at a nanoscale level, having such a small thing in his hands. In biology for example, almost everything can be perceived at a nano level, the DNA, proteins, viruses, cell components, etc. Furthermore, in order to measure these things, one has to control the tools also at a nanometer size, "and that's why it's so fascinating... such a very interesting technology". Dr. van den Berg gave as a good example the following situation. Your watch gets broken, you want to repair it and you only have a big hammer or a big pin set- you can not really manipulate it. So, if you want to fix the watch, you would need micro instruments, you would have to manipulate it on a nanoscale. And this makes nanotechnologies superior to other classic technologies. Moving on to the implementation of nanotechnology in healthcare, dr van den Berg highlighted the field of nanomedicine and its importance. There are different applications of nanotechnology in medicine. For instance, you can package your medication in a little nano balloon, decorated at the outside with receptors that bind only to the organ, tissue or cell that you want to attack with your medicine. In the case of cancer, the medication is normally very toxic, but if you package it in a nano balloon, it attaches to the cancer tissue, it opens and then the toxic molecule will only go to the cancer tissue and not to the rest of the body tissues. Dr van den Berg also explained that nanoparticles can significantly improve the imaging quality of an imaging technique. These particles improve the resolution and contrast of MRIs or CT scans for example. In regards to the implementation of nanotechnology in more hospitals, dr van den Berg said that little steps are taken everyday towards that direction, but from the big businesses such as the pharmaceutical industry and diagnostics industry, not universities for example, as they don't do the big business with hospitals. "The testing of Corona is also now being done using nano devices. And that is, for instance, how it already happens. And also in hospitals, they typically use commercially available nano systems and nano particles. But of course, we also work together with many hospitals to develop new technologies and that normally takes maybe five to 10 years between the research done at university together with medical hospitals, and the moment that it's commercial". It is nevertheless extremely important that the medical implementation process is handled carefully.

> "and that's why it's so **fascinating**... such a **very interesting technology**
>
> - Albert van den Berg

“ privacy is a very

There are restrictions and limitations set upon nanotechnology which prevents it from entering the medical sector. Dr. van den Berg highlighted that it’s people fearing nanotechnology that restricts it, and he said that people do not have to be afraid as the researchers are the ones that are first exposed to these technologies. As a result, they work closely with regulative bodies such as the European Medicines Agency (EMA), to make sure that they remain safe while developing the nanotechnology further. He also explained that there are three levels of acceptance; technical readiness (how applicable the technology is), societal readiness (how willing is the general public to accept it) and regulatory readiness (does the technology meet the requirements of current rules and regulations). He stated that all these levels need to be developed together.

Following the theme of people fearing nanotechnology, dr. van den Berg emphasized that they work and take no risks. As a result, they check the different effects that nanotechnology has on our body in a multitude of ways. A project he featured, tissue on chip, includes growing a culture of skin cells onto a chip. The skin cells will then be put under testing of cosmetics, to ensure minimal side effects. He invites people to see the inner workings of the research by inviting people to his lab where he is open to criticism to improve how acceptable his innovation is.

A concern by many people is privacy, Dr. van den Berg chimed in on the issue. He said that there were plans to make a ‘digital twin’ of every citizen. All information regarding yourself will be saved to this twin, from what your name is to how much sunlight you get. This twin will be saved in the cloud. Dr. van den Berg stated that this would greatly benefit doctors, which will have all the complete information regarding you thus a more precise diagnostic will be possible and treatment of a patient will be easier. Not only doctors, researchers will be able to benefit from this, if the data will be anonymized, researchers will be able to develop better medication with additional information. However, he stressed on privacy being important, “privacy is a very important issue, because you don’t want everybody to be able to access your medical data of course”.

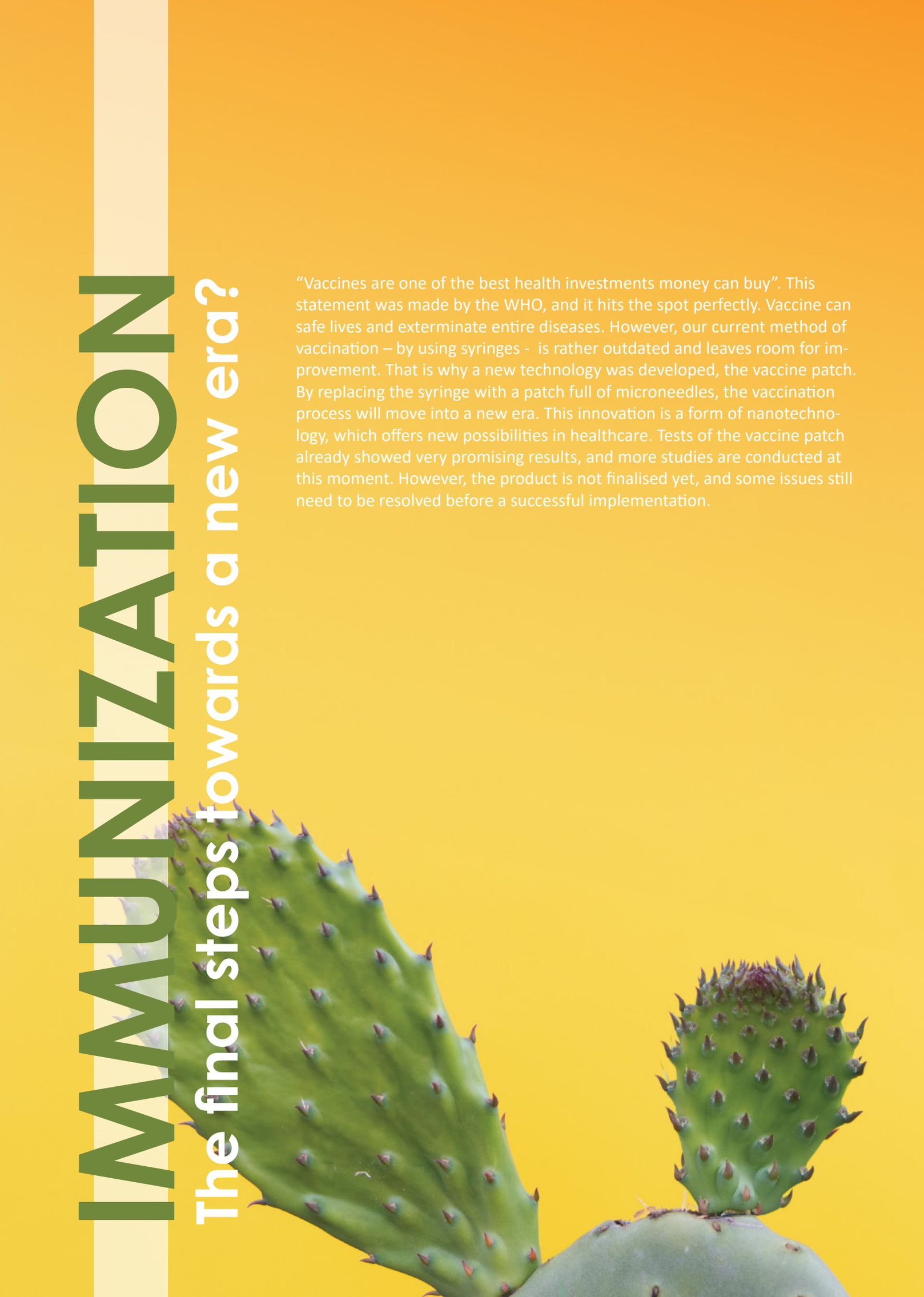
Lastly, we asked what dr. van den Berg. is working on right now. He voiced that there are several projects focused on early detection of COVID-19. He is also working on ‘organ on chip’ projects. One of them is that when you contract COVID-19, you also develop thrombosis which in the long run will cause problems. So dr. van den Berg is developing micro-blood vessels on a chip to see if he can mimic some of the effects of COVID-19 in the blood. He believes that this is the most promising development that he has done in terms of health research for his research group.

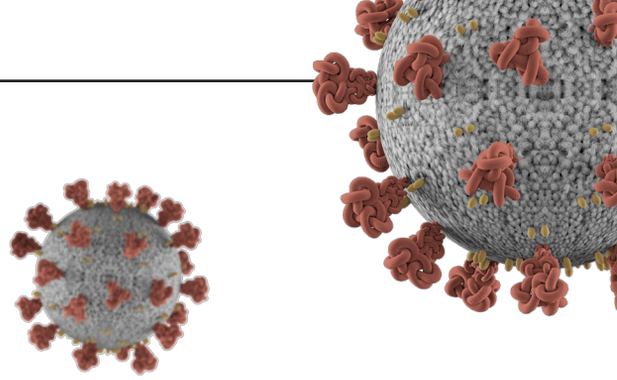
important issue, because you don't want everybody to be able to access your medical data."

IMMUNIZATION

The final steps towards a new era?

“Vaccines are one of the best health investments money can buy”. This statement was made by the WHO, and it hits the spot perfectly. Vaccine can safe lives and exterminate entire diseases. However, our current method of vaccination – by using syringes - is rather outdated and leaves room for improvement. That is why a new technology was developed, the vaccine patch. By replacing the syringe with a patch full of microneedles, the vaccination process will move into a new era. This innovation is a form of nanotechnology, which offers new possibilities in healthcare. Tests of the vaccine patch already showed very promising results, and more studies are conducted at this moment. However, the product is not finalised yet, and some issues still need to be resolved before a successful implementation.



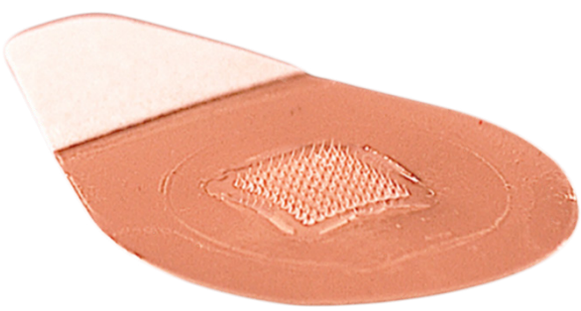


ONE PATCH, BUT HUNDREDS OF TINY NEEDLES

To make it a bit easier to understand, think of a normal band aid. Instead of the white part that covers a wound, there is an area containing hundreds of small needles, each between 0,1 or 1mm long, depending on the specific technology.
To administer the vaccine, there are two different options: dissolvable and coated needles. In the first version, needles are coated with a dried vaccine which then is absorbed by the skin a few minutes after application. Dissolvable needles are made out of sugar and 'dissolve'- as the name already suggests - after a certain amount of time after application.
To administer the patch, you simply place it on your skin, for example on the wrist. After a few minutes, the patch can be removed and the vaccine transferred into the body where it leads to immunity against the virus. The immunization itself works the same way as it does with traditional vaccines. In the first step, a vaccine containing an inactive form of the disease is introduced to the body through the patch. The body reacts to it by producing antibodies, which work as sword and shield and protect you against the virus.

WHAT MAKES IT BETTER THAN A 'NORMAL' VACCINE?

You might think, all well and good but why should I use this new technology if it does the same thing as your 'normal' vaccines. Let me say, not only needle-phobics can profit from using those patches. Current tests show vaccine patches to be just as, or in some cases even more effective than syringe solutions. This was proven though clinical trials conducted with both animals and human participants.
Patches transmit the vaccine in a very different way from traditional vaccines. Whereas syringes need to be injected in muscle tissue to be effective, patches are placed on areas of the body with thin layers of skin, making them a lot easier and convenient to administer.



In fact, patches are claimed to be easy enough to place that they can be self-administered by the general public. But not only that, vaccine patches also solve another issue of current syringe vaccinations that makes a lot of us tremble in fear: pain caused by the needle. Instead of concentrating all pressure on one large needle, the incredibly small needles of a vaccine patch distribute the contact area and are as good as painless. And if you wonder how expensive such a technology must be- not expensive at all. A traditional vaccine costs almost twice as much as vaccination delivered through a vaccine patch. This and the fact that it has very low transport requirements, makes it a valuable weapon to tackle the low vaccination rates in developing countries.against the virus.

HOW THIS TINY PATCH MIGHT FIGHT A GLOBAL PANDEMIC

There are many obstacles to overcome during the Covid-19 pandemic, and finding a vaccine is not going to solve everything at a glance. Current vaccines require administration by medical personnel and therefore personal contact, something we are trying to avoid at all costs right now. So how could a tiny patch help us? One huge advantage of the vaccine patches over traditional vaccines is that they can be self-administered.
The process requires zero to little skill and could technically done by a child. Simply put the vaccine patch on a thin layer of skin. Done. This process can offer huge practical advantages during the time when Covid-19 vaccines become more available.
The shift from a centralised vaccination place such as the general practitioner or the hospital to a decentralised place such as one's own home would allow it to reduce contact to a minimum. The patch can be picked up at the pharmacy or transported to you by mail. This reduction of contact prevents Covid-19 from spreading in the first place and moreover frees medical professionals to focus on important treatments. Even if vaccine patches are not our answer to this pandemic, it can give us a perspective for the future, and maybe even prevent the next pandemic.

IS IT TOO GOOD TO BE TRUE?

Would you trust this new technology? Many people don't, especially if they do not understand it fully yet. And why would you use something new if the current version also works? Adapting a new technique takes effort. If people do not see the advantages of the vaccine patch, they are not willing to switch to it. Technologies, such as this one, that require drastic changes are usually met with suspicion. This can also be seen in academic studies. A focus group recently conducted at the University of Twente showed, that people´s main concern about vaccine patches is safety and other personal worries, including worries about the correct use of the patch and potential abuse for illegal drugs. Imagine for example parents that administer the vaccine patch to their child and due to a small unnoticed mistake don´t know about the missing potection against that certain disease.

> "I think if the **effectiveness of the patches** is the same or better, [...] it's better to use patches. But if not, then I'll stick to the injections"
>
> - Focus group study at the University of Twente

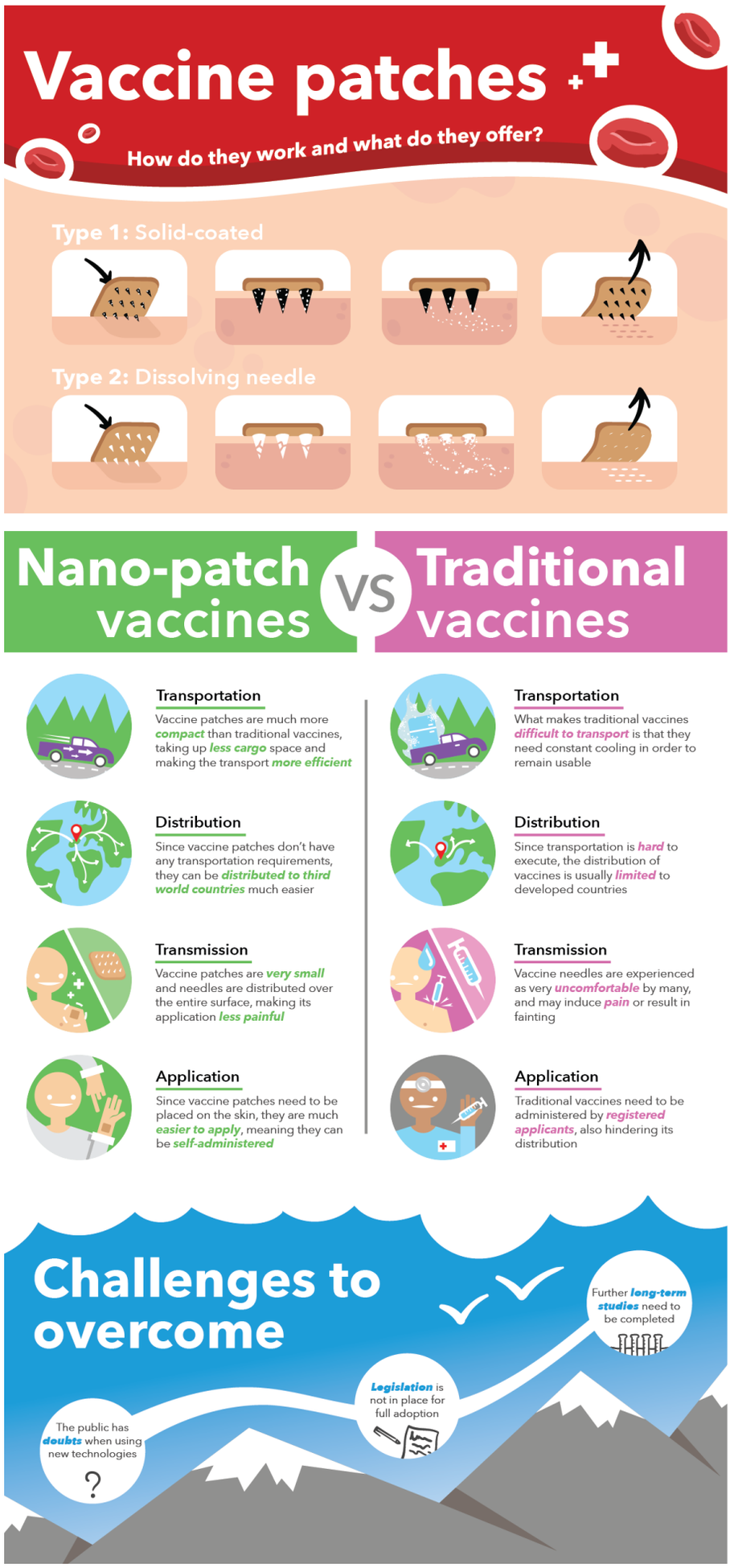
But that´s not all yet. There are more problems to be solved when it comes to the actual use of vaccine patches, just think of the following examples: What about anti-vaxxers pretending to have used the patch and faking their vaccination record? What about people with skin diseases that can negatively influence the immunization process with a vaccine patch? What about potential side effects like skin rashes? These are all important points that might influence the safety of vaccine patches and need to be investigated further.

WHY YOU CAN´T GET A VACCINE PATCH IN THE PHARMACY YET

Of course, there are some uncertainties left with vaccine patches, but is any technology ever perfect? Vaccine patches might be used for drug abuse, but so are syringes. So why can´t you get a vaccine patch yet, even though they are so effective, cheap and easy to use? The answer is not

so simple, as there are multiple reasons explaining why vaccine patches have not been adopted by the market so far. Those mainly come down to economic and legislative reasons. First of all, legislation for syringe vaccines has been in development since the 1950's and vaccine patches have only been around since 2015, which is a rather short period of time. As you might remember from an earlier part of this article, new innovations are usually met with suspicion, however public acceptance needs to be built up to bring legislation forward. Furthermore, to ensure that vaccine patches, are safe enough to use, research in form of clinical trials is necessary, but the funding of clinical trials is expensive. Certainly, you know the saying "Time is money", but in this case it is the other way around. Money actually influences how much longer we need to wait until vaccine patches enter the market.

As it has become clear, the vaccine patch is a great innovation with a lot of potential. They are promising and have benefits for the individual and also for society. In the long term, they can revolutionize our vaccination experience and make it much more comfortable and safe for everyone. However, there is no need to rush. Our current method of vaccination also works, and vaccine patches are still in the development phase. Even after passing clinical trials, there are many steps before they will become our "new normal". Until the development and testing of the vaccine patch is entirely completed, we have to use the methods at hand. But once the patches are ready to use, we will experience a new era of vaccination, which holds many new opportunities. What about you? Can you imagine switching to such a vaccine patch? New technologies can be exiting and entail many advantages, like you probably experienced with your smartphone, or your grandma's new hearing aids. It may still feel strange right now, but once you tried it, you won't want to go back.



PUZZLE PAGE

ADMINISTRATION
BLOOD
BOWEL
CANCER
COLONOSCOPY
DOCTOR
DONOR
ENZYMES
FUTURE
HEALTHCARE
HOSPITAL
INNOVATION
LIVER
LIVES
MEDICINE
MICROSCOPIC
NANO
NANOPILL
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PATCH
POSSIBILITIES
REJECTION
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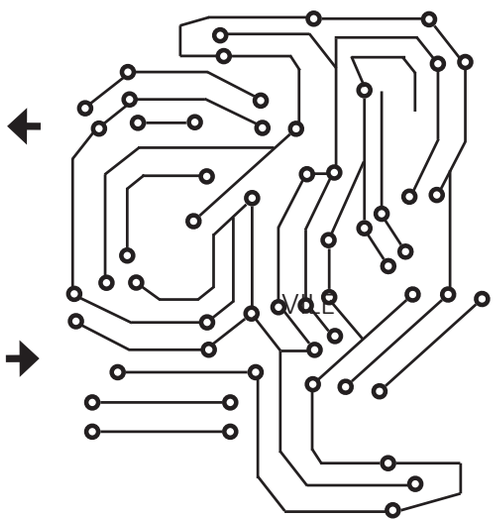

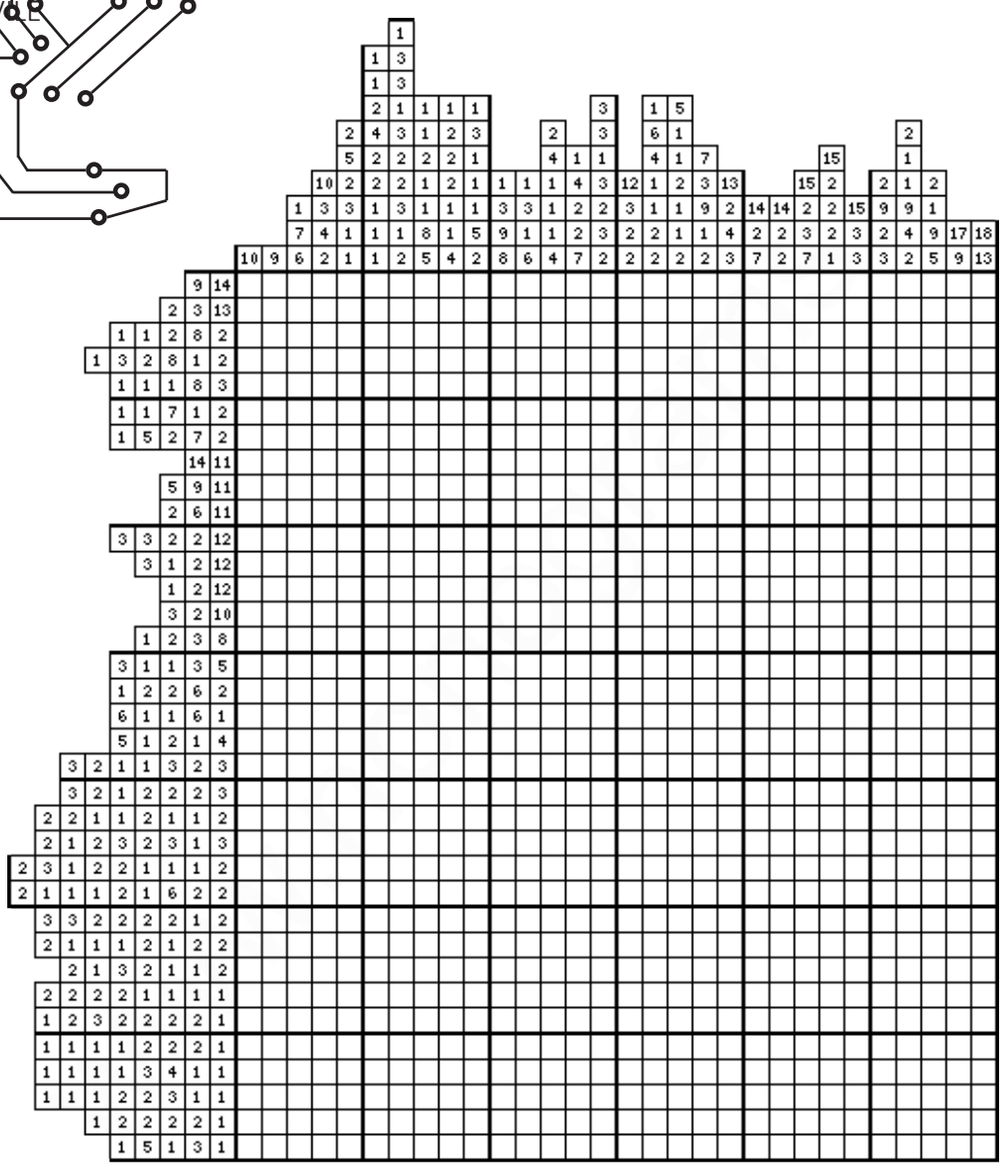

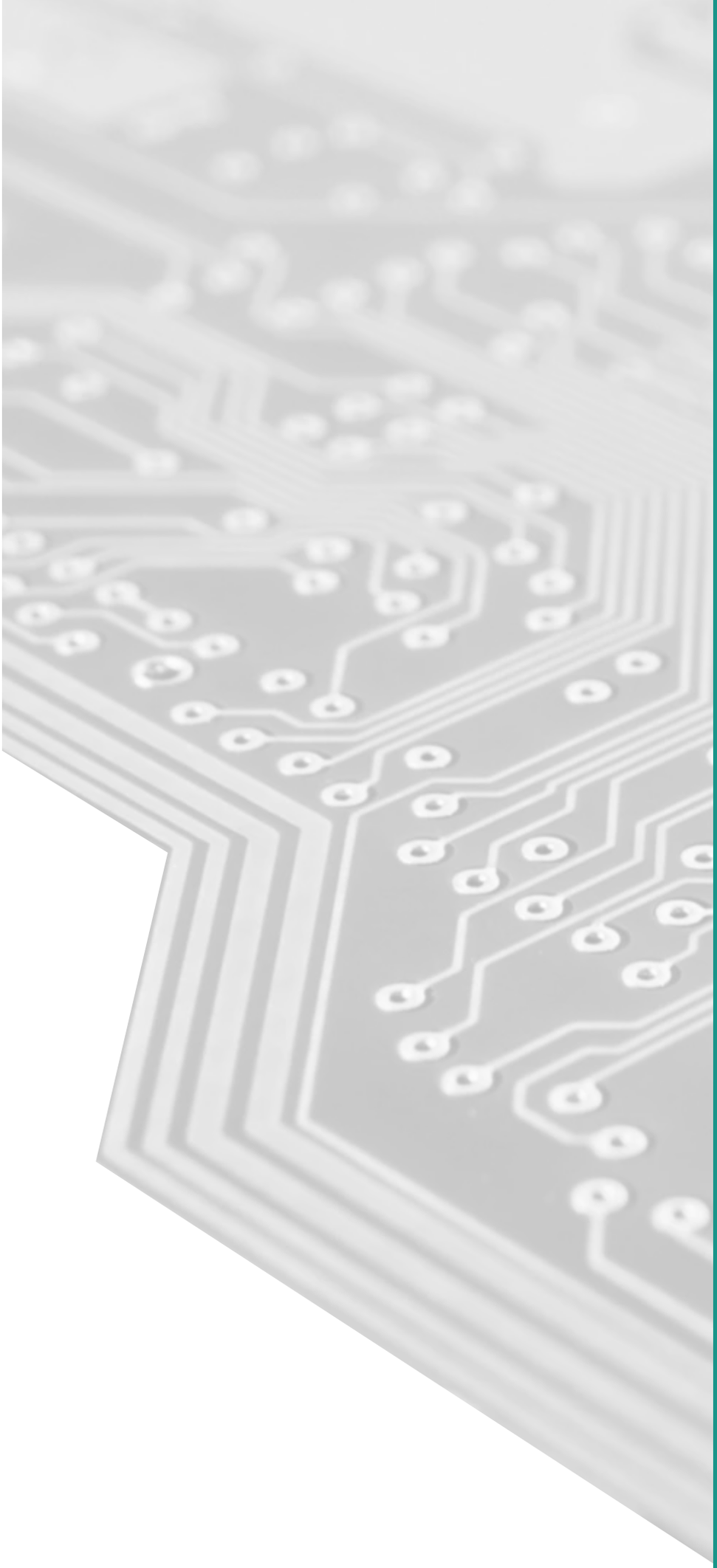

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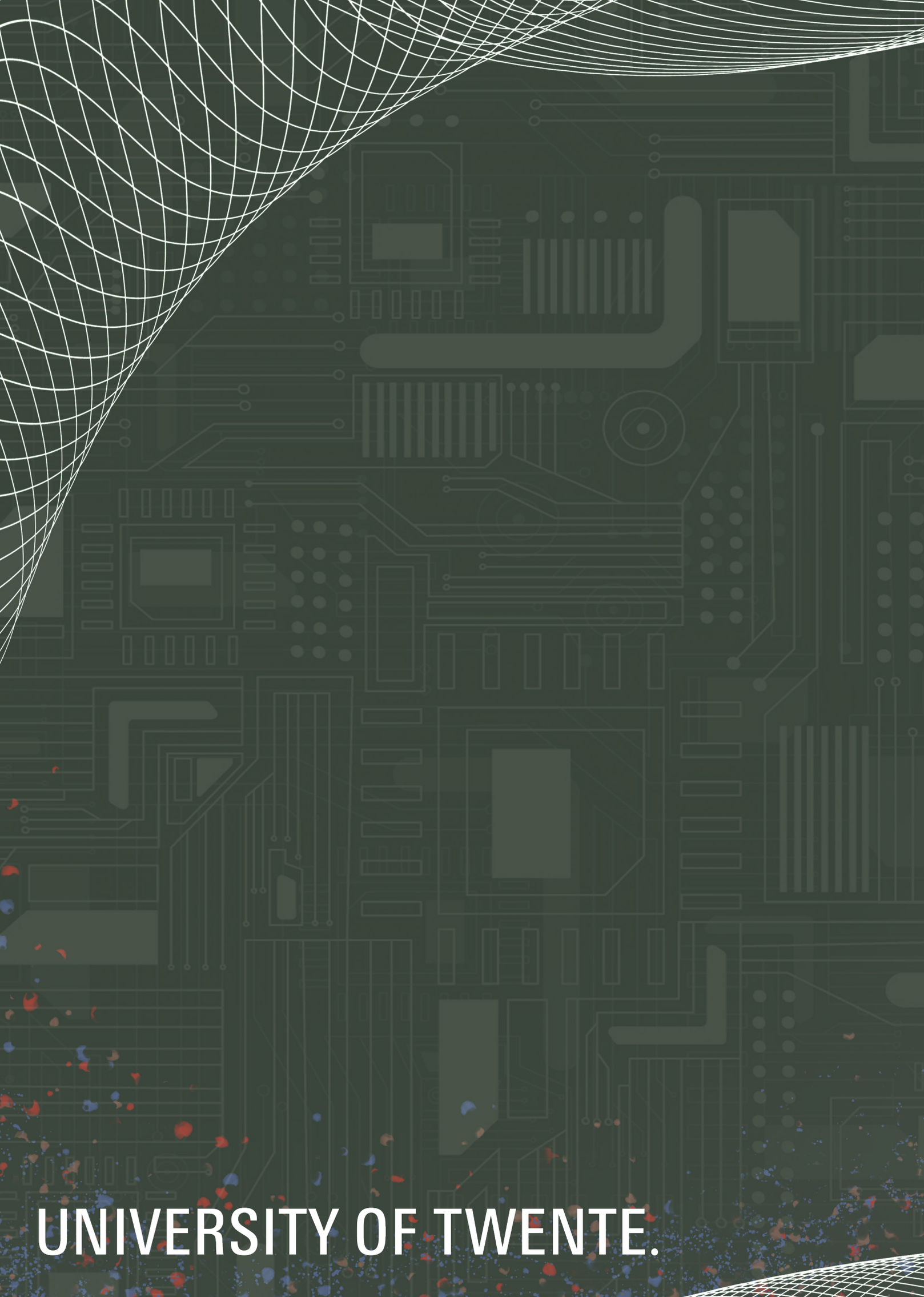
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