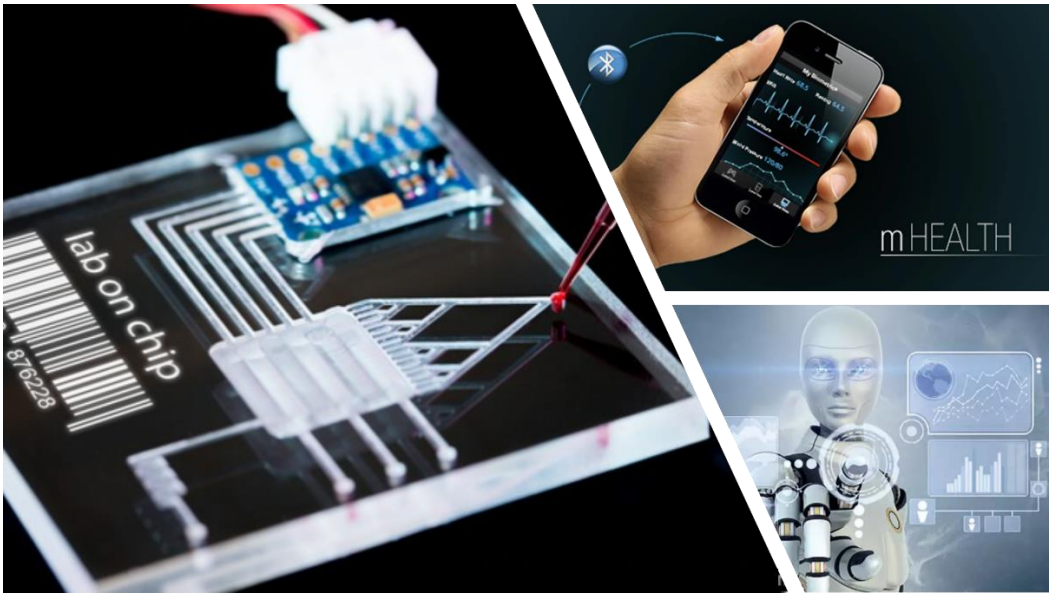


Market insights regarding micro- and nano electronics for healthcare in Flanders-Belgium

REPORT COMMISIONED BY THE PROVINCE OF FLEMISH BRABANT – SMART HUB HEALTH

CLUSTER EXCELLENCE IN LIFE SCIENCES – INTERNATIONALIZATION OF SMES (CELIS)

Johan Lecocq | V1.0 | 2/10/2020

SMART HUB FLEMISH BRABANT

ESCP X CELIS Partnership

Content

Introduction

Flanders, the Dutch speaking region of Belgium, has a strong tradition in micro- and nano electronics (MNE). Already for many decades our universities offer education programs on microelectronics which can compete on global scale. The founding of the research center imec in 1984[1] was certainly the milestone putting Flanders finally on the map as a leading region for micro and nanoelectronics skills and expertise, something which is continuing even today.

Micro and nanoelectronics is one of the key enabling technologies (KETs). It is in fact driving a lot of the high tech innovations happening today and still to expect in the near future. And this is certainly true for innovations in health care. If you ask journalists or market research companies about the main technological trends in health care they all come up with similar lists. And without any exception all trends are strongly relying on the availability of state of the art micro and nanoelectronics.

As a result, the use of semiconductors in healthcare has been increasing owing to the revolutionary changes in the domain such as digitization and automation of various activities such as surgery for which robotic assistance is being employed. The digitization has been enabling in the implementation of such automation. The use of sensors and other wireless technology are being used for remote patient monitoring. A wide range of solutions are still in the development phase to harness data from connected devices and other electronic ecosystems to enable better patient care. 3D printing of organs and medical devices has also been one of the recent developments which are expected to increase the use of semiconductor.

The semiconductor industry will play a pivotal role in designing and developing portable and affordable medical devices. The connectivity enabled by semiconductor technology (wired or wireless) will drive applications such as telemedicine that will facilitate access to the required level of healthcare.

Some of the key drivers for the growth of semiconductors in the health care are[2]:

- Technological advancements
- Increased use of connected devices
- Digitization of a vast array of previously manually operations in the healthcare industry

[1] Interuniversity Microelectronics Centre is an international research & development and innovation hub, active in the fields of nanoelectronics and digital technologies. (https://www.imec-int.com/en)

[2] https://www.transparencymarketresearch.com/semiconductors-healthcare-applications-market.html

- To process the vast volumes of digital data developed by connected devices and digitized processes, the demand for effective data processing tools is becoming stronger with the passing day
- The development of portable, self-care and small therapeutic and diagnostic devices

Scope of the report

Regional focus

This report provides an overview of the economic activities and related market opportunities in Flanders related to micro and nanoelectronics in health care. However market information is often not available on the level of Flanders only. In that case Belgium is taken as the focus region instead.

And if the information is available, specific attention will be paid to the province of Flemish-Brabant as this is home of imec and of KU Leuven, the most innovative university in Europe and the 7th worldwide[3].

Which economic activities

Companies, research organizations and universities are taken into account for the analysis of the ecosystem.

All companies and organizations active on the value chain of health related applications for which micro and nanoelectronics is an enabling technology are considered for this report. This means that at least the following types of activities will be taken along:

- Companies developing micro and nanoelectronics components that can be applied in health products
- Companies using micro and nanoelectronics components in their health products
- Companies relying on platforms that are strongly based on micro and nanoelectronics

The process technologies used to integrate electronic systems on semiconductor material can also be used to develop miniaturized systems other than pure electronics. Examples are BioMEMS and micro-fluidics. Also these applications of the micro and nano(electronics) technology are considered for this report.

[3] https://www.arts.kuleuven.be/english/education/why-choose-ku-leuven/meest-innovatieve-universiteit-van-europa

The ecosystem for micro and nanoelectronics for healthcare in Flanders

Although some (very limited though) information can be found on the life sciences sector in Flanders, no information is (freely) available on the cross-section of life sciences and micro and nanoelectronics. In order to make an overview of the ecosystem, available reports on the life sciences sector, are combined with knowledge available in the relevant regional cluster organizations like DSP Valley and the RTOs[4] that are closely collaborating with the industry. Life sciences reports can be found with the Belgian Foreign Trade Agency[5] and Flanders Investment and Trade[6].
Three main categories of actors are considered: research (incl. academia), component and sub-system developers and application builders. A special category are the companies delivering product design services. They can be found as a sub list in the overview of application builders. An overview of the main regional players in these categories is depicted below.

Research/Academia

Flanders has a well-developed education program for micro and nano electronics. All universities are offering master programs in engineering disciplines related to micro- and nano-electronics. The education program is complemented by strong research programs. The four universities in Flanders offering research programs that are competitive on global scale in micro and nanoelectronics are:

- University of Leuven (KUL)
- University of Ghent (UGENT)
- University of Brussels (VUB)
- University of Antwerp (UAntwerpen)

Next to the academic institutes, Flanders has established several applied research organisations active in fields relevant for the industry and society. One of those is focusing on micro and nanoelectronics research. imec, the inter university microelectronics center, was founded in 1984 as a result of a program of the Flemish government to strengthen the microelectronics industry in Flanders. In 2009 the brain research lab NERF (Neuro-Electronics Research Flanders) was founded as a cross disciplinary collaboration between imec, KUL and VIB. The latter is the Flemish Institute of Biotechnology.

[4] Research and Technology Organisation
[5] https://www.abh-ace.be/en/importers/sectoral_publications/belgian_life_sciences_2019
[6] https://www.flandersinvestmentandtrade.com/invest/en/sectors/life-sciences-health

Components and sub-systems

The presence of highly skilled people, the different research programs at the universities and the presence of the research institute imec have resulted in many entrepreneurial initiatives in the area of micro and nanoelectronics. One main category are those companies that design components or sub-systems. Some of them offer design services towards customer specific solutions, others have dedicated components or technologies in their portfolio. Because of the typical enabling nature of micro and nanoelectronics, these companies are often serving multiple market segments. For this overview we only consider those companies that have a significant part of their turnover in healthcare or at least consider this as an important growth segment.

Components & sub-systems	Location	HQ	Focus	Spin off	Founding date
Gpixel	Antwerpen	China	imaging sensors		2018
Caeleste	Mechelen	Belgium	imaging sensors	imec (Fillf	2006
Cmosis (acq by AMS in 2015)	Antwerpen	Austria	imaging sensors	imec (Fillf	2007
ON Semi (acq Cypress Semi in 2011)	Mechelen	US	imaging sensors		2002
IC Sense (acq by TDK in 2017)	Leuven	Japan	ASIC design		2004
Ansem (acq by Cyient in 2018)	Leuven	India	ASIC design	imec	1998
Melexis	Tessenderlo	Belgium	sensors		1993
Easics	Leuven	Belgium	ASIC design	imec	1992
NXP	Leuven	The Nethe	varia		2006
Cochlear TCE	Mechelen	Australia	ASIC design		1990
Spectricity	Mechelen	Belgium	optical spectral sensing	imec	2018
Quad Industries	St Niklaas	Belgium	flexible electronics		1998
Sony Depthsensing Solutions (acq SoftKinetic in 2017)	Brussel	Japan	3D time of flight sensors	VUB	2007
Pharmafluidics	Gent	Belgium	microtubes for chromotography	VUB	2010

Applications

In this category all companies that develop products or services for the healthcare market are considered. To enable further analysis and because the list of companies is quite long additional sub-categories have been defined.

The first list shows companies that develop clinical diagnostics devices. Several of those companies follow a strong cross-disciplinary approach by combining biotechnology and micro and nanoelectronics.

Clinical Diagnostics devices	Location	HQ	Focus	Spin off	Founding date
miDiagnostics	Leuven	Belgium	nanofluidic processors	imec	2015
Antelope DX	Zwijnaarde	Belgium	portable diagnostics devices	MyCartis	2019
Biocartis	Mechelen	Belgium	portable diagnostics devices		2007
Trinean (acq by Unchained labs)	Gent	US	spectrofotometer	imec	2006
Pepric (acq by Sygma)	Leuven	Russia	direct imaging of magnetic labels	imec + UGent	2009
Barco	Kortrijk	Belgium	Diagnositics		1934
Minze	Antwerpen	Belgium	Urology	imec	2015
Indigo Diabetes	Gent	Belgium	Diabetes	imec	2016
MyCartis	Zwijnaarde	Belgium	Point of Care diagnostics		2015
Nischala Technologies	Antwerpen	Belgium	AI assisted blood sample testing		2019
Ovizio	Brussel	Belgium	light based digital holographic microscopy		2009
Agfa	Antwerpen	Belgium	imaging IT		1894
BeWell	Ranst	Belgium	self test kiosk		2010
3.LIFE	St Agatha Be	Belgium	platform connecting health devices		2019
HippoCreates	BlueHealth	Belgium	allergy test		2020

The next sub-category are companies developing solutions for pre-clinical test and measurement. One of the typical applications in this field is lab equipment used for drug discovery. But also brain probes to perform tests on animals or PET scans dedicated for animal testing belong to this category.

Pre-clinical test & measurement	Location	HQ	Focus	Spin off	Founding date
BioSensource	Vilvoorde	Belgium	Drug Discovery	imec & VUB	2016
Molecubes	Gent	Belgium	Diagnostics Research	imec + Ugent	2015
Atlas Neuroengineering	Leuven	Belgium	Diagnostics Research	imec	2012
Cellsine	Leuven	Belgium	Drug Discovery	KUL-VUB	2015
Peira (part of Exmore group)	Beerse	Belgium	Instruments for research		2007
Fox Biosystems	Diepenbeek	Belgium	Diagnostics Research	KUL	2017

The next sub- category are companies producing personalized “passive” implants. This category has been added because Flanders has a strong tradition on 3D printing and several of those companies are also targeting the healthcare market.

Implants	Location	HQ	Focus	Spin off	Founding date
Materialise	Leuven	Belgium	Implants		1990
Layerwise (acq by 3D Systems in 2014)	Leuven	US	Implants		2008
CADskills	Gent	Belgium	Implants		1996

A fourth sub-category are the therapeutic devices.

Therapeutic devices	Location	HQ	Focus	Spin off	Founding date
Morrow Optics	Zwijnaarde	Belgium	Digital glasses	imec	2016
Tokai Optecs (acq EYEcoEYEco)	Tienen	Belgium	Digital glasses	imec	2016
Elmedics	Leuven	Belgium	Controlled heat treatment for pancreatic cancer	UA	2016
Moonbird	Keerbergen	Belgium	Supporting breathing ecercises		2019
Cochlear TCE	Mechelen	Australia	Hearing implants		1990
Creative Therapy	Gent	Belgium	Interactive mat	UGent	2019
Sequanamedical	Zwijnaarde	Belgium	Pump for fluid inbalance disorders		2006

The wearable solutions are combined in a fifth sub-category. Although you can argue that some of those solutions could also belong to the diagnostics or therapeutic devices, we have put them in a separate category because in many market analysis reports, wearables are mentioned separately.

Wearables	Location	HQ	Focus	Spin off	Founding date
Bloomlife	Genk	US	Pragnancy monitoring	imec	2014
Crescent (acq Uest - Zembro)	Leuven	Belgium	Monitoring elderly people	imec	2015
Onera	Eindhoven	US	Sleep monitoring	imec	2018
Pulsify Medical	Leuven	Belgium	Ultrasound patches	imec	2018
Byteflies	Antwerpen	Belgium	Monitoring of several parameters		2015
Epihunter	Hasselt	Belgium	Epilepsi seizure detection		2017
Noho	Brussel	Belgium	Lymphedema treatment		2015
Gabi Smartcare	Brussel	Belgium	Monitor respiratory conditions		2017
Heart Kinetics	Brussel	Belgium	Cardiac monitoring system	ULB	2019
Ectosense	Leuven	Belgium	Sleep apnea		2015
Bainisha	Lokeren	Belgium	Monitoring of body movements		2014

This study not only focuses on hardware but also on software which is strongly relying on the enabling micro and nanoelectronics technology. In this sixth sub-category you will find a mix of solutions going from data analytics services (which could also be offered for non-healthcare applications), diagnostics , monitoring to even therapeutics services. All these companies make use of off the shelf platforms to offer their services.

Algorithms, AI, ...(on standard platforms	Location	HQ	Focus	Spin off	Founding date
Ontoforce	Gent	Belgium	Data analytics	imec	2011
ArtiQ	Leuven	Belgium	AI based interpretation of lung function tests		2019
Datastories	Turnhout	Belgium	Data analytics		2011
Lindacare	Leuven	Belgium	Cloud based remote monitoring implanted cardiac devices	imec	2015
Epilog	Gent	Belgium	EEG analysis for Epilepsi	imec - UA	2016
Helpilepsy (Epione)	Brussel	Belgium	Monitoring		2017
` MoveUP	Brussel	Belgium	Digital Therapy		2015
My Medicoach	Etterbeek	Belgium	Digital Therapy		2012
icometrix	Leuven	Belgium	AI based brain image analysis	KUL - UA	2011
MyNeo	Gent	Belgium	Identification and prediction of neoantigens		2018
Biolizard	Gent	Belgium	bioinformatics		2018
Emweb	Leuven	Belgium	AI based virus identification		2008
Fibricheck (Qompium NV)	Hasselt	Belgium	heart rhytm monitoring with smartphone		2014
Sentiance	Antwerpen	Belgium	insights and tips for healthier lifestyles based on data science		2015
Robovision	Gent	Belgium	deep learning & medical imaging		2009
Biorics	Leuven	Belgium	Monitoring of sports teams and people at work	KUL	2006
Sneezz	Aarschot	Belgium	allergy insights based on sensor networks		2017
Cubigo	Hasselt	Belgium	Care platform	Uhasselt	2011
eSaturnus (acq by Sony in 2016)	Leuven	Japan	digital imaging data handling	KUL	2003
Cartagenia (acq by Agilent in 2015)	Leuven	US	analytics SW for genetic labs	KUL	2008
ASYLIA DIAGNOSTICS	Beerse	Belgium	Immonotherapy safety prediction	imec	2016
Bingli	Antwerpen	Belgium	Medical interview, chatbox		2017
DEO	Genk	Belgium	OR efficiency platform		2018
Epcon	Antwerpen	Belgium	Epidemic control		2018
Lynxcare	Leuven	US	Data analytics		2015
Nephroflow (now nipro)	Brugge	Belgium	Process flow support for Dialysis		2013
Bluebee (acq by Illumina in 2020)	Mechelen	US	Analysis of genetic data		2011
Oehoe datasciences	Hasselt	Belgium	Data analytics		2015

A seventh category is called medical infrastructure. These companies are offering solutions which are mainly supportive for the care of patients. A button at the hospital bed to call a nurse or a tool to track the assets in an hospital are examples.

Medical infrastructure	Location	HQ	Focus	Spin off	Founding date
Televic	Izegem	Belgium	safety, comfort		1946
Blooloc	Hasselt	Belgium	asset tracking		2018
Kaspard	Brussel	Belgium	fall detection		2017
FamilyEye	Gent	Belgium	fall detection		2012
Blyott (former Sensinxs)	Brugge	Belgium	asset tracking		2017
Pozyx	Gent	Belgium	Localisation	UGent	2015
Epic Blue	Leuven	Belgium	localisation		2016

The last category are those companies that provide design services.

Product design services for medical proc	Location	HQ	Focus	Spin off	Founding date
Verhaert	Kruibeke	Belgium	product design		1969
Comate	Leuven	Belgium	product design		2010
Zenso	Leuven	Belgium	product design	KUL	2007
Dekimo	Gent	Belgium	product design		1987
Voxdale	Antwerpen	Belgium	product design		2005
Ninix Technologies	Brugge	Belgium	product design		2001
Commeto	Ham	Belgium	embedded SW		2001
Covartim	Brussel	Belgium	product design		1992
Connect group	Kampenhout	Belgium	product design		1996
Achilles design	Mechelen	Belgium	product design		1994
pilipili	Kortrijk	Belgium	product design		1996

State of the art of micro and nanoelectronics for health applications in Flanders

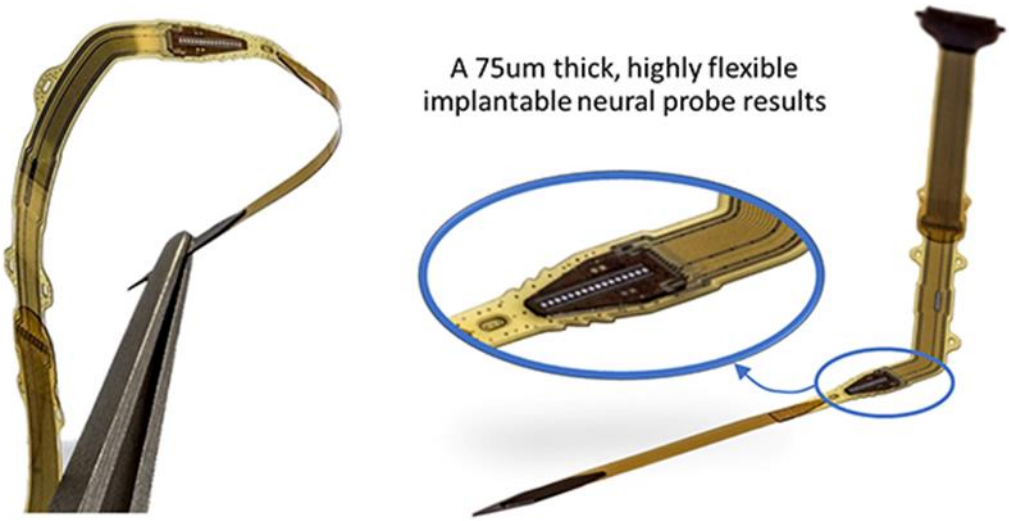
To provide insight in the state of the art developments ongoing in Flanders in the area of micro and nanoelectronics for health applications, a few examples of on going research activities are described in this chapter. This overview is not intended to be comprehensive but just want to give a flavor.

SMALLER, THINNER AND SOFT IMPLANT ENCAPSULATION TECHNOLOGY (IMEC & UNIVERSITY OF GHENT)

Active medical implants are gaining increasing interest as smart supporting devices. One example is a pacemaker that monitors the patient's heartbeat and only interferes when needed. However, electronics and the human body are not always best friends. When a device is implanted, the body's immune system will react to it, often resulting in a thick layer of scar tissue surrounding the implant. Direct exposure to fluids will damage electronic components. But, at the same time, since the smart electronics are not biocompatible, the body needs to be protected from leaching of substances. Therefore, active implants require an encapsulation with a hermetic bi-directional diffusion barrier.

The conventional encapsulation/packaging technology based on titanium or glass package is bulky and results in a pronounced tissue reaction which may affect device functioning. A smaller, thinner and soft implant encapsulation technology has significant advantages. Because it allows for smaller devices, the implantation procedure will be much less invasive, and the tissue reaction will be less pronounced.

The combination of thin biocompatible polymer films and high-quality ceramic nanolayers proves to fulfil the hermeticity needs of long-term implantable medical devices. The technology was successfully applied to a flexible, thin neural probe, optimized for intra-fascicular nerve insertion.



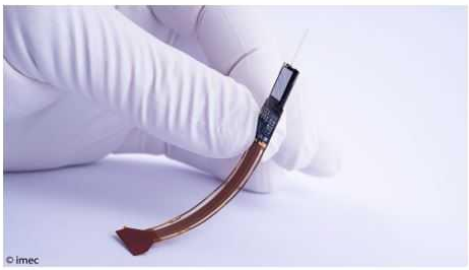
An article was published on this technology in MedTech Intelligence:
https://www.medtechintelligence.com/feature_article/novel-long-term-hermetic-ultrathin-implant-packaging-technology-based-on-ceramic-nanolayers/

FROM WEARABLES TO CAREABLES: CLOSING THE LOOP IN CONNECTED HEALTH (IMEC)

Thanks to the miniaturization of sensors and actuators, and thanks to the enormous progress made in artificial intelligence and deep-learning algorithms, it becomes possible to close the loop on health: not only sensing vital signs but also interpreting the data, getting actionable insights, and triggering some action.

This leads the way to artificial organs, drug-device combinations, the targeted treatment of depression and chronic pain, and many other applications. Every closed-loop therapy system will look different and will rely on (a combination of) different form factors (wearable, implantable, invisible) and building blocks to find the perfect fit for a specific application.

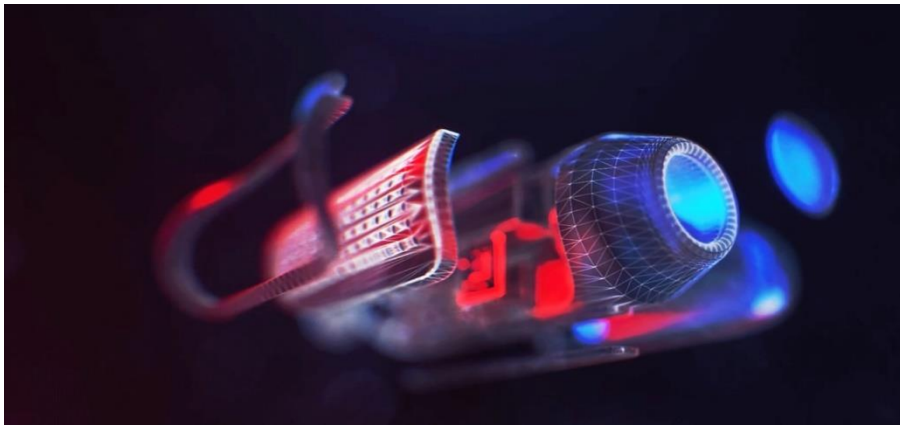
imec researches and develops the key building blocks for such a closed-loop therapy system of the future. Together with application and research partners, this technology can be translated into a tailored solution for specific patient conditions.



e.g. imec develops both microneedles and implantable nodes for electrical sensing and stimulation of nerve cells.

More information: https://www.imec-int.com/en/articles/wearables-careables-closing-loop-connected-health

ALL-IN-ONE INGESTIBLE SENSOR (IMEC)



imec is working on technology that will enable an ingestible sensor that's small enough to swallow, yet packed with technology: sensors, signal processing and power management. Once in the digestive system, the ingestibles could, in real time, sense and transmit mechanical movements of the gastro-intestinal tract, electrical stimuli that govern the muscle contractions and chemical processes, involving hormones and enzymes, that break down the food.

That data could then be transmitted to a wearable device, such as the imec health patch. This requires fundamental innovations as there are:

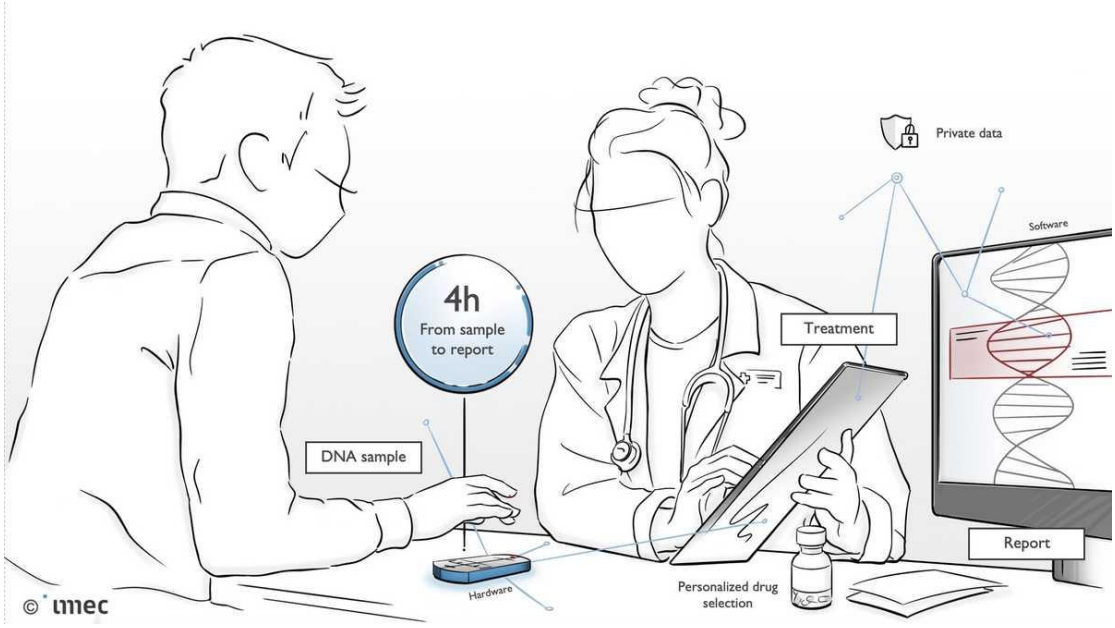
- miniature electro-chemical sensors that provide high specificity in a challenging environment
- ultra-low-power miniature interfaces and signal processing electronics, co-designed with the sensors
- volume-constrained wireless power and data communication technology, crucial to enable truly ingestible sensors
- bio-compatible thin and safe packaging

More information: https://www.imec-int.com/en/ingestibles

PERSONALIZED MOBILE SEQUENCING: FROM SAMPLE TO DNA IN FOUR HOURS (IMEC)

For personalized and mobile sequencing, you need two ingredients: a device and population genomics. The device must allow you to go from a raw sample to an analyzed result in 4 hours (instead of 3.5 days). Because the whole process - from sample to result - occurs in the same device, it also runs much more efficiently.

According to imec personalized and mobile sequencing is a game changer for rare diseases. Imagine that the doctor can't immediately tell what is wrong with your baby, you will in principle be able to upload a sample on the maternity ward and 4 hours later find out if it is a known rare disease. In this way you are not dependent on the doctor's knowledge of all rare diseases, and the odyssey has immediately become much shorter.



Personalized mobile sequencing brings the sequencing time down to 4 hours.

But to be able to make such diagnoses, you also need DNA … a lot of it. In rare diseases you have to look at the whole genome because this is not about one disease but a collection of diseases. Additionally, apart from the DNA, you need a lot of information about all these different rare diseases because before you can say that there is a case of a rare disease, a lot of analyses must have already been done. This is what we call large-scale population genomics.

A solution in the near future:

The next couple of years, imec wishes to cover both aspects: in general for personalized medicine, but also specifically for rare diseases. We already have a lot of the technological building blocks to achieve the 4 hours, e.g. our work on microfluidics, the actual sequencing chips, the specific software and the work on neuromorphic computing to make the analyses quicker. However, work is still required to integrate all the elements. imec believes that a personalized and mobile sequencing device can be achieved in 4 to 5 years.

More information can be found here:

https://www.imec-int.com/en/imec-magazine/imec-magazine-february-2020/new-software-makes-the-diagnosis-of-rare-diseases-less-of-an-odyssey

IMEC AND GHENT UNIVERSITY PRESENT A SMART CONTACT LENS MIMICKING THE HUMAN IRIS TO COMBAT EYE DEFICIENCIES

Ghent (Belgium), September 4, 2020 — imec, a world-leading research and innovation hub in nanoelectronics and digital technologies and CMST (an imec-affiliated research group at Ghent University), together with their partners the Instituto de Investigación Sanitaria Fundación Jiménez Díaz (Madrid, Spain) and Holst Centre (an open innovation initiative from imec and TNO, the Netherlands) today presented an artificial iris embedded in a smart contact lens. The iris aperture is tunable through concentric rings on an integrated liquid crystal display (LCD). The smart contact lens is designed to operate for an entire day thanks to an ultra-low power design, offering a practical solution for people who suffer from human eye iris deficiencies like aniridia, high order aberrations like keratoconus, and light sensitivity or photophobia. The first performance assessment of the artificial iris is reported today in Scientific Reports from Nature, demonstrating its potential to expand the visual sharpness, decrease optical aberrations and reduce the amount of light entering the eye in a dynamic manner. The prototype presented today will be further developed into a medical device within the framework of the spin-off incubation initiative Azalea Vision, from imec and Ghent University.

The human iris controls the pupil size in response to light, hence regulating the amount of light that reaches the retina. Patients suffering from human eye iris deficiencies like aniridia, higher order aberrations like keratoconus, and light sensitivity or photophobia, which is highly prevalent in patients with chronic migraine, and Dry-Eye Syndrome (DES) could use this platform inside a contact lens. The prevalence for these groups adds up to more than 20 million patients. Current solutions such as contact lenses with a fixed iris, artificial iris implants or glasses with variable transparency, do not entirely mimic the normal functionality of the iris. For example, they do not affect the depth-of-focus, hence impeding a sharp vision. The artificial iris lens is capable of dynamically changing the pupil size, bringing back two levels of functionality of the eye, being light adaptation and expanded depth-of-focus.

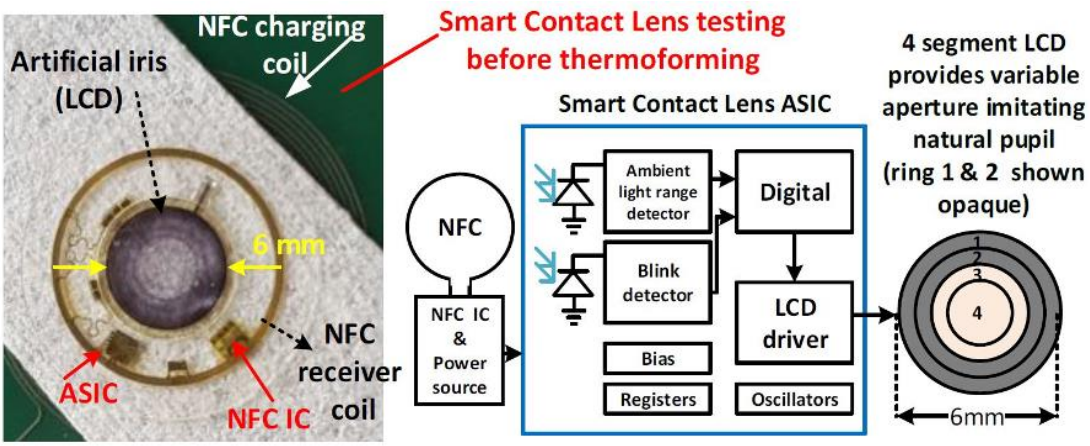
Currently the Azalea Vision team is focused on validating this device with patients and volunteers under clinical investigations in order to provide a functional, robust and safe device for diverse eye disorders with light sensitivity and lack of visual sharpness.

“By combining our expertise on miniaturized flexible electronics, low-power ASIC design and hybrid integration, we have demonstrated the capacity to develop a solution for people who suffer from iris deficiencies, higher order aberrations and photophobia, a common yet debilitating symptom seen in many neuro-ophthalmic disorders”, says researcher prof. Andrés Vásquez Quintero at imec/UGent. “Our smart contact lens can control the level of incoming light mimicking a human iris and offering a potential solution to vision correction – by expanding depth-of-field with automatic control of pupil size. This way, our approach can surpass current solutions to combat human eye iris deficiencies. Its beneficial optical effects will be further clinically validated and developed into a medical device.”

“It is imec’s aim to create added value for the society and bring our research to the market”, said Luc Van den hove, president and CEO of imec. “We are convinced that

this artificial iris prototype has all the potential to become a game changer in ophthalmic treatment. Therefore, we have launched an incubation project together with imec.xpand to fully support the team's ambition to mature and validate the technology and support their efforts to commercialize via a strong business case as a spin-off."

"The Azalea Vision initiative adds to our longstanding track record of creating spin-off's in the photonics and microsystems area", said Rik Van de Walle, rector of Ghent University. "Many of these new companies target important medical problems and several more startup initiatives are in preparation."



More information can be found here: https://www.imec-int.com/en/press/imec-and-ghent-university-present-smart-contact-lens-mimicking-human-iris-combat-eye

GAP Analysis

Flanders is often perceived as a top region for micro and nanoelectronics. The presence of highly ranked universities and the world famous research center imec have made this possible. Every year highly skilled engineers are graduating and many spin offs are originating from both the universities and imec. However for those companies focusing on micro and nanoelectronics technology, the market is mainly outside of Flanders. This is mainly caused by a lack of medical device companies requiring customer specific micro and nanoelectronics solutions. This gap was also identified by a GAP analysis study commissioned by the province of Flemish Brabant in 2015[7]. Although it was not seen as an immediate problem for the companies (they will go where the customer are), a presence of larger players could benefit the local ecosystem on the longer term and makes the Flemish technology players less dependent of international unexpected events. (e.g. pandemic, war, ...). Therefore it is important that the policy of the region of Flanders should certainly consider any measure that encourages potential entrepreneurs

[7] Geert Adriaens, F. H. (2015). *Gap-analyse medtech/biotech/combitech.* Leuven.

(certainly not discourage) to enter the medical device market relying on locally developed micro and nanoelectronics technology and also help to increase the chance that small companies relying on customer specific micro and nanoelectronics technology will successfully grow and become a larger player (selling quantities). Other measures that could be considered are building good relationships with other regions and as such enlarging the ecosystem for the own companies.

Market insights

GLOBAL VIEW

Health spending or expenditure gives a good indication on how important the health related market is in certain countries. According to the OECD[8], health spending is defined as follows:

Health spending measures the final consumption of health care goods and services (i.e. current health expenditure) including personal health care (curative care, rehabilitative care, long-term care, ancillary services and medical goods) and collective services (prevention and public health services as well as health administration), but excluding spending on investments.

An overview of the health care expenditures in the main global markets in 2017 is given in Figure 1. The main markets are the US and EU followed by China and Japan. Also the individual countries of the CELIS project have been explicitly mentioned. Switzerland has been added because it is the European country (but no-EU) with the highest proportional expenditures in Europe. It is also known for its medical industry. Sources for this kind of information are for instance The World Bank[9], Eurostat[10] and Population Pyramid[11].

Healthcare expenditures 2017									
	US	EU-27	China	Japan	Germany	Belgium	Estonia	Denmark	Switzerland
GDP (Billion)	$19.520,00	$17.350,00	$12.060,00	$4.860,00	$3.660,00	$500,00	$30,00	$330,00	$680,00
% of GDP	17,80%	9,90%	5,15%	10,94%	11,30%	10,30%	6,40%	10,10%	12,40%
expenditures	$3.474,56	$1.717,65	$621,09	$531,68	$413,58	$51,50	$1,92	$33,33	$84,32
population (Million)	325	511	1421	127,5	82,66	11,42	1,319	5,732	8,456
per capita	$10.690,95	$3.361,35	$437,08	$4.170,07	$5.003,39	$4.509,63	$1.455,65	$5.814,72	$9.971,62

Figure 1: Health Expenditures 2017

The reason why the US is often considered as the place to be for Health Tech companies can be easily understood when studying the amount of healthcare spending per country. The US is by far the biggest healthcare spender in the world. Proportionally to the GDP, they are spending almost double of the EU and 3.5 times of China. Secondly, the US is known as the global high-tech leader and related to that the availability of highly skilled

[8] https://data.oecd.org/healthres/health-spending.htm
[9] https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS
[10] https://ec.europa.eu/eurostat/web/products-eurostat-news/-/DDN-20200331-1
[11] https://www.populationpyramid.net/population-size-per-country/2017/

people. In China, most of the expenditures are at this moment still in the basic technology.

EUROPEAN VIEW

In Europe, Germany and France are the greatest spenders in healthcare both on absolute level as proportionally to the GDP. But when looking to the spending per capita (see Figure 3), the Scandinavian countries Sweden and Denmark are clearly number 1 and 2.

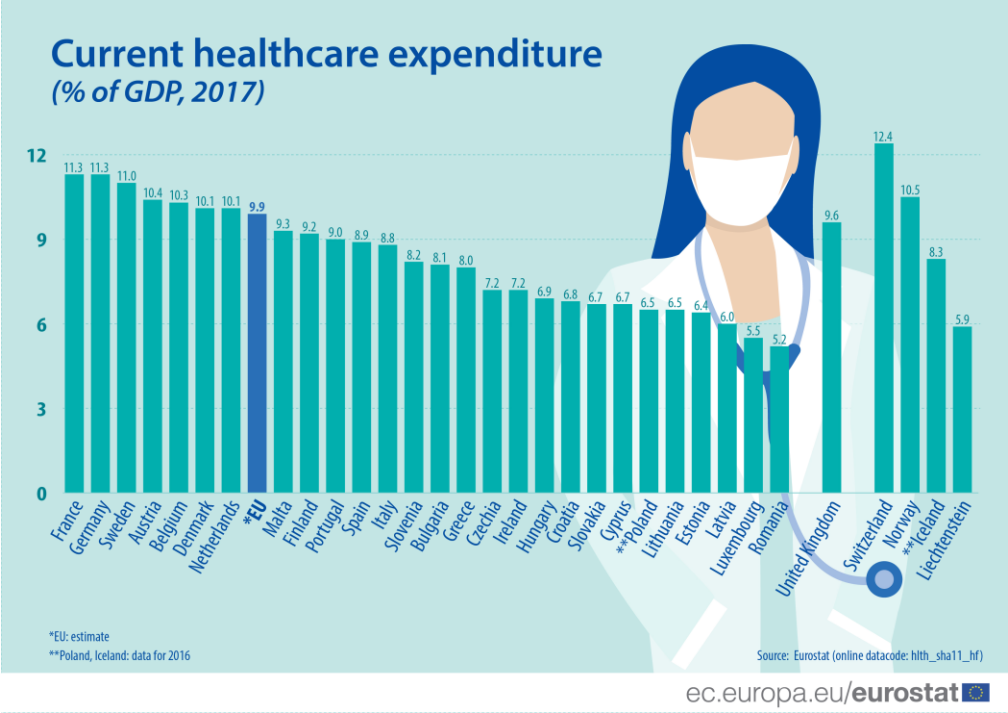


Figure 2: European Healthcare expenditures proportional to the GDP

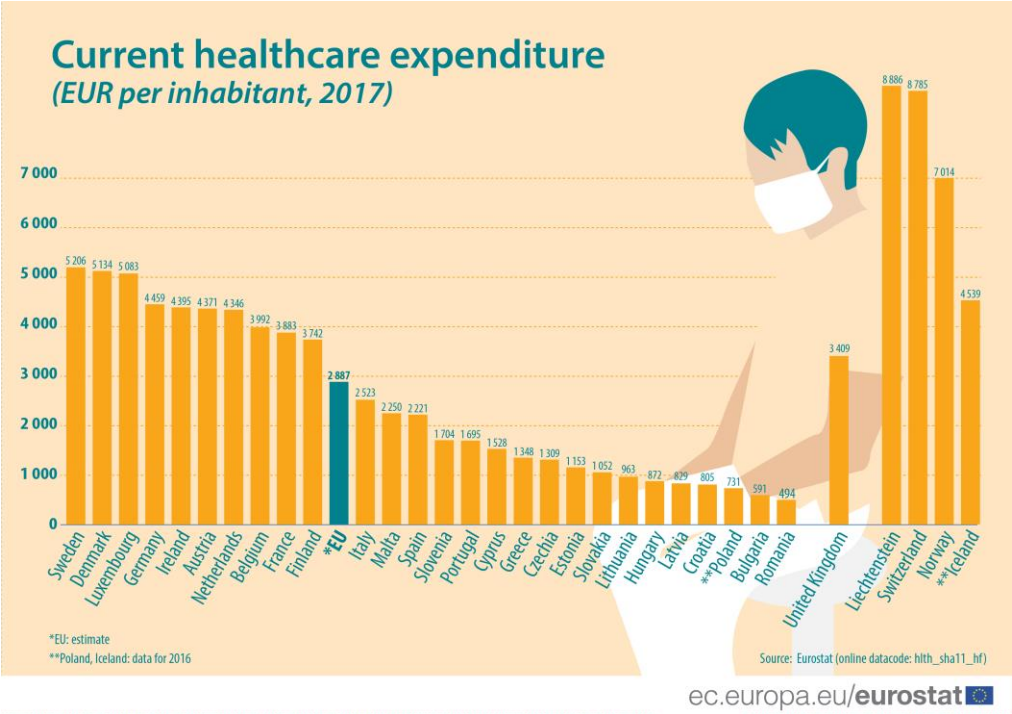


Figure 3: European healthcare expenditures per capita

MedTech Europe, the European trade association representing the medical technology industries, from diagnosis to cure, publishes yearly on overview of this industry [12]. A few highlights relevant for his report are mentioned below.

The next figure shows the top 7 countries with highest direct employment in the medical technology industry. As can be expected, there is a relation with the size of the country, except for Switzerland though.

[12] https://www.medtecheurope.org/resource-library/the-european-medical-technology-industry-in-figures-2019/

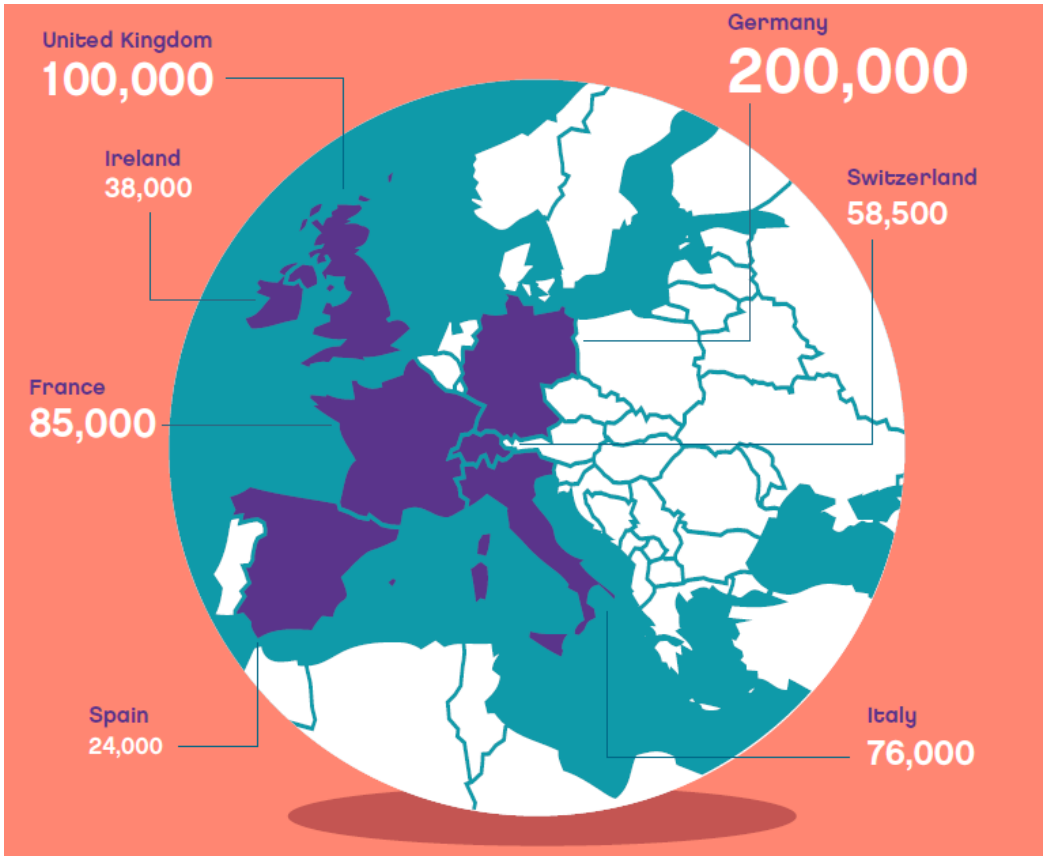


Figure 4: Top 7 countries with highest direct employment in the medical technology industry, 2017

This is clearly seen when the number of people directly employed in the medical technology industry per 10,000 inhabitants is measured (see). The countries with a significant higher employment rate are Ireland and Switzerland. But also Demark, Germany and Belgium are among the highly ranked countries.

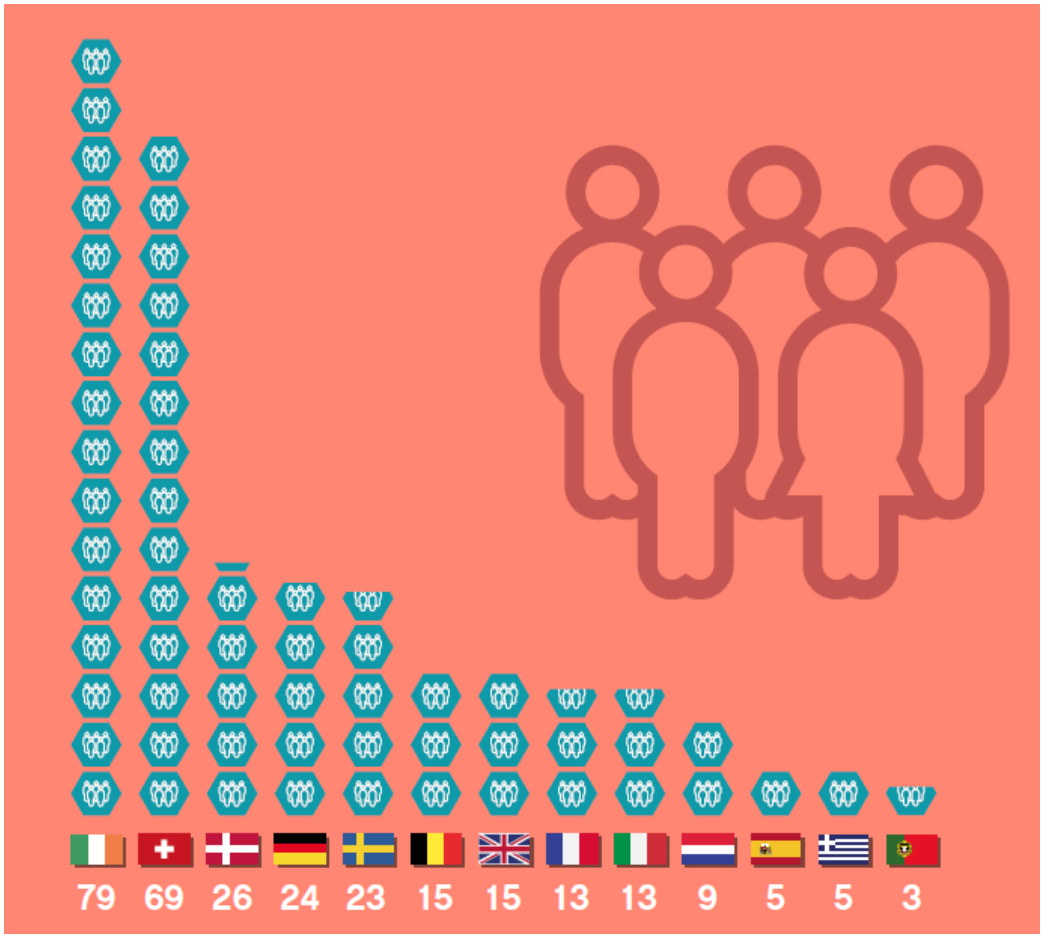


Figure 5: Number of people directly employed in the medical technology industry per 10,000 inhabitants, 2017

When the breakdown of the healthcare expenditures in Europe is made, we see that more than 7% is related to medical technology and about 16% to pharmaceuticals and other non-durables. Medical technology as defined in the study of Medtech Europe is the combination of medical devices and in vitro diagnostics. It is not containing digital health. Although not all medical technologies are based on micro and nanoelectronics (e.g. stethoscope or a catheter are examples of technology without micro and nanoelectronics), we can claim that a lot of innovations are enabled by micro and nanoelectronics. And because digital health solutions are often based on standard ICT solutions (e.g. cell phone, computers, ..) combined with dedicated SW platforms, we can consider the medical technology share as the main target market for micro and nanoelectronics dedicated for health. As such we get a rough idea on which part of the healthcare market is impacted by micro and nanoelectronics.

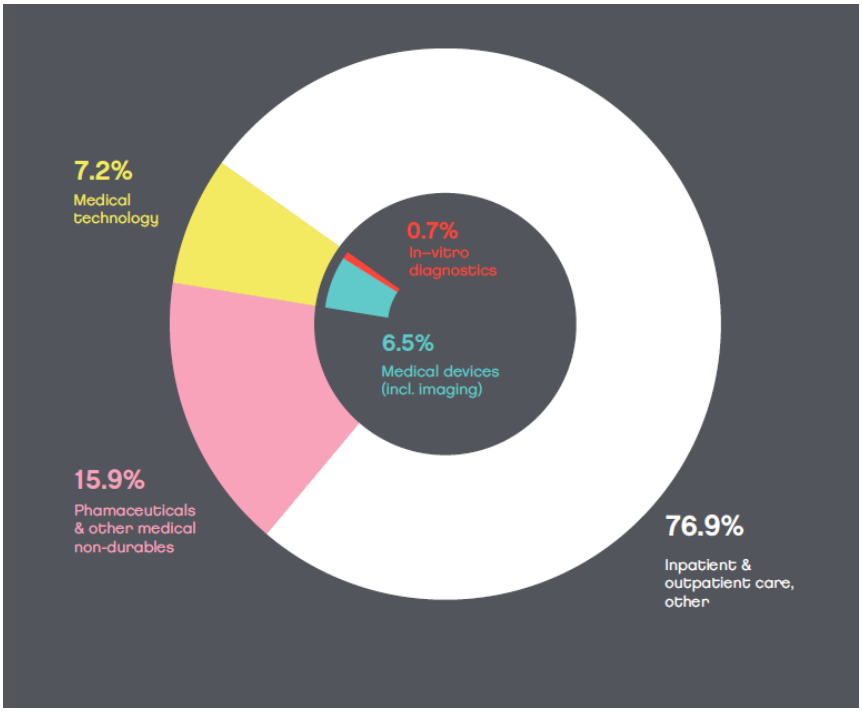
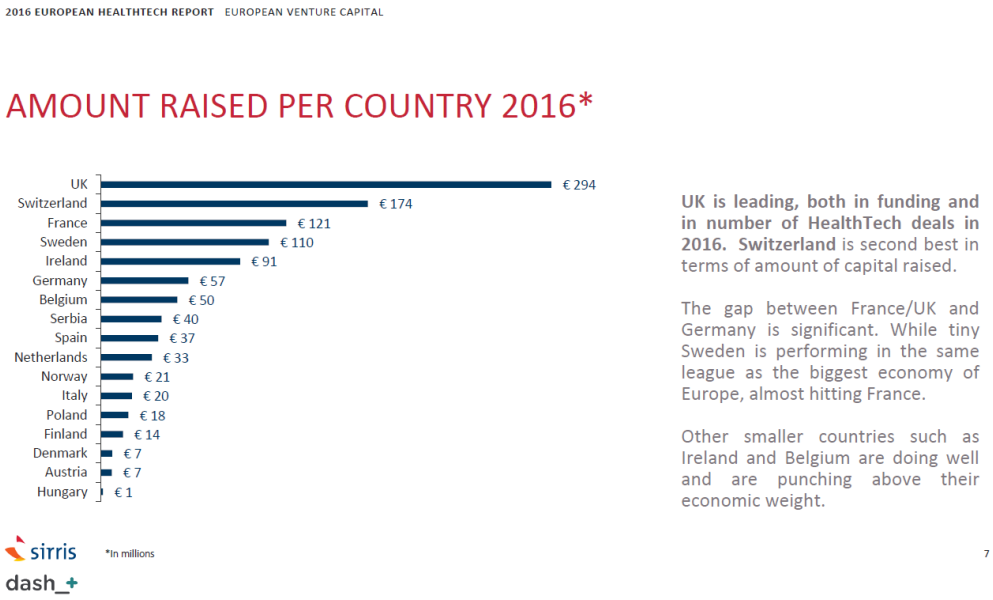


Figure 6: Breakdown of total healthcare expenditure in Europe, 2017

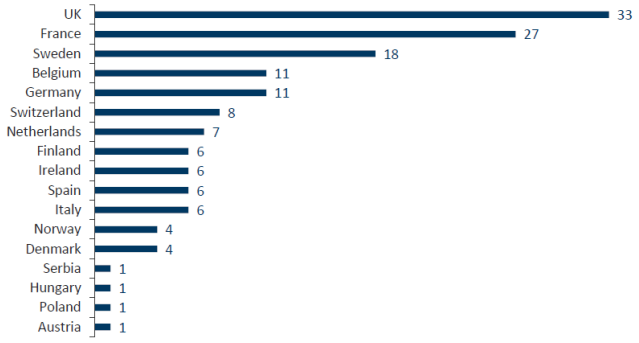
In 2016, Sirris in cooperation with Dash + have published a report on the European Health tech industry. That report[13] focuses on the investments done in European health scale ups. It shows that at least in 2016, Belgium is not doing bad with respect to attracting investments.



[13] https://www.slideshare.net/omohout/europe-health-tech-report-2016

2016 EUROPEAN HEALTHTECH REPORT EUROPEAN VENTURE CAPITAL

DEALS PER COUNTRY 2016



UK and France are leading. Sweden and Belgium are taking a very interesting 3rd and 4th position. No doubt **Sweden** is the rising star in Health, leaving Germany and Switzerland behind in amount of deals in 2016.

Belgium is doing great. It seems like public agenda setting for digital transformation and creation of a startup ecosystem are paying off..

Germany has HealthTech growth potential. Compared to its other sectors, HealthTech investments are lagging behind.

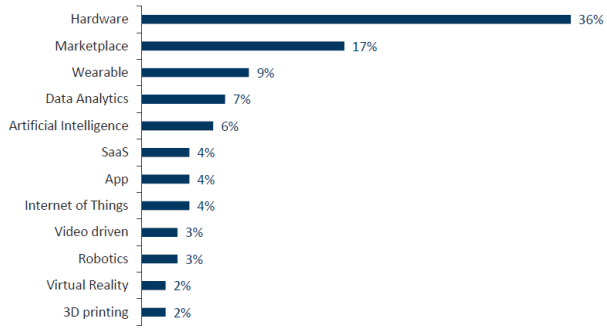
sirris
dash_+

8

And according to the authors most health tech scale ups in Belgium are AI based.

2016 EUROPEAN HEALTHTECH REPORT EUROPEAN VENTURE CAPITAL

TYPE OF BUSINESS MODELS/TECHNOLOGY 2016



Not surprisingly, hardware, traditionally very strong in the engineering cultures of European countries, **is the leading business model for scaleups**, counting for 34% of the total.

France is leading in hardware and IoT while market places, robotics, video and apps is dominated by the UK. Sweden is the #1 spot for wearables and SaaS; Switzerland for 3D printing and video; Finland for data analytics, and Belgium for AI.

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dash_+

18

FOCUS ON SEMICONDUCTORS

According to most of the market analysis reports, the market of semiconductor devices comprises of Integrated Circuits, Optoelectronics, Sensors and Discrete Components. General purpose devices applied in health care applications as well as application specific devices are considered.

Most market research companies forecast for semiconductors in the healthcare market a CAGR of about 10% per year in the forecast period 2020 – 2025.

The US and Europe are the biggest markets but the highest growth rates are expected in the Asia-Pacific region according to the report "Semiconductor in Healthcare Market - Growth, Trends, and Forecast (2020 - 2025)"[14] as can be seen on Figure 7.

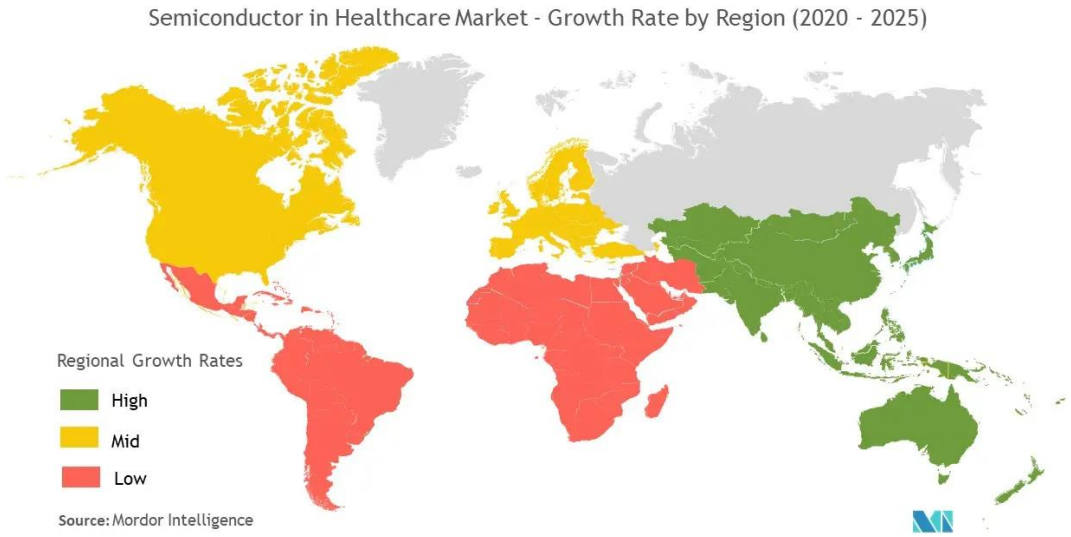

Figure 7: Semiconductor in Healthcare market – Growth Rate by region (2020 – 2025)

The main reasons for this high growth in the Asia-Pacific region are: [15]

- Major factors supporting the growth are increasing investments in research and innovation centers, government programs, and governmental policies favoring the IT healthcare equipment and devices markets.
- Moreover, the region is the biggest market for semiconductors across the globe with countries like China, Japan, India, Taiwan, South Korea and Singapore, contributing to the growth of the healthcare segment.
- With the rapid expansion of population, a rise in hypertension diseases is creating a high demand for remote monitoring devices, such as blood pressure monitor, which is effectively increasing the growth of the market.
- There is also an increase in the incidence of diseases and cancer, increasing the demand for advanced diagnostic tools like MRI. Japan holds a major share in the Asia Pacific region with a high per capita income and advanced technology, which shows the growth of the market.
- According to the World Health Organization (WHO), there are around 430 million diabetics worldwide, where 60% of diabetics are Asian, so the rate

[14] https://www.mordorintelligence.com/industry-reports/semi-conductor-applications-in-healthcare-market
[15] https://www.researchandmarkets.com/reports/4602225/semiconductor-in-healthcare-market-growth

of the glucose monitoring device is increasing, which increases the growth of semiconductor in the healthcare market.

Typical trends mentioned in market analysis reports driving the growth rate of semiconductor devices in healthcare applications are:

- The revolutionary changes in the domain such as digitization and automation of various activities such as surgery for which robotic assistance is being employed.
- Sensors in devices or within the human body have the power to link data collection to powerful algorithms, which will transform the existing practices and take the healthcare sector to a new level of individualized care.
- Increasing uptake of wireless technology coupled with rise in development of semiconductor technology devices such as mobile cardiac monitors, mobile insulin pumps & ECG machines drives demand for semiconductors in healthcare applications market.
- 3D printing of organs and medical devices has also been one of the recent developments which are expected to increase the use of semiconductors.
- Growth of connected devices in healthcare is driving the market and is expected to increase from 10 billion to 50 billion units over the next decade. Manufacturers are turning to digital connectivity, to improve the coordination and delivery of patient care by transmitting monitored data through devices to address the real-time health functioning.
- Rising prevalence of chronic diseases is driving the market, by which the demand for remote monitoring, mobile health (mHealth) apps, and wearables, such as activity trackers are increasing globally.

Yole is one of the market research companies that strongly focuses on the semiconductor market and its applications. They have published several rapports related to several aspects of the health care market. For this report we can of course only use the freely available samples. But this snapshot already gives a good indication of the potential of this market.

As already mentioned above, sensors are clearly one of the drivers of the semiconductor market in healthcare applications. Figure 8 gives an overview of body related parameters that can be measured by sensors. At the same time it gives a picture on the variation of sensors used in the health context as there are microphones, pressure sensors, temperature sensors, light sensors, bio sensors, etc.

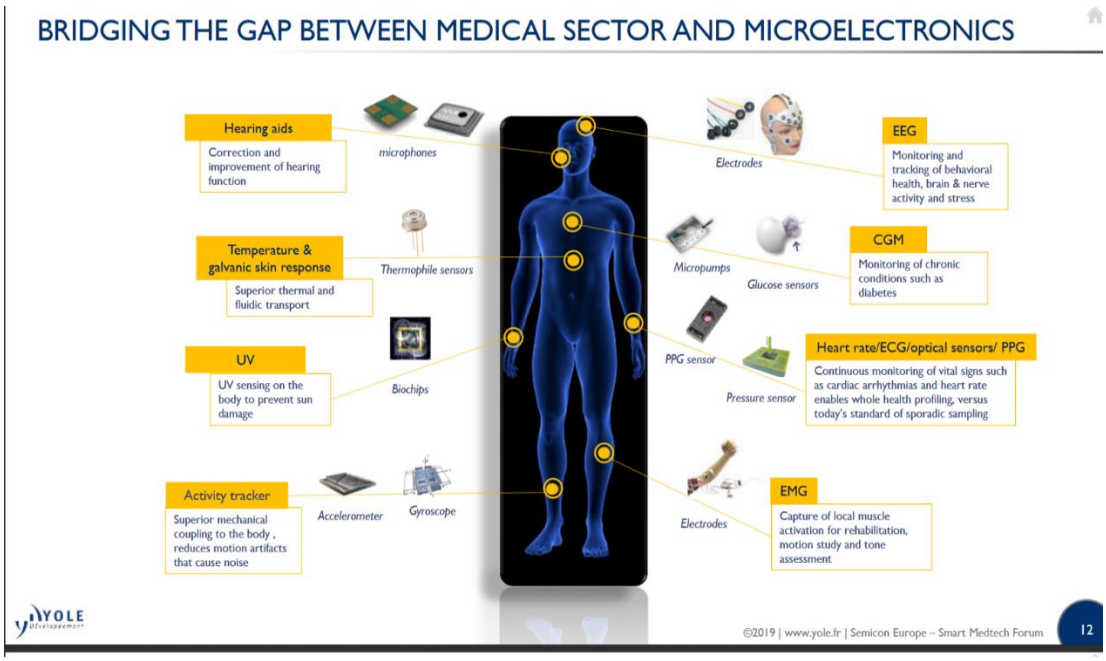

Figure 8: Body related parameters that can be measured by sensors

The wearable market which is the driver for the sensor market is expected to grow significantly according to the market analysts. Yole expects this market to grow over 20% on a yearly basis[16]. The market of the belonging sensors will grow accordingly.

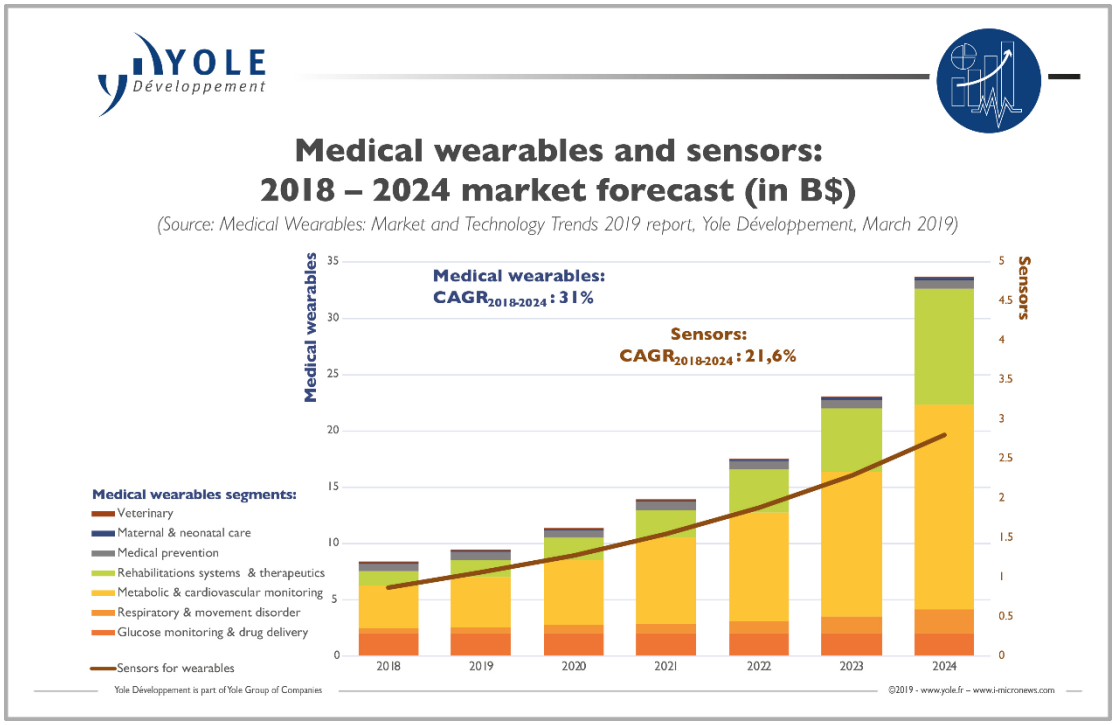

Figure 9: Medical wearables and sensors: 2018 – 2024 market forecast

[16] http://www.yole.fr/2014-galery-MedTech.aspx#10005da02

One specific category of sensors which is widely used in medical applications are the detectors for medical imaging going from Xray detectors, ultrasound detectors to miniature camera's for endoscopy. Next figure gives an overview of this market showing a yearly growth rate of over 7%. [17]

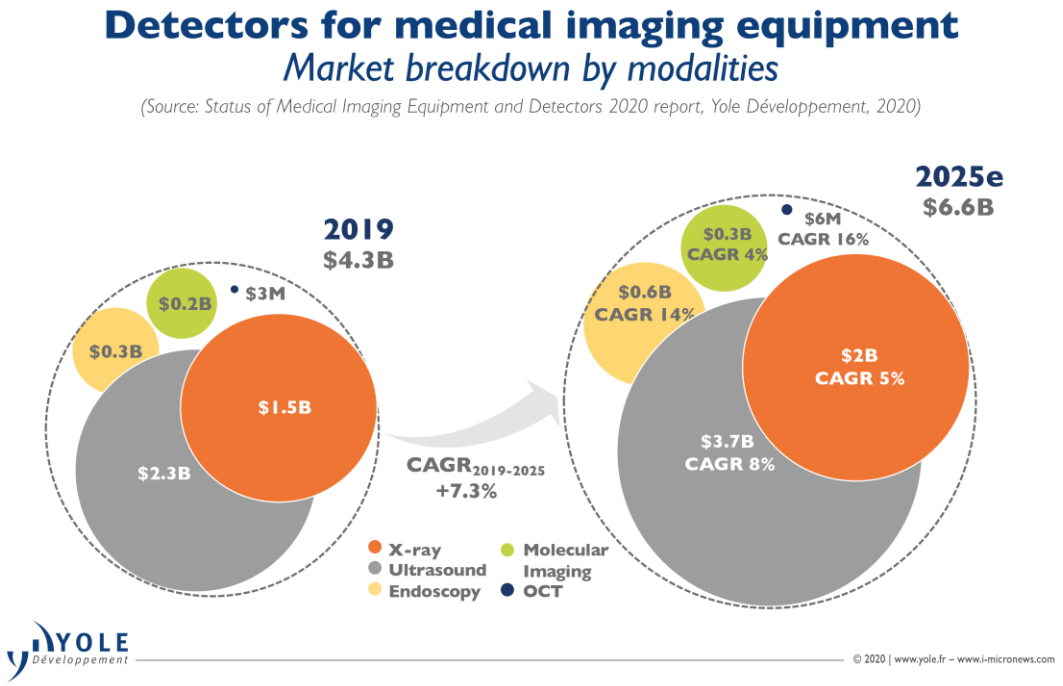

Figure 10: Market of detectors for medical imaging equipement

Future trends in the healthcare market

As a final chapter for this report it makes sense to refer to a list of trends in healthcare that are identified by multiple publications. And what makes this overview of trends so interesting? Most of the trends observed are more or less enabled by micro- and nano-electronics. The list of trends defined by Forbes[18] is a good reference:

1. AI and Machine Learning

As the world population continues to grow, and age, artificial intelligence, and machine learning offer new and better ways to identify disease, diagnose conditions, crowdsource and develop treatment plans, monitor health epidemics, create efficiencies in medical research and clinical trials, and make operations more efficient to handle the increased

[17] http://www.yole.fr/MedicalImaging_Equipment_Detectors_Overview.aspx
[18] https://www.forbes.com/sites/bernardmarr/2019/11/01/the-9-biggest-technology-trends-that-will-transform-medicine-and-healthcare-in-2020/#3507815b72cd

demands on the healthcare system. By 2020, medical data will double every 73 days. McKinsey estimates that there could be $100 billion in annual savings for medicine and pharma by leaning on big data as well as the artificial intelligence and machine learning tools to process it. Artificial intelligence algorithms powered by recent advances in computational power learn from the data and can predict the probability of a condition to help doctors provide a diagnosis and treatment plans. Ultimately, AI and machine learning can assist with many clinical problems as long as governing and regulatory bodies can determine how to regulate the use of algorithms in healthcare.

2. Robotics

When it comes to life or death, would you trust a robot with yours? Currently, collaborative robots - such as the da Vinci surgical robot - are already assisting humans with tasks in the operating room. However, the potential for robots in healthcare expands beyond surgical uses. With tremendous growth expected in the industry - the global medical robotics market is expected to reach $20 billion by 2023 - there's no doubt that robots used in healthcare will continue to conduct more varied tasks. These already include helping doctors examine and treat patients in rural areas via "telepresence," transporting medical supplies, disinfecting hospital rooms, helping patients with rehabilitation or with prosthetics, and automating labs and packaging medical devices. Other medical robots that are promising include a micro-bot that can target therapy to a specific part of the body, such as radiation to a tumor or clear bacterial infections.

3. Computer and Machine Vision

Training computers to "see" the world and understand visual input is no small feat. Since there has been significant progress in machine vision, there are more ways computers and machine vision are being used in medicine for diagnostics, viewing scans and medical images, surgery, and more. Machine vision is helping doctors definitively know how much blood a woman loses in childbirth so that appropriate care can be given to reduce the mortality of mothers from post-partum hemorrhaging. Computers provide accurate intel, while previously this was a guessing game. The applications where computers are being used to view CT scans to detect neurological and cardiovascular illnesses and spot tumors in X-ray images are growing rapidly.

4. Wearable Tech

Wearable fitness technology can do much more than tell you how many steps you walk each day. With more than 80% of people willing to wear wearable tech, there are tremendous opportunities to use these devices for healthcare. Today's smartwatches can not only track your steps but can monitor your heart rhythms. Other forms of wearable devices are ECG monitors that can detect atrial fibrillation and send reports to your doctor, blood pressure monitors, self-adhesive biosensor patches that track your temperature, heart rate, and more. Wearable tech will help consumers proactively get health support if there are anomalies in their trackers.

5. Genomics

Artificial intelligence and machine learning help advance genomic medicine—when a person's genomic info is used to determine personalized treatment plans and clinical care. In pharmacology, oncology, infectious diseases, and more, genomic medicine is making an impact. Computers make the analysis of genes and gene mutations that cause medical conditions much quicker. This helps the medical community better understand how diseases occur, but also how to treat the condition or even eradicate it. There are many research projects in place covering such medical conditions as organ transplant rejection, cystic fibrosis, and cancers to determine how best to treat these conditions through personalized medicine.

6. 3D Printing

Just as it's done for other industries, 3D printing enabled prototyping, customization, research, and manufacturing for healthcare. Surgeons can replicate patient-specific organs with 3D printing to help prepare for procedures, and many medical devices and surgical tools can be 3D printed. 3D printing makes it easier to cost-effectively develop comfortable prosthetic limbs for patients and print tissues and organs for transplant. Also, 3D printing is used in dentistry and orthodontics.

7. Extended Reality (Virtual, Augmented and Mixed Reality)

Extended reality is not just for entertainment; it’s being used for important purposes in healthcare. The VR/AR healthcare market should reach $5.1 billion by 2025. Not only is this technology extremely beneficial for training and surgery simulation, but it's also playing an important part in patient care and treatment. Virtual reality has helped patients with visual impairment, depression, cancer, and autism. Augmented reality helps provide another layer of support for healthcare practitioners and aided physicians during brain surgery and reconnecting blood vessels. In mixed reality, the virtual and real worlds are intertwined, so it provides important education capabilities for medical professionals as well as to help patients understand their conditions or treatment plans.

8. Digital Twins

A digital twin is a near real-time replica of something in the physical world—in healthcare, that replica is the life-long data record of an individual. Digital twins can assist a doctor in determining the possibilities for a successful outcome of a procedure, help make therapy decisions, and manage chronic diseases. Ultimately, digital twins can help improve patient experience through effective, patient-centric care. The use of digital twins in healthcare is still in its early stages, but its potential is extraordinary.

9. 5G

As the capabilities for healthcare centers to provide care in remote or under-served areas through telemedicine increase, the quality and speed of the network are imperative for positive outcomes. 5G can better support healthcare organizations by enabling the

transmission of large imaging files so specialists can review and advise on care; allow for the use of AI and Internet of Things technology; enhance a doctor's ability to deliver treatments through AR, VR and mixed reality; and allow for remote and reliable monitoring of patients.

Conclusions

Micro and nanoelectronics is one of the key enabling technologies (KETs) for many applications but certainly for health applications. Over the years Flanders has built a strong reputation in the field of micro and nanoelectronics resulting in many spin-offs from our research organisations and many other initiatives that took advantage of the available skills and expertise. In this report over 100 companies were identified that are active on the cross-over between micro and nanoelectronics and health and more than 35 of those spun off from one of the research organisations. In order to provide an impression of the ongoing developments and showing the state of the art expertise available in our research centers, a few concrete cases have been described.

Based on available European and global market reports we could derive a few but rather limited conclusions for our region, Belgium (including Flanders) is among the regions in Europe with a relatively high number of employees active in the medical industry. But as this industry is much broader than the one enabled by micro and nanoelectronics only no direct conclusions could be drawn on this particular segment. And despite the challenge for attracting investment money, according to a study in 2016 Belgium (including Flanders) could also attract some reasonable investment money for promising medical technology scale-ups. Because of its small size, the presence of mainly SMEs and a lack of large integrators, internationalization is very important for the Flemish micro and nanoelectronics industry. For medical applications, the US market is still number one, both for its market size and the level of innovation going on. But considering growth, the Asia-Pacific region with countries like China, Japan, India, Taiwan, South Korea and Singapore is certainly the most important region for our micro and nanoelectronics industry. In Europe the countries with the largest expenditure on healthcare are certainly Germany, France UK and Italy. But for the technology companies the size of the medical industry is more relevant. The countries with the *highest* employment rate in the medical industry are Germany, UK, France, Italy and Switzerland. But calculated per inhabitant the top three is Ireland, Switzerland and Denmark.

Sensors are clearly one of the enabling components for many medical applications going from medical imaging over, wearable health applications to point of care diagnostics devices. Because Flanders is strong in the field of sensors, this (world)market clearly shows a large potential.

And as a final conclusion, if you look at the major trends in health care applications, and knowing micro and nanoelectronics are one of the major enabling technologies to realise those trends, a large opportunity is there for the micro and nanotechnology industry in Flanders.