Emerging Medical Domains
for the ECS industry

White Paper

November 2020

Health.E
Moore for Medical

ECSEL Joint Undertaking
Electronic Components and Systems for European Leadership

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Colophon

This White Paper is a publication of the Health.E Lighthouse (https://www.health-lighthouse.eu/).

The Health.E Lighthouse is an initiative of the ECSEL Joint Undertaking (https://www.ecsel.eu/lighthouse-initiatives).

The Health.E Lighthouse is supported by the **He**alth.E **L**ighth**o**use **S**upport Initiative (HELoS)
ECSEL Coordination & Support Action (ECSEL-CSA)
grant agreement: 871394

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Health.E Moore for Medical

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ECSEL Joint Undertaking

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1 Executive Summary

The population is aging and the cost of healthcare is increasing, therefore healthcare is changing. It is becoming more and more decentralized, personalized and focused on prevention. Insurance companies change their reimbursement models from pay per treatment to pay per cure.

These changes are enabled by the advent of new healthcare technologies. This has resulted in the fading of the borders between MedTech, Pharma and the Electronic Components and Systems (ECS) industry. At these interfaces new medical domains are developing that offer diagnosis and treatment solutions that address the needs in healthcare.
Many of these new medical domains offer attractive opportunities for the ECS industry as they rely on digital instruments, advanced electronic sensors and photonics, MEMS, and the high volume, high quality low cost production capabilities of the ECS industry.

The objective of this document is to make an inventory of the emerging medical domains that can be served, now and in the near future, by the ECS industry. The Health.E Lighthouse Initiative[1] has conducted a consultation amongst RTOs, projects connected to the Lighthouse, and other stakeholders, such as policymakers and healthcare organizations. This has resulted in the following un-prioritized list, which will be detailed out in Section 2 of this white paper:

- Bioelectronic medicines
- Organ-on-Chip
- Personal ultrasound
- Radiation free diagnostics and interventions
- Smart minimally invasive instruments
- Second generation of surgical robots
- Smart drug delivery
- Intelligent wound care
- Ambulatory monitoring
- Point-of-care diagnostics
- Remote sensing and monitoring
- E-health
- Advanced therapies using genes, cells and tissues

Despite its great promise for society and industry, the speed of innovation in electronic medical devices is relatively slow compared to the speed of innovation in the consumer domain. This is only partly due to the strict regulations that apply to medical devices. A major obstacle to innovation in the medical domain is the absence of generic technologies that can be shared by all developers of medical devices. Consequently, a lot of resources are being spent for the development of expensive point solutions.

As added value is shifting from technology towards algorithms and software solutions, open technology platforms have become commonplace in all facets of the ECS industry. Open technologies platforms have accelerated the pace of innovations, reduced risk and lowered costs. There is no reason, apart from convention, why open technology platforms could not be implemented for medical devices.

In a next phase, the Health.E Lighthouse working group will make an inventory of the technologies that have the capability to enable the emerging medical domains that are identified in this document. These technologies will be ranked based on their innovative impact. Finally, recommendations on their implementation into *open* technology platforms will be made.

[1] https://www.health-lighthouse.eu/

2 Accelerating Innovation in Electronic Medical Devices

The healthcare challenge

Europe's aging population is a tribute to the success of our healthcare systems as these have been put into place after the Second World War, but it poses also a challenge for the future. If healthcare had not made as many advances as it has, we would not be seeing the steady rise in life expectancy in all European countries. However, this success comes at a price: older populations are susceptible to diseases that typically are more prevalent as age increases. These include an array of chronic diseases such as cancer, diabetes, heart and respiratory diseases, stroke, dementia and depression. As a result, the financial burden of caring for the chronically ill is growing at an alarming rate. Although there are large differences in healthcare spending for the different European member states, the average figure at the moment amounts to approximately 10% of the Gross Domestic Product (GDP) of the EU, or € 1.6 trillion.

Healthcare is changing

To cope with this increasing financial burden, stakeholders such as governments, caregivers, and insurance companies are implementing scenarios to reduce or at least contain the cost of healthcare. The key terms reflecting these policies are:

- **Decentralization**
  There is a strong drive to treat and diagnose people as much as possible in their home environments. It is well known that people stay longer healthy and recover faster in the comfort of their homes. This will make it necessary to track patients remotely through ambulatory or remote devices to monitor their condition and effect of their therapies, for example to check if they take their medicines as prescribed.
- **Personalization**
  A medicine or therapy that works for one patient, may be completely ineffective for others. Since the complete sequencing of the human genome in 2000, the insight into the origin and curing of diseases in relation to a person's genetics has grown exponentially. This will make it possible to tailor therapies to groups of patients with similar genetic profiles. In the treatment of mental diseases advancements in machine learning and artificial intelligence will make it possible to diagnose people more accurately and create highly personalized therapies.
- **Empowering patients**
  The WHO has defined empowerment as "a process through which people gain greater control over decisions and actions affecting their health." Empowered patients ultimately understand their health condition and the effects of treatment on their body so that they can participate in decision-making with their healthcare professionals to make informed choices about prevention and treatment. Keeping people healthy longer is perhaps one of the strongest instruments to curtail the increasing cost of healthcare.
- **Pay for cure**
  Pay for cure rather than pay for treatment can be an effective way to increase the efficiency of healthcare by avoiding unnecessary tests, therapies and prescriptions. Together with empowered patients, care givers should be able to come to better informed and more effective choices for treatment.

Enabling innovative technologies

We live in an exciting time where a number of technological and biological breakthroughs (Table 1) is opening up completely new medical domains, which will change healthcare in its broadest sense.

Technological	Biological / Medical
• Digital revolution	• Sequencing of the human genome
• Big data	• Fluorescent protein tags
• BioMEMS	• Induced pluripotent stem cells (iPSC)
• Microfluidics	• Biological drugs
• MEMS ultrasound	• DNA editing (CRISPR-Cas)
• Conformable and wearable electronics	• Minimally invasive surgery
• Artificial Intelligence	

Table 1 Some of the most important technological and biological/medical breakthroughs that are currently the drivers behind the development of completely new medical disciplines and domains.

The connection of "human avatars" or "digital twins" with the individual citizen and the medical doctor constitutes a triangle that will cause a paradigmatic shift towards personalized and preventive healthcare. The goal is to deliver more efficient error-free personalized treatments and to enable feedback data loops for preventive healthcare strategies.

The success of the digital twin concept, however, largely depends on the quality of the gathered data and the possibility to translate the outcomes of the decision making processes into effective therapies. The ongoing digitization of healthcare in its broadest sense is promising and necessary, but its success will largely depend on the availability and quality of the underlying "physical layer."

Fading borders

The changes in healthcare combined with technological innovations are resulting in the fading of the borders between the different communities of Pharma, MedTech and the Electronic Components and Systems industry (ECS). At the intersections between these domains new technologies are emerging that offer great opportunities for industry, as well as for society in the form of better and affordable healthcare (Fig. 1).

The pharmaceutical industry, for instance, has so far been primarily focussed on the development of chemical and biological compounds that are developed and screened *in vitro* in massive parallel biological assays, and *in vivo* in hugely expensive clinical trials. There is however a strong drive to bring clinical trials from the hospital to the home where subjects can be monitored remotely in their natural environment by means of implantable or wearable devices. At the same time, organ-on-chip devices combine human cells with microfluidic structures and sensors to form the basic elements of human organs. These devices offer better and more representative models for drug development than cells cultured in well plates or animal testing. At the same time, a revolution is taking place in therapy, as small implantable neuromodulators will be used to stimulate the autonomous part of the nerve system to complement and sometimes even replace traditional chemical and biological pharmaceutics, especially in the treatment of autoimmune diseases.

Likewise, the MedTech industry is facing new opportunities and challenges in the transition from an industry that was primarily producing multi-million euro high-end hospital equipment, to an industry that will increasingly serve point-of-care professionals and even consumers. For example, scalable and affordable ultrasound imaging and diagnostics based on MEMS technology will increasingly replace traditional X-ray imaging. The potential for low-cost mass pro-

Figure 1 *The fading of the borders between the traditional communities of Pharma, MedTech and the ECS industry creates emerging application domains with a huge potential for society and industry.*

duction will bring this equipment out of the hospital into the world.
It is obvious that the ECS industry with its capabilities in miniaturization, embedded intelligence, connectivity and high-volume low-cost manufacturing has enormous potential to play a pivotal role in creating the devices and systems that are needed to make these emerging opportunities a reality.
In Chapter 3 of this white paper a number of identified emerging medical domains will be discussed in relation to the societal impact, relevance for the ECS industry and the technology platforms that are needed to manufacture the new medical devices.

R&D efficiency

The current practice of research and development for new medical devices is disappointingly inefficient. Academia, industry and RTOs spend enormous resources on R&D of new medical devices and technologies, resulting in countless spin-outs and start-ups that aim to commercialize the new technologies. In Europe alone, there are more than 25.000 SMEs active in the field of medical devices. Unfortunately, despite this enormous activity, only very few breakthrough innovations reach the patient or the clinic.

In 2012 Scannell et al. published a landmark paper on their investigation into the R&D efficiency of the pharmaceutical industry (Fig. 2). They found that since 1950 the price per drug launched onto the market has been doubling roughly every 9 years. With some irony they named this trend Eroom's Law of Pharma (Moore reversed). In their analysis they identified several causes; not surprisingly, the enormous cost associated with the extensive clinical trials required to comply with FDA regulations was among the most important factors. In other words, it is not so much the cost of the

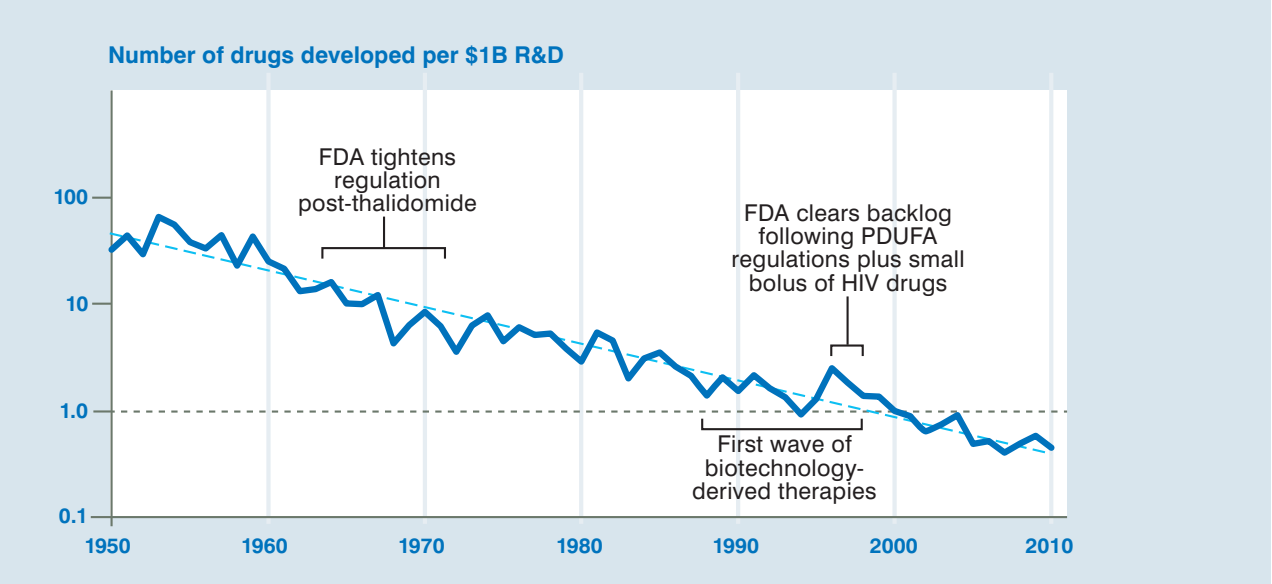


Figure 2 *The number of pharmaceutical drugs developed per $1B has been steady declining since 1950. For medical device R&D a similar decline is happening although no factual data is available yet. (source: Scannell et al., Nature Reviews Drug Development, Vol.11, March 2012, p.191)*

basic research into new drugs that reduces the R&D efficiency, as well as the cost associated with their industrialization. Although similar data as those for the R&D efficiency for pharmaceutics (Fig. 2) are not readily available for the R&D efficiency for electronic medical devices, it is obvious that these will follow the same trend. This is indicated by the fact that the number of patents generated per $1B revenue in MedTech is significantly larger than the same metric for pharma and even for the ECS industry for similar or lower revenues (Fig. 3). Similarly to pharma, it is not so much the cost associated with the basic research of a new device that is prohibitive, but rather the enormous initial cost associated with industrialization. This especially holds when some form of microfabrication is involved as is the case with many innovative medical instruments.

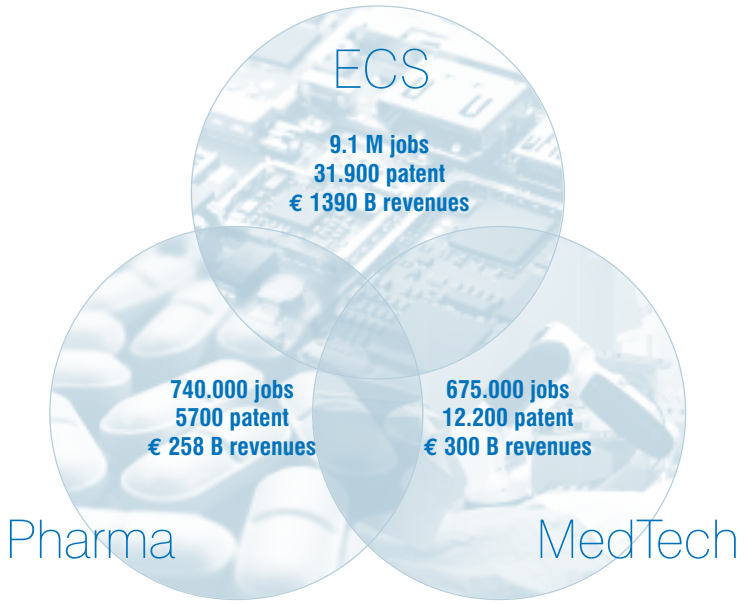


Figure 3 *Selected statistics for the European ECS, MedTech and Pharma industries.*
(sources: The Pharmaceutical industry in figures, efpia 2018, The European Medical Technology Industry in figures, MedTech Europe 2018, European Patent Office 2016)

The lack of Moore's Law in medical devices and technologies

In the ECS industry, the drive towards volume combined with high performance, low-cost and high flexibility has led to a technology consolidation that has resulted in high-end open technology platforms that encompass the whole value chain, starting from devices, packages, assembly, all the way up to systems, connectivity and software platforms. The most well-known example is without doubt CMOS technology, where the combined production volume of all the customers that use the CMOS platforms justifies the immense investments that are required to build and operate foundries. At the same time the revenues generated make it possible to continuously develop new process generations. It is this mechanism which has driven "Moore's law" for the past five decades.

This mechanism is almost completely lacking in the medical device industry. Diagnostic ultrasound may serve as an everyday example. Figure 4 shows the three basic components of a common diagnostic ultrasound system: the device level (the transducer), the electronic readout system and the data level. It is clear that the system as well as the data level can hugely benefit from hardware and software technologies that are being developed for the consumer industry. However, on the device level, the transducer, innovation proceeds much slower; the volumes here are small while the cost of innovation is high, which results in a slow absorption of innovations that come out of research.

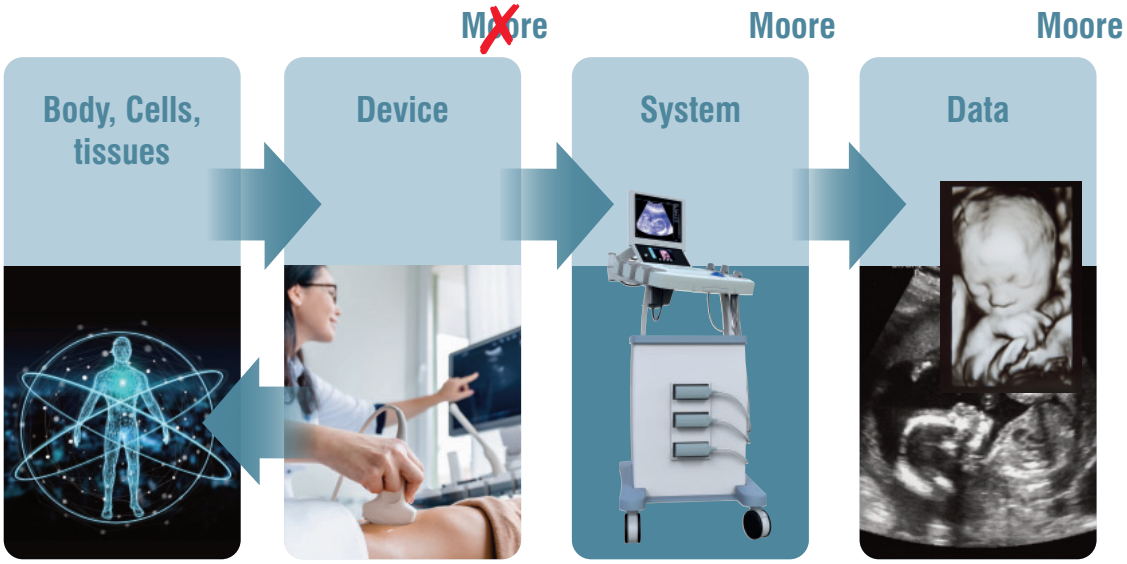


Figure 4 Traditional diagnostic ultrasound is a typical example of a medical device where innovation speed is limited by innovation at the device level.

The situation is even worse for emerging medical devices and technologies. Enormous resources are being spent on academic and industrial research for the development of new promising medical devices, but actually very few of these reach the market and become a medical and economical success. One of the primary reasons for this is that the developed technologies are mostly proprietary "point solutions," and not supported by roadmaps. Many good ideas die in infancy because their market potential simply does not justify the enormous investments needed to develop a concept into a manufacturable and qualified product.

Open technology platforms for medical devices

The success of the non-medical ECS industry is largely due to the endorsement of open technology platforms and shared standards, while open technology platforms are scarce in the medical device industry.

It is however very well possible to create open technology platforms for medical devices. A good example is the technology platform for the next generation smart catheters that is currently being developed in the ECSEL JU POSITION-II project. Driven by the objective to develop technology with a production volume that will allow for

continuous innovation, Philips took the initiative to develop, together with partners, technology platforms that are open also to other parties.

This example also nicely illustrates the concept of open platforms. It is a common misunderstanding that open technology means that there is no IP and no ownership, in other words that "the technology is on the street." This is obviously not the case. An open technology platform, at least in the context of this proposal, is a platform that is owned and maintained by the platform owner, but accessible to others on a normal commercial base.

Apart from the aspect of production volume, open technology platforms offer several other advantages to their users:

- Focus on applications rather than technology development;
- Shorter time to market;
- Reduced risk;
- Lower cost.

Established markets and technologies are not very well suitable for the introduction of open technology platforms. Therefore, the Health.E lighthouse is promoting the development of open technology for *emerging* medical domains, with the objective to accelerate innovation.

Sharing resources – a lesson learned from the semiconductor industry

In the early days of the semiconductor industry, semiconductor manufacturers owned the complete value chain from silicon wafer manufacturing up to and including the end products. As the (complexity of) the industry grew, most manufacturers started to rely on specialized manufacturers for their silicon starting material. Subsequently, the standardized substrate wafer became the first open technology platform in the industry. Next, packaging became a commodity that was easily shared with other semiconductor manufacturers, mostly in the Asia. For many years most manufacturers kept clinging to their IC processes as these were considered to be an important part of their IP portfolios. Today, as the costs associated with the development of new CMOS nodes have become astronomically high, many semiconductor companies have been forced to become more or less fab-less and share foundry services with others, even competitors.

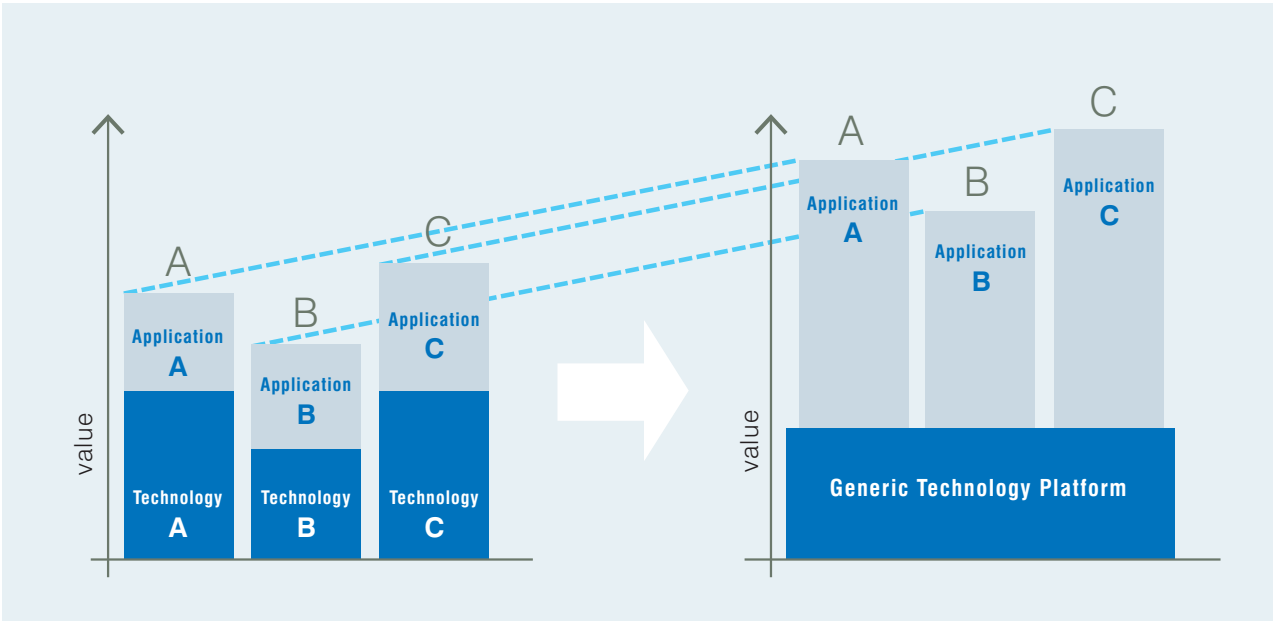


Figure 5 *Left, companies (A,B,C) that use and develop proprietary technologies have to divide their resources between technology and applications. Right, the implementation of open technology platforms allows companies to fully focus on applications, increasing the value of their products.*

As this transition was taking place, many OEMs feared the prospect of losing control of the basic technologies. The new situation turned out to be much more favourable than many had expected. Before the transition, every individual company had to spend a significant amount of resources on technology development, which left less resources for development of the applications (Fig. 5 left). After the transition, when open technology foundry services had replaced proprietary technologies, all resources became available for application development (ASIC and chip design Fig. 5 right).

In the end, the transition to foundry services with open technology platforms has enormously accelerated the entire industry, from which all actors are benefiting. Foundries gather the accumulated production load, which makes it possible for them to continuously invest in technology to keep up with Moore's Law. Semiconductor companies can concentrate fully on innovative products that benefit from continuous technology updates, and last but not least end-users benefit from the best solutions at very low costs. It is no exaggeration to state that the adoption of open technology platforms by the semiconductor industry has enabled the evolution of the ICT-based society as we know it.

Finally, it should be mentioned that the move towards high-end foundry services has enabled and stimulated the growth of a legion of SME design houses that design custom integrated circuits (ASICs), which in their turn enable new products.

Reduce duplication

Apart from historical and cultural conventions there is no reason why such an "innovation accelerator" cannot be implemented for medical devices. On the contrary, many new medical device concepts are in an urgent need for platforms and standards that will enable them to bridge the gap between their academic proof-of-concept, and large scale acceptance by patients, clinics and pharma.

Organ-on-chip has already been used as an example a number of times in this document. Since this is an entirely new branch of science/technology, there is no large industry that can take the lead here to give the new industry a "push" in the right direction. In contrast, the field is driven by SMEs that all develop their own private solutions. Any form of standardization is lacking. The result is that the systems are costly, clumsy to use (especially for biologists with limited

Figure 6 An impression of the smart well plate that is currently being developed in the ECSEL JU project Moore4Medical. It is designed to bring the organ-on-chip devices of different manufacturers in a standard format.

engineering skills), and that the pharmaceutical companies are overwhelmed by offerings that are mutually incompatible. Figure 6 shows a precompetitive microfluidic "packaging" solution that is currently being developed in the ECSEL JU project Moore4Medical[2]. It brings the organ-on-chip devices of different manufacturers in a standard well plate format with the goal to replace the different point solutions, making it possible for companies to dedicate their resources to the chip and the organ, while pharma can readily adopt the new devices in their standard workflows.

Now is the time!

The emergence of entirely new medical domains is the ideal moment to change the culture in the MedTech industry and start with the introduction of open technologies. Nearly all of the new domains have elements that could heavily benefit from the endless technology portfolio of the ECS industry.

On top of this, there is a general consensus that added value is shifting from technology towards algorithms, applications and solutions.

Of the approximately 25.000 SME MedTech companies in Europe, many are eager to also bring their ideas and products - very often in these new domains - to the market.

Now is the time to join forces and make it happen!

[2] https://moore4medical.eu/

3 Emerging Medical Domains

Innovations and new insights in technology and biology have triggered the emergence of completely new electronic medical devices and applications that provide answers to the call for a more decentralized and personalized form of healthcare. These emerging domains not only hold great promise for society and patients, but also for the ECS industry as they increasingly rely on the industry's capabilities in microfabrication, miniaturization, and embedded intelligence in combination with high-volume, low-cost manufacturing.

It is one of the central objectives of the Health.E Lighthouse Initiative to create awareness among the ECS industry about these emerging opportunities in the medical domain. In order to generate an overview, the Lighthouse has conducted a consultation among RTOs, projects connected to the Lighthouse and other stakeholders. The overview is limited to technologies that in a broad sense are linked to the ECS industry. Furthermore, the emerging medical domains are distinguished from innovative research ideas and concepts that are still at a low TRL level. For this white paper the following criteria are used to define an emerging medical domain:

- Disruptive in nature;
- Demonstrated in a relevant setting;
- Not yet in volume production;
- Not integrated in clinical and pharmaceutical workflows.

This has resulted in an un-prioritized list. In the next Sections the emerging domains that were identified will be discussed, and their societal impact and relevance for the ECS industry will be highlighted. Each Section ends with an analysis of the technology platforms needed to accelerate the pace of innovation for each particular domain.

- Bioelectronic medicines
- Organ-on-Chip
- Personal ultrasound
- Radiation free diagnostics and interventions
- Smart minimally invasive instruments
- Second generation of surgical robots
- Smart drug delivery
- Intelligent wound care
- Ambulatory monitoring
- Point-of-care diagnostic
- Remote sensing and monitoring
- E-health
- Advanced therapies using genes, cells and tissues

3.1 Bioelectronic Medicines
Towards an electrical cure for chronic diseases

Active implantable devices have been used for years to treat chronic conditions with minimal side effects: pacemakers and defibrillators (cardiac rhythm management), cochlear implants (deafness), deep brain stimulation (Parkinson's disease), spinal cord stimulation (chronic pain) etc.

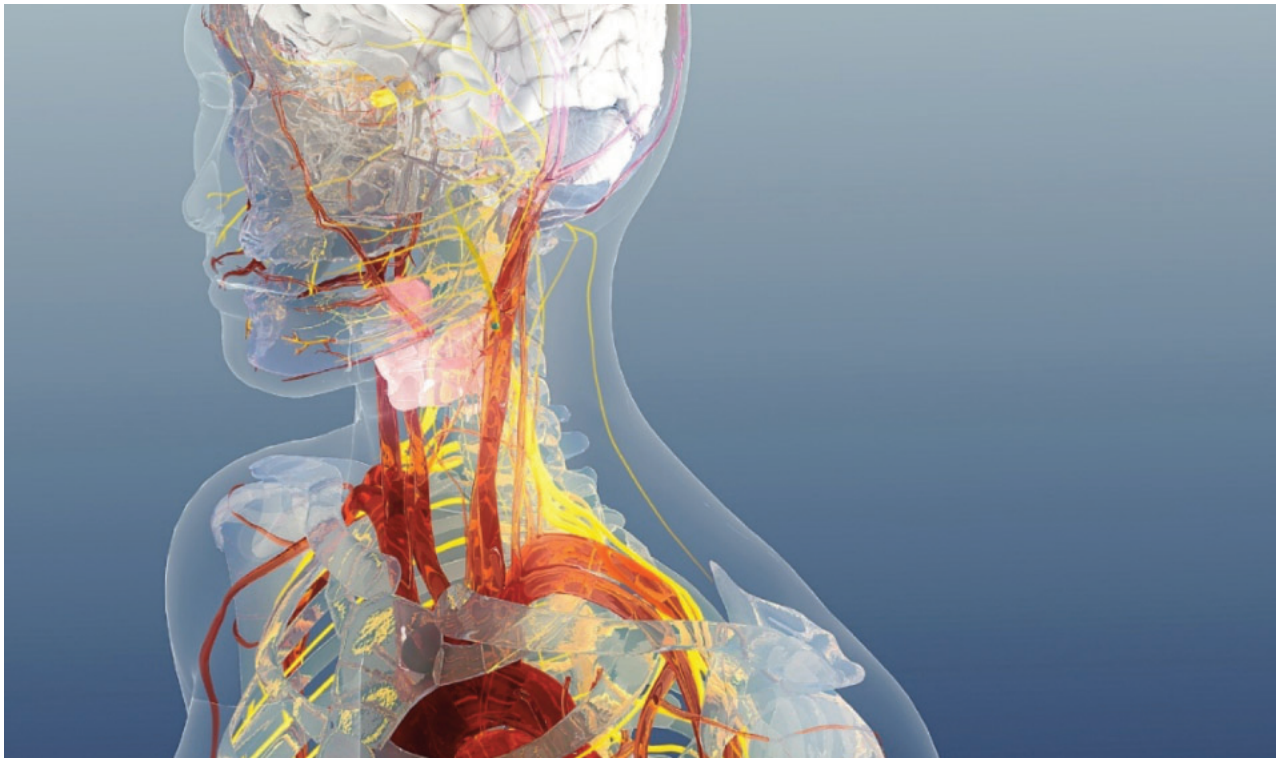
Recently the interest in nerve stimulation has surged because it has been found that mild vagal nerve stimulation can be used as a complementary, or even replacement treatment for (chronic) autoimmune diseases such as, rheumatoid arthritis, Crohn's disease, colitis, congestive heart failure, psoriasis, multiple sclerosis, asthma, Alzheimer, Parkinson etc.

To make bioelectronic medicines a practical reality, the next generation of smart implantable devices will need to be highly miniaturized, autonomous and cost effective, so that they can be implanted on the selected nerve by a simple minimally invasive procedure.

Societal impact

With an increasingly aging population, the (cost) effective treatment of chronic diseases is becoming increasingly important to curb the burden of the cost of healthcare. It is widely recognized that many chronic diseases find their roots in inflammatory abnormalities, often involving an overactive immune system.

Today, the treatment of chronic autoimmune related diseases with biological cytokine suppressors places a heavy impact on our healthcare systems. Therapies with modern biological compounds such as Etanercept, Adalimumab, and Infliximab cost between $15,000 and $25,000 a year per patient, and even these are effective in only 40% of the cases.



The prospect of a therapy that can be administered with less side effects, lower total costs and with higher efficacy, is daunting. Based on the preliminary results obtained so far, it is even justified to consider bioelectronic medicines not only as a last resort, but as a second or first line of therapy.

Relevance for the Electronic Components and Systems (ECS) industry

The prospect of bioelectronic medicines that can be deployed on a large scale for the treatment of a wide variety of chronic diseases poses an enormous opportunity for the electronic industry with its expertise and miniaturization, assembly, encapsulation, low power processing, wireless communication and high volume low-cost manufacturing. To enable this, the ECS industry will need to take the initiative in the development of the next generation of implantable neuromodulator devices that will be:

- Highly miniaturized, so that they can be precisely delivered on target nerves with minimally invasive procedures;
- Specific, so that they precisely target specific groups of neurons (fascicles) with minimal side effects;
- Wirelessly powered by RF, ultrasound or energy harvesting;
- Active only when needed through closed loop operation.

Enabling technology platforms

The development of the emerging field of bioelectronic medicines can be significantly accelerated by the development of a number of open technology platforms that address common technological challenges and that will serve a variety of bioelectronic medicine devices. These include platforms for:

- *Miniaturization of complex heterogeneous systems* to allow for minimally invasive device delivery on the target nerve;
- *Power management* covering storage (battery or capacitor) and remote charging (inductive, ultrasound, scavenging);
- *Secure communication;*
- *Low-power edge AI computing* for autonomous closed loop operation;
- *Small efficient electrodes* for bioelectronic devices that need to interface in a sensitive organ/neuron environment;
- *Encapsulation* in relation to reliability, bio-stability, weight, manufacturability and cost.

Links:

- Bioelectronic Medicine Roadmap, A publication by the Semiconductor Research Cooperation of the USA. *https://www.src.org/program/bem/*
- Bioelectronic magazine, a part of Springer Nature. *https://bioelecmed.biomedcentral.com/*
- SetPoint Medical website. *https://setpointmedical.com/files/SetPoint_The_Evolution_Of_Bioelectronic_Medicine.pdf*
- Galvani Bioelectronics website. *https://galvani.bio/*
- Salvia BioElectronics website. *https://www.salvianeuro.com/*

Further Reading:

- Emily Waltz, "A spark at the periphery," Nature Biotechnology, vol.34, no. 9, September 2016 *http://www.emilywaltz.com/Peripheral_Nerve_Stimulation_-_Sept_2016.pdf*
- Douglas Fox, "The electric cure," Nature 545, p 20–22, 4 May 2017. *https://www.nature.com/news/the-shock-tactics-set-to-shake-up-immunology-1.21918*
- Anthony Arnold, "The evolution of bioelectronic medicine, Reprogramming the body to fight disease with electricity," a whitepaper by Setpoint Medical. *https://setpointmedical.com/files/SetPoint_The_Evolution_Of_Bioelectronic_Medicine.pdf*

3.2 Organ-on-Chip
Towards precision medicine in future healthcare

A major problem in developing new medicines is the limited availability of human model systems for preclinical research on disease target identification, drug efficacy and toxicity. Laboratory animals or cells in standard tissue cultures, even if they are human, often do not respond to medication in the way cells in contact human organs in the body do. Organ-on-chip (OoC) technology based on human cells may present solutions to this challenge of creating near-human test systems.

In an organ-on-chip the smallest functional unit of an organ is replicated. A typical organ-on-chip comprises the following elements:

- Multiple cell types in a 3D culture, with the cells interacting with each other as they would do in the real organ. The cells are derived by means of iPSC technology from individuals and thus have the genetic characteristics of a particular individual (patients-on-chips);
- A microfluidic device that contains the cells and that provides perfusion and other physiological relevant stimuli such as: stretch, shear stress and chemical gradients;
- A readout, which can simply be optical, but also electrical for electrically active cells, and that can include a whole range of chemical and physical sensors.

Societal impact

Organs-on-chips can significantly reduce the costs of healthcare, because they will allow drug development to become better, safer, faster and cheaper. Presently the development of a new drug from start-to-market takes about 12 years, and costs minimally 1 billion euro per drug. This is due to inefficient drug development pipelines, with too many drugs failing late in development. Organs-on-chips will:

- Speed up development of new drugs, thereby reducing costs;
- Enable precise screening of drugs for unwanted side effects and toxicity (clinical trials on a chip);
- Greatly reduce animal testing supporting the 3Rs guiding principles of reduction, refinement and replacement of animal experiments.

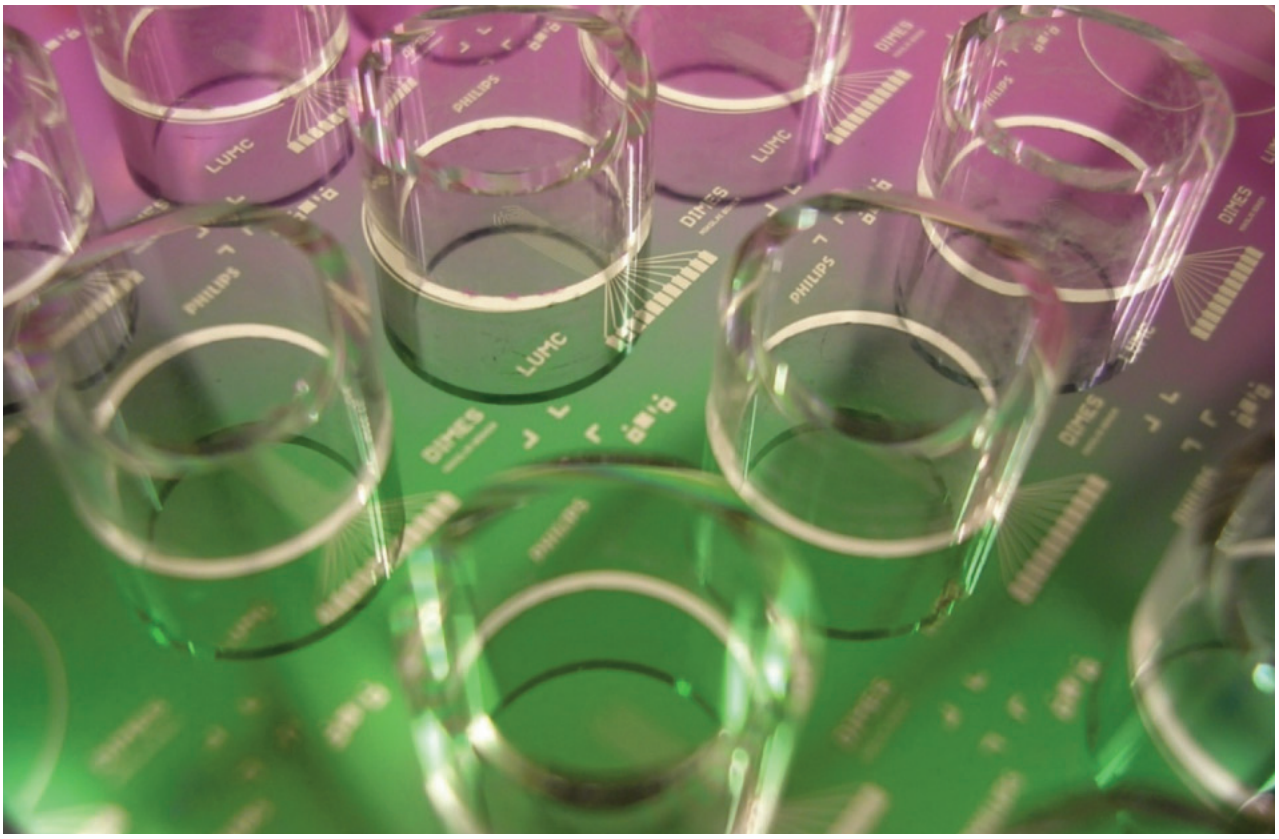
Relevance for the Electronic Components and Systems (ECS) industry

Despite its great promise, the maturity of organ-on-chip technology, with a few exceptions, at present remains mainly stuck at the academic level. Handmade PDMS molded devices, interfaced with a multitude of tubes to external pumps are not compatible with the standardized work flow in biology and pharmaceutical labs. The ECS industry can play an important role in maturing the organ-on-chip concept by developing:

- Technology platforms for large volume, low cost fabrication of organ-on-chip devices utilizing the enormous infrastructure available for the production of microfabricated and microfluidic devices;
- Platform “packaging” concepts that bring the organ-on-chip devices into the standard well plate format used by biologist and the pharmaceutical industry. These “smart well plates” need to contain unobtrusive perfusion and (wireless) electrical interfaces to let them blend in standard work flows;
- Readout equipment that collects the large amounts of data generated by the integrated electrodes and sensors and uses AI to assist in data interpretation.

Enabling technology platforms

The essential capabilities underlying the organ-on-chip field are primarily *embedded microfluidics* and the *processing of polymers* in a microfabrication environment. Ideally, the industry should formulate one or more open technology platforms that will allow for the production of a range of different organ-on-chip devices on a foundry service base.



Additionally, the industry should come to standardization of the microfluidic and (when applicable) electronic interfaces on organ-on-chip devices. This will allow individual organ-on-chip devices to be applied in larger systems that are compatible with standard work flows (smart well plates). *Smart sensors* can be used as readout devices, while *edge AI* will be essential in data interpretation and reduction.

Critical to a wide adoption of OoC will also be the peripheral component integration (i.e., metabolics management, oxygenation, etc.), which has often a larger size than the OoC device itself. Therefore, the interfacing of peripherals for the OoC device should also be a part of the standardization concept.

Links:

- The European Organ-on-Chip Society *https://euroocs.eu/*
- The Organ-on-Chip in Development (ORCHID) project *https://h2020-orchid.eu/*
- The human Disease Model Technology (hDMT) institute *https://www.hdmt.technology/*

Further Reading:

- Organ-on-Chip white paper, an hDMT publication.
- Towards an organ-on-chip roadmap, an ORCHID publication.
- Impact of organ-on-a-chip technology on pharmaceutical R&D costs, N. Franzen et al. Drug Discovery Today, Volume 24, Issue 9, September 2019, Pages 1720-1724.
- *Mini-organs on chips*, publication by Biowetenschappen en Maatschappij.

3.3 Personal ultrasound

MEMS ultrasound transducers are taking ultrasound diagnostics out of the clinic

Ultrasound imaging has developed into an extremely versatile diagnostic tool that is serving almost all branches of professional medical care. Despite its versatility, ultrasound diagnostics is still mainly used in clinical settings for three reasons:

1. The required skill to use it in the right way and acquire diagnostically relevant images;
2. The required expertise to translate these images into diagnostic conclusions;
3. The high cost and limited availability of this equipment.

The development of mass producible MEMS ultrasound transducers is enabling the cost-effective production of highly complex 2D ultrasound imaging arrays capable of capturing 3D volumes. This, combined with efficient edge AI to guide data acquisition and interpretation, will enable the development of ultrasound diagnostic appliances that can be operated by users with limited medical knowledge and even offer mobile use scenarios.

Societal impact

The development of high volume and low cost MEMS ultrasound transducer technologies and edge AI will make ultrasound imaging available to semi-professional, remote diagnostics and even consumer markets.

Today, the first products for these potentially huge markets are being introduced. With prices dropping rapidly from several thousands of dollars down to hundreds of dollars, ultrasound imaging is now moving out of the clinic. It will not

only find its way to (semi)professionals like physiotherapists, obstetricians, midwives, sports physicians etc., but it will also bring diagnostic imaging to rural areas (remote diagnostics) in developing countries. However, the largest market will probably be in home fetal monitoring.

Relevance for the Electronic Components and Systems (ECS) industry

Traditional ultrasound is based on dedicated, non-scalable and proprietary piezo-ceramic production technologies operated by the MedTech industry. The development of low cost silicon based MEMS ultrasound transducer technologies is bringing ultrasound diagnostics within the reach of the ECS industry. As no other, the ECS industry has the instruments and production technologies to transform these into high volume consumer products. As such, they present a huge opportunity for the ECS industry, not only in terms of square meters of silicon, but also in terms of the electronics needed to drive the transducers and the many different applications that these transducers will enable. It is even envisaged that a category of these devices will be disposable wearables. Consequently, it is expected that MEMS ultrasound will enable a completely new industry.

Enabling technology platforms

The *MEMS ultrasound transducer* is the enabling platform technology driving this completely new industry. MEMS ultrasound transducers come in many flavors: capacitive (CMUT) and thin-film piezo (PMUT), processed as standalone or on ASIC etc. In the ECSEL JU project POSITION-II[1], a European benchmark is executed to map the different technologies on the application space.

The second enabling platform to allow US imaging to be executed by laymen is *edge AI* to assist the user in data acquisition and data interpretation.

Links:

- "An open platform CMUT ultrasound transducer platform," Philips Innovation Services. *https://www.innovationservices.philips.com/looking-expertise/mems-micro-devices/mems-applications/capacitive-micromachined-ultrasonic-transducers-cmut/*
- Butterfly website, *https://www.butterflynetwork.com/*
- PulseNmore website, *https://pulsenmore.com/*
- Lumify website, *https://www.philips.co.uk/healthcare?locale_code=en_gb*

Further Reading:

- Dave Fornell, "5 Key Trends in New Ultrasound Technology," *Ultrasound Imaging,* February 07, 2019.
- Rob van Schaijk, "CMUT and PMUT: New Technology Platform for Medical Ultrasound," Philips Innovation Services.

[1] http://position-2.eu/

3.4 Radiation free diagnostics and interventions

Innovations in photonics and MEMS enable in body guidance without radiation

New technologies are being developed that can largely eliminate the need for harmful X-ray radiation during minimally invasive procedures:

- Optical tracking of instruments is combined with pre-operative scans and augmented reality, to show the surgeon the position of his instruments with respect to internal physiology;
- Electromagnetic and acoustic sensors show the position of the tip of an instrument with respect to a pre-operative scan or directly in a live ultrasound image;
- Breakthrough innovations in photonics are enabling optical shape sensing techniques that can reconstruct the shape of a catheter over its entire length;
- MEMS ultrasound technology will enable segmented large area body conformal ultrasound transducers that are capable of imaging large parts of the body without the need for a sonographer, to guide surgeons in a multitude of minimally invasive interventions.

Societal impact

The move from open surgery to minimally invasive interventions has led to a drastic reduction in hospitalization and post-surgical complications. As such it is one of the most effective instruments to reduce the cost of healthcare. Not surprisingly, minimally invasive surgery is now being used in almost every branch of surgery, and as a result the number of minimally invasive interventions has grown explosively over the past two decades.

Moving from open to minimally invasive surgery, image guidance is needed. X-ray imaging was a first logical step, but apart from the fact that it requires bulky equipment that is often obstructing the surgeon, it poses a considerable health risk to the patient and especially to the surgeon, while it only provides a 2D representation of the 3D physiology and 3D shape of the devices.

Innovative radiation free 3D device guidance will allow for a natural and easy navigation in the body resulting in more precise and successful interventions while minimizing radiation concerns. It will further reduce the need for open surgery and is therefore a significant driver in the reduction of healthcare cost.

Relevance for the Electronic Components and Systems (ECS) industry

Europe has a leading position in cath lab infrastructures with a world market share in excess of 76%. Next to this, it is a prominent producer of X-ray diagnostic equipment. To consolidate and expand this important market position, it is of paramount importance for Europe to be a forefront innovator in non-ionizing guidance and diagnostic imaging technologies.

These new technologies cover almost every aspect of the ECS value chain ranging from MEMS fabrication and photonics to massive edge computing and AI for image reconstruction.

New non-ionizing diagnostic imaging modalities will additionally find their way from the clinical setting to general practitioners and other professional users (see also “Personal Ultrasound”, Section 3.3).

Enabling technology platforms

Nearly all technologies covered by the ECS value chain will be essential in the reduction or even elimination of X-ray for guidance and to a certain extent for diagnostics. However, the main technology platforms that are driving this innovation are:

- *Integrated photonics;*
- *MEMS ultrasound;*
- *Flexible and conformal electronics;*
- *Low power edge computing and AI;*
- *Data integration into clinical systems;*
- *Terahertz imaging systems for healthcare applications.*

Links:

- Fiber Optic RealShape (FORS) Technology. *https://www.philips.com/a-w/research/research-programs/fors.html*
- Fiber Optic RealShape (FORS) technology – FIH clinical Study. *https://www.youtube.com/watch?v=rVGWPwv4jq4&feature=youtu.be*
- VOSTARS project website. *https://www.vostars.eu/*

Further Reading:

- Adrian Elmi-Terander et al. “Feasibility and accuracy of thoracolumbar minimally invasive pedicle screw placement with augmented reality navigation technology,” Spine. 43(14):1018-1023, July 15, 2018.

3.5 Smart minimally invasive instruments

Electrical and optical systems at the tip of minimally invasive instruments add eyes and ears at the point where surgeons need them the most

The capabilities of the ECS industry in miniaturization, integration, embedded intelligence, communication and sensing will have an enormous impact on the next generations of smart minimally invasive devices.While our phones, cars and houses are filled with low-cost, unobtrusive sensors able to provide a wealth of information, most minimally invasive devices today, aside from some smart catheters used in cardiac interventions, are unintelligent instruments without sensor functionality at all. Many interventions such as biopsies, ablations, intravenous infusions and epidural needle placements, lead extractions etc. are all still performed based on experience, or simply guided by ultrasound or fluoroscopy. Highly miniaturized electrical and optical systems using advanced cost-effective platform technologies will bring extensive imaging and sensing capabilities to these devices and enable the second minimally invasive surgery revolution.

Societal impact

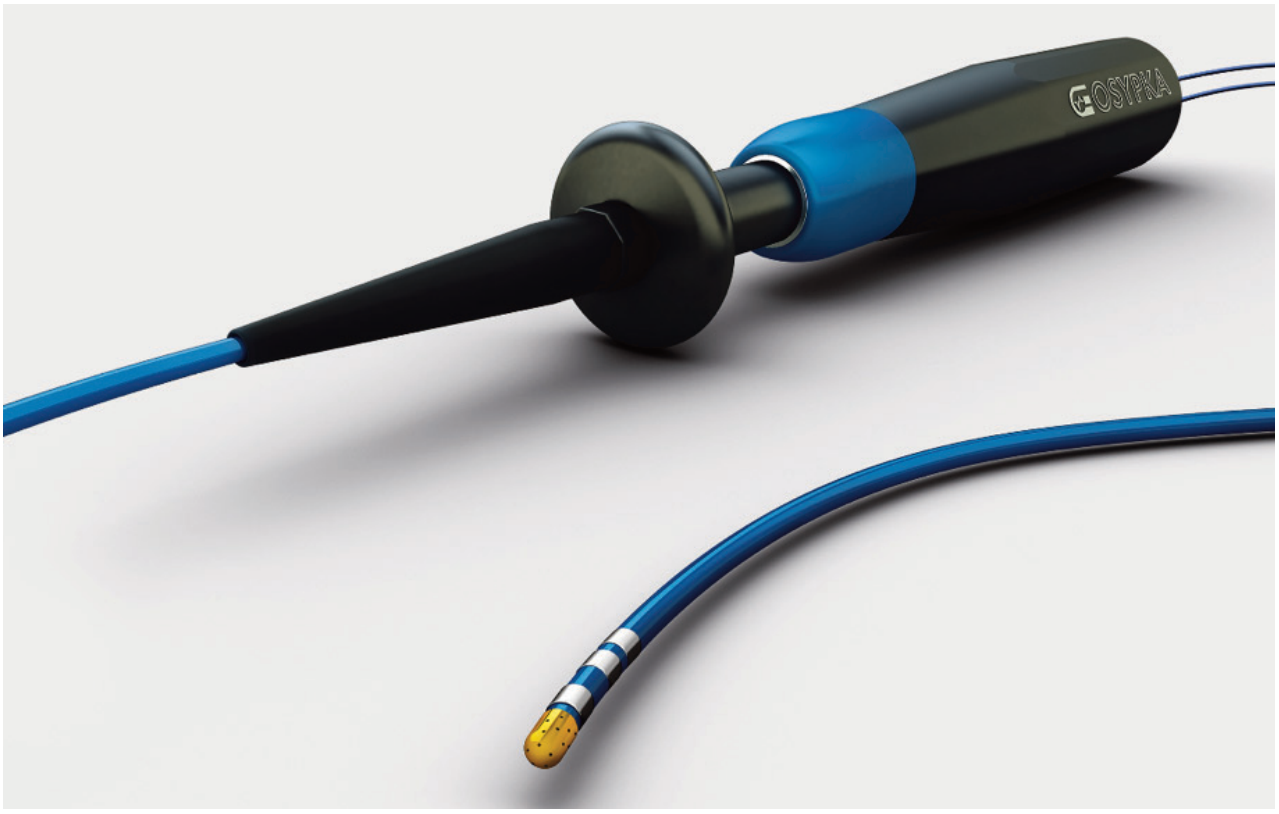
Minimally invasive surgery is one of the most effective instruments to reduce the cost of healthcare. Compared to open surgery it has led to a drastic reduction in hospitalization, trauma to the patient and post-surgical complications. Not surprisingly, minimally invasive surgery is now being used in almost every branch of surgery, and as a result, the number of minimally invasive interventions has grown immensely over the past two decades.

An example in which minimally invasive procedures will have a tremendous impact is in the treatment of atrial fibrillation (AF). In the last 20 years AF, which is strongly related to age, has become one of the most important public health problems. It is estimated that the patient population with AF in Europe will have reached 14-17 million in 2030, with between 120 and 215 thousand new cases of AF each year. Until recently, the only therapies available have been either the prescription of drugs or - extremely impactful - open heart surgery. Today, a growing number of patients is treated using a minimally invasive procedure. Smart catheters will increasingly enable the surgeon to know where he or she has to treat, how to reach the position, and how deep the ablation is progressing. This will shorten procedures and improve procedure outcomes, enabling the cost effective treatment of a growing number of patients.

Relevance for the Electronic Components and Systems (ECS) industry

Today, the potential of highly miniaturized electrical and optical systems for smart minimally invasive instruments is largely untapped. Application of electronic sensing functionality remains primarily limited to coronary interventions, and even there the products in the market today use outdated analog technologies based on expensive point solutions.
The field is desperately waiting for universal open technology platforms that can be used to fold, wrap, and squeeze complex electronic sensing systems into the tip of these tiny instruments. Digitization at the tip will lead to serialization of data, which in turn will result in standardization of communication protocols. Seamless integration of these products in the cath lab infrastructures will further promote their proliferation.

With approximately 7-10% of the aging population expected to undergo at one moment in their life a cardiac intervention, this type of interventions alone, which are entirely based on disposable devices, will represent a significant business prospect for the ECS community.



Enabling technology platforms

To realize the next generation smart catheters, a broad spectrum of advanced ECS capabilities will need to be brought together, foremost in dedicated platforms for *heterogeneous miniaturization* and *integrated photonics*. These platforms are complemented with platforms for *embedded ultrasound*, *low power edge computing and AI* and *digital health platform integration.* Finally, it should be mentioned that the development of the next generation of smart minimally invasive instruments will go hand in hand with the development of new navigation techniques that do not rely on X-ray (see emerging domain "Towards radiation free interventions").

Links:

- POSITION-II project website. *http://position-2.eu/*

Further Reading:

- H. Bezerra & G.S. Mintz, "Intravascular OCT and IVUS in PCI, an expert review," American College *of* Cardiology, Jun. 13, 2016.
- P. Tonino et al. "Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention," Jan 15, 2009, N Engl J Med 2009; 360:213-224.
- A. Darge, "Advances in Atrial Fibrillation Ablation," J Invasive Cardiol. 2009 May; 21(5): 247–254.

3.6 The second generation of surgical robotics
Surgery is about to get "digitized"

The use of robotics started in the manufacturing industry in the 1950s, but their entry into the realm of surgery was not until the '90s. This came together with the demand for minimally invasive surgery. Surgeons who used the first wave of surgical robotic systems, already experienced enhanced precision, improved dexterity and intuitive remote control, along with improved stereo visualization inside the patient when compared with traditional techniques.

Where the first wave was focused on improving the surgeons device manipulation and sensing abilities, the next waves will focus on providing consistent and high quality surgical services, improving outcomes and increasing efficiency in the operating room by automating simple tasks and actively assisting surgeons in more complex procedures. Before fully autonomous surgical suites are realized, many technical, social, and regulatory challenges must be overcome. The existing capabilities of the ECS industry as well as breakthroughs in miniaturization, actuation, integration, embedded intelligence, communication, and sensing are all essential enablers for the next wave of surgical robotics.

Societal impact

Surgical robotics address 3 major components of surgery, repetitive tasks (e.g., hair follicle harvesting), access and dexterity (e.g., keyhole abdominal surgery) and precision (e.g., spine screw placement, biopsy).

Surgical robotics have a clear impact on the society by improving the outcomes of procedures and reducing procedure-associated complications, which has a significant economic benefit in addition to cost savings by reduction of post-operative care and length of stay at hospitals. This has been shown for initial applications in minimally invasive joint replacement and prostate cancer treatment procedures. So far only ~2% of procedures are performed with robotic assistance worldwide. Therefore, it is essential to continue to develop and deploy robot systems in medical procedures

to cover more procedures and enable wider access, essentially democratizing surgery and reducing the overall cost of care. As surgical robot companies grow fueled by technological breakthroughs and increased adoption, product costs will decrease while providing increased quality, leading routine procedure costs to decrease.

Relevance for the Electronic Components and Systems (ECS) industry

From a technical perspective, innovations should focus on improving the surgeon's and their team's experience, always improving patient outcomes, and therefore increasing (operating room) efficiency and ultimately reducing healthcare cost. This will be achieved through innovations that simplify application of surgical treatment, even if they require greater technological sophistication. Improvements in visualization, including better incorporation of pre-operative and intraoperative (e.g., x-ray) imaging, sensing and augmented reality interfaces will make robot-assisted surgery more natural and intuitive, and enable surgeons to execute surgical plans more precisely and efficiently. Artificial Intelligence driven by increased collection of data passing through these robotic systems like motion tracking, sensing and imaging will enable exponential improvements and innovations. Key innovations will improve and simplify workflow, provide active assistance in the form of automated maneuvers, present enhanced real-time guidance from information fusion and add system redundancies for robustness. These changes will improve the quality of existing procedures while reducing costs and building confidence to expend into new surgical applications. The capabilities of the ECS industry in miniaturization, integration, embedded intelligence, communication and sensing are all needed to help succeed those technical innovations.

Enabling technology platforms

The ECS value chain will be essential in the development of the second wave of surgical robotic systems. The main technology platforms that are driving this innovation are:

- Low power edge computing;
- Automation;
- Sensing;
- Miniaturization of sensors and actuators;
- Control systems;
- Artificial Intelligence for perception;
- Artificial Intelligence for 'robotics' control;
- Integration platform (e.g., Open protocols / OpenIGTLink);
- Device and data interoperability standards e.g., DICOM2.0.

Links and further reading:

- https://pubmed.ncbi.nlm.nih.gov/32270913/
- https://www.philips.com/a-w/about/news/archive/blogs/innovation-matters/robots-humans-and-healthcare.html
- https://www.philips.com/a-w/about/news/archive/future-health-index/articles/20170512-medical-drones-and-robot-surgeons-visions-of-the-medical-futurist.html

3.7 Smart drug delivery

Intelligent drug delivery platforms will improve patient adherence and help to move healthcare from hospital to home

Recent years have seen significant increases in the prevalence of chronic diseases such as diabetes and autoimmune conditions. The very high cost of the drugs (> € 10k/yr) and treatment regimens associated with these conditions has intensified the pressure to shift medication administration from traditional settings to cost-effective alternatives.

One alternative location is the patient's home, where treatments are now regularly self-injected. Diabetics may require multiple doses of insulin daily, while high-value biologics for autoimmune conditions may be administered as infrequently as once every 2-3 months.

However, homecare settings lead to poor patient adherence (i.e., the failure to take medication as prescribed). To address these issues, the development of smart drug delivery platforms and intelligent auto-injectors is required.

Societal impact

The greatest societal impact of smart drug delivery platforms will be seen in improved public health arising from increased patient adherence. Poor adherence is linked to demographic factors, incorrect patient beliefs about costs and benefits, and perceived patient burden regarding obtaining and using medication. It is estimated that up to 50% of patients fail to medicate as planned, and for chronic diseases such as rheumatoid arthritis, this can cause deterioration of the joints from physical wear of the bones, leading to further hospitalization, patient distress and financial burden.

Ultimately, non-adherence contributes to the premature deaths of nearly 200,000 Europeans annually. Conversely, the potential societal impact of improved adherence is huge – in one study, patients who showed improved adherence had a 13% reduction in the risk of hospitalization or emergency room visits – and emerging drug delivery technologies will further accelerate this trend.

Relevance for the Electronic Components and Systems (ECS) industry

Use of technology, connectivity and loyalty-style programs improves adherence rates and facilitates remote treatment outside of the hospital, and so a clear need exists for the development of next-generation drug delivery systems. These will form part of the "Internet of Medical Things" (IoMT) - medical devices and applications that link with healthcare systems using wireless connectivity. Already, 3.7 million connected medical devices are used worldwide today.

However, the More-than-Moore technologies needed to realize the next generation of sensorized and wearable delivery devices still need to be developed, and there are significant opportunities for European ECS in this regard, especially as the industry is already strong in the MedTech sector. Particular emphasis should be placed on the development of new medical-grade microsystems technologies, including transdermal interface components, closed-loop diagnostics, artificial intelligence and low-power communications.

Enabling technology platforms

Enabling platforms are required in order to facilitate a transition from the legacy mechanical components seen in current autoinjectors and wearable drug delivery pumps, to highly integrated, patch-like microsystems. These include:

- *High-performance sensors and actuators* for drug delivery, monitoring and control;
- *On-board microfluidics* for in-situ preparation and delivery of formulations;
- *Minimally invasive needles and electrodes* for transdermal interfacing, delivery and diagnostics;
- *ECS-controlled smart materials* for targeted drug release;
- *New materials, containers and power sources* that will meet stringent environmental and clinical waste disposal standards, and that may even allow biodegradation or dissolution in vivo (which may include dissolvable/biodegradable electronics for e.g., temporary drug delivery treatments);
- *Body-worn communications technologies* for IoMT integration and clinical interfacing;
- *Edge AI* for closed-loop control, adherence assessment, and clinical trial monitoring.

Links:

- MT Brown *et al*, "Medication Adherence: Truth and Consequences", *Am J Med Sci*. **351**(4), pp. 387-99, 2016.
  https://pubmed.ncbi.nlm.nih.gov/27079345/
- AK Jha *et al*., "Greater adherence to diabetes drugs is linked to less hospital use and could save nearly $5 billion annually", *Health Affairs* **31**(8), pp. 1836-46, 2012.
  https://pubmed.ncbi.nlm.nih.gov/22869663/

Further Reading:

- S. Al-Lawati, "A report on patient non-adherence in Ireland",Pfizer Healthcare Ireland/Irish Pharmacy Union/Irish Patients' Association, March 2014.
- OnDrug Delivery Magazine Issue No #103, "Connecting Drug Delivery", December 7th, 2019.

3.8 Intelligent wound care
Smart Dressings – towards Intelligent, autonomous wound care

Among the emerging applications of advanced MedTech, one that has especially high potential for social and economic impact is that of 'smart wound care' *i.e.* the merger of highly miniaturized electronic, optical and communications technologies with conventional wound dressing materials.

The resulting smart dressings will be capable of autonomously monitoring and managing the condition of chronic wounds in the home and will have enormous impact in the early diagnosis, efficient management and advanced treatment of conditions such as diabetic, venous and pressure ulcers.

Unsurprisingly, wound care is a challenging environment; dressings must be comfortable and unobtrusive to wear, deployable by untrained personnel, highly flexible, and safely disposable. Successful exploitation of the new technology will therefore depend on the development of medical-grade technology platforms for flexible and biodegradable electronics, body-worn communications, and advanced packaging.

Societal impact

A chronic wound is defined as one that does not heal after three months of treatment. The economic cost of prolonged wound care is enormous; annual care of a single chronic ulcer is approximately € 10,000, and global cost is expected to top € 13.5B by 2025.

The social cost is immeasurable. Chronic wounds are painful, curtail social and economic activities, place a significant burden on families, and are life- and limb-threatening – worldwide, a diabetic foot is amputated every twenty seconds. Sadly, the prevalence of chronic wounds is increasing, due in part to the rising average age of the population, along with growth in the prevalence of obesity, diabetes and lower extremity disease.

Smart dressing technologies will facilitate remote care and alleviate the burden on healthcare infrastructure and national budgets.

Relevance for the Electronic Components and Systems (ECS) industry

Today, the field of intelligent wound care remains in the early R&D phase, and there is no 'smart dressing' on the market today, for example, despite substantial patent activity in the background.

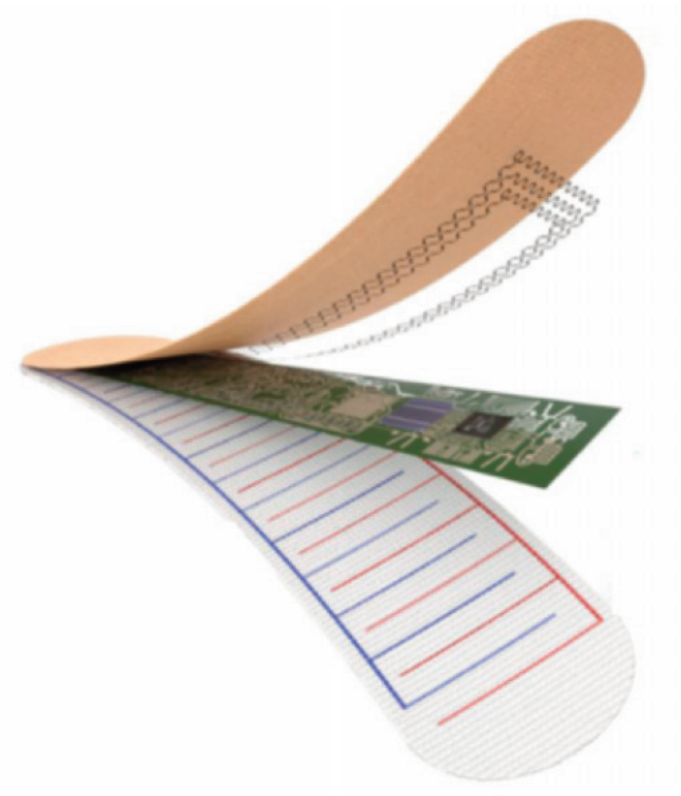
The European ECS industry has the tools and expertise required to make connected dressings a reality, but these must now be repurposed with renewed focus on the specific challenges of the wound care industry. New capabilities will also overlap with requirements in other emerging domains such as point of care diagnostics and minimally invasive surgery, suggesting that common platforms could be beneficial across a range of sectors.

Significant opportunities therefore exist for the ECS community to develop this entirely new industry, at a time when population demographics and lifestyle changes demand it most. Early development and adoption of the necessary technology platforms will furthermore position the sector as global leaders in advanced healthcare.

Enabling technology platforms

While much progress has been made in wearable technologies over the past decade, new platforms must be developed and integrated in order to enable the rapid rollout of intelligent wound care. These include:

- *Flexible and low-profile electronics,* including circuits, optical components, sensors and transducers, suitable for embedding within conventional dressings;
- *Advanced manufacturing techniques* for reliable integration of microelectronic technologies with foam- and polymer-based dressing materials;
- *Biodegradable materials, substrates and power sources* that will meet stringent environmental and clinical waste disposal standards;
- *Body-worn communications* technologies for low-power transmission of wound status;
- *Edge AI* to assist the clinical user in data acquisition and data interpretation.



Links:

- "Get smart – advances in dressing technology", Practical Patient Care magazine, November 2016. *http://www.practical-patient-care.com/features/featureget-smart-advances-in-dressing-technology-5683876/*
- "Could bandages be going digital? Monitor dressing and electric pulses to revolutionise wound treatment", Health Europa, July 2019. *https://www.healtheuropa.eu/could-bandages-be-going-digital-monitor-dressing-and-electric-pulses-to-revolutionise-wound-treatment/92591/*
- "Smart bandages designed to monitor and tailor treatment for chronic wounds", Tufts University, July 2018. *https://now.tufts.edu/news-releases/smart-bandages-designed-monitor-and-tailor-treatment-chronic-wounds*

Further Reading:

- James Davis, "*Smart Bandage Technology: Design and Application,* Academic Press (Cambridge, MA), 2016.
- H. Derakhshandeh *et al*. "Smart bandages: the future of wound care", Trends in Biotechnology **36** (12), pp. 1259-1274, 2018.
- S. O'Callaghan et al, "'Smart Dressings' for Advanced Woundcare: A Review", Journal of Woundcare 29(7), pp. 394-406, 2020. DOI: 10.12968/jowc.2020.29.7.394.

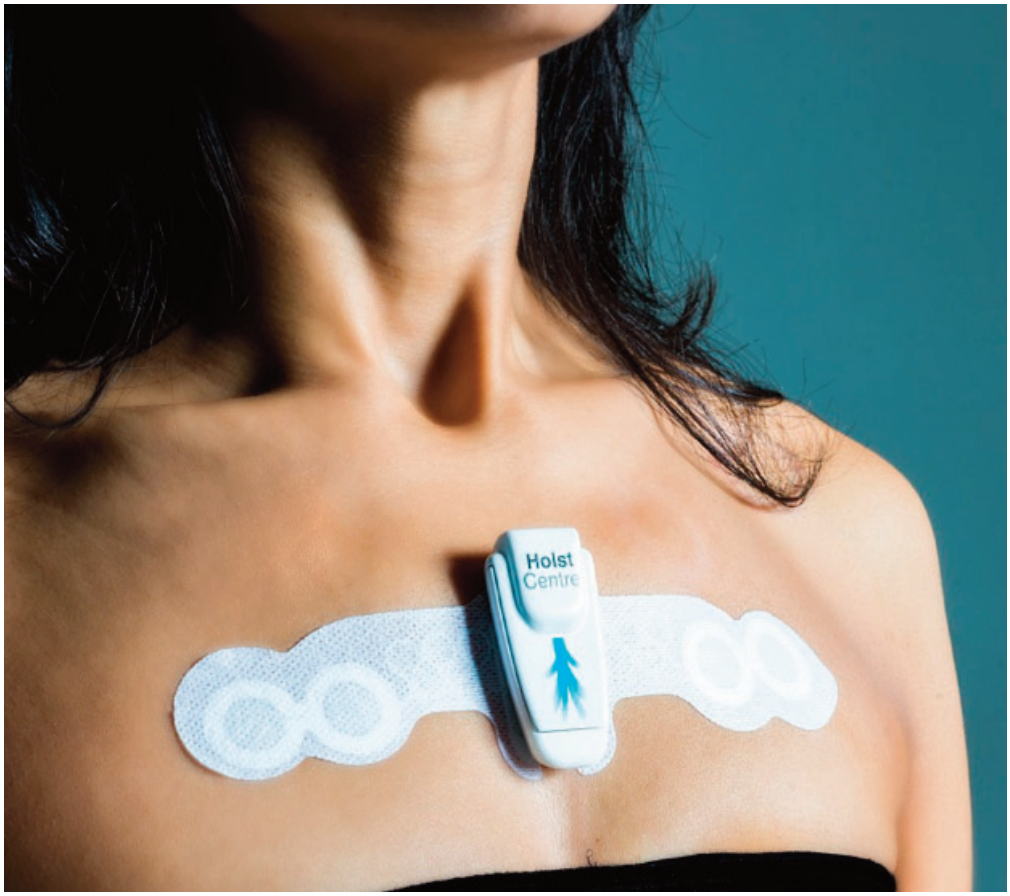
3.9 Ambulatory monitoring

Wearable Healthcare – towards unobtrusive, long term, objective monitoring at home

The measurement of physiological signals is fully integrated in the daily medical practice. Vital signals are monitored to detect acute life-threatening events, but also to determine the general health status of a patient. More and more, also physical activity parameters and stress parameters are determined. These parameters play an important signaling role in the onset of chronic diseases and therefore, also their cure and prevention.

Vital signs are often measured at the medical practice. In addition, physical activity and stress parameters are usually determined by means of a questionnaire. This provides care professionals with only a short term, partially subjective insight in a patient's health status while being at the medical practice.

Recent technological developments (e.g., miniaturization, wireless communication, and flexible electronics) have supported the development of wearable devices and patches for the measurement of physiological signals. These devices are worn on the body and are well suited for long term, objective ambulatory monitoring of patients in their home environment. However, for the use of wearable devices and patches to follow Moore's law, next steps in the development of platform technology have to be made to make ambulatory monitoring more unobtrusive. In extension to this, these technologies may enable ingestibles that can perform transient, unobtrusive monitoring of some vital functions from inside the body.



Societal impact

Long term objective ambulatory monitoring has an important impact on several aspects of the health system:

With an increasingly aging population, the (cost) effective treatment of chronic diseases is becoming increasingly important to curb the burden of the cost of healthcare. It is widely recognized that many chronic diseases find their roots in an unhealthy lifestyle, for example little physical activity, sedentary behavior, restless sleep, stress, loneliness. Ambulatory monitoring provides personal insights in a patient's health status that can support the treatment or deceleration of these diseases. It can also be used as a preventive tool to support a healthy lifestyle.

Shortening the duration of hospitalization also has great economic and social impact. It reduces the high costs of hospitalization and sick leave. More importantly, it greatly reduces the social and physiological burden of being hospitalized. Ambulatory monitoring of physiological signals provides the opportunity for personalized preparation for hospitalization (optimal physical fitness, biopsychosocial profile) and early discharge after treatment (vital signs monitoring, rehabilitation and lifestyle support).

Finally, ambulatory monitoring can play an important role speeding up and reducing the costs of development of new drugs by replacing costly tests to prove the effect of the newly developed drugs in clinical trials.

Relevance for the Electronic Components and Systems (ECS) industry

The prospect of the deployment of ambulatory monitoring on a large scale for the treatment (ranging from prevention to cure and aftercare) of a wide variety of diseases, poses an enormous opportunity for the electronic components, systems and embedded intelligence industry. Moreover, because their input is required in three areas:

- Wearable devices and patches, were the actual monitoring takes place;
- Data infrastructure, required to collect and store data (e.g. gateways, data warehouses);
- Feedback tools, to provide relevant feedback to patients and care professionals (e.g., smartphones, smart domestic devices, electronic medical records (EMR)).

Enabling technology platforms

The ECS industry plays an important role in bringing ambulatory monitoring to the next level. Important aspects are reducing costs, improving user friendliness (e.g. easy to wear/use devices, interoperable gateways, reduction of patient follow-up systems) and data security. The following enabling technology platforms can contribute to this:

- *Low power technology*, for sensors, microprocessors, data storage and wireless communication modules etc.;
- *Miniaturization technology*, for sensors, microprocessors, data storage and wireless communication modules etc.;
- *Printed electronics technology*, for textile integration and patch-type housing of electronics;
- *Low power Edge AI computing*, for data analysis and data reduction;
- *Data communication technology*, for interoperability of (wireless) data infrastructure hardware (wearable device connections) and software (data sharing between data warehouses for analysis and with patient follow-up systems for feedback);
- *Encapsulation* for ensuring the performance and the stability of the final device in critical fluids (gastric and intestinal secretions and microbiota);
- *Data security technology*, for interoperability between security hardware and software components.

Links:

- https://www.wearable-technologies.com/

Further Reading:

- https://www.idtechex.com/en/reports/wearable-technology/52

3.10 Point of care diagnostics
Near-patient diagnostics: accurate, fast and friendly

Point of Care Testing (PoCT) represents a reasonably young but continuously expanding emerging domain based on two simple concepts: perform frequent but accurate medical tests, and perform them closer to the patient's home, both approaches leading to a better diagnostic efficiency, and to a considerable reduction of diagnostic costs. PoCT methodology encompasses different approaches from the self-monitoring of glucose or pregnancy, to more professional testing of infectious diseases or cardiac problems.

From an economical point of view the enhancing role of PoCT aims to reduce the diagnostic related expenses currently concentrated in secondary and tertiary hospitals, and increase significantly the diagnostic efforts in the places of primary care, with clear benefits for the well-being of our society and undeniable gain for the quality of healthcare.

Societal impact

Early diagnosis is a key factor for the successful treatment of both modest and challenging medical conditions of the patient. In case of available routine therapy, anticipating the treatment brings enormous benefits to the health of the patient and reduces the costs of medical services to the minimum. For more challenging diseases, early diagnosis and hence early therapies may even result in a full recovery or possibly stabilization of the patient's condition. In the most serious case of missing therapies, an accurate and well comprehended diagnosis represents the only possible way for the development of future cures and solutions, and catching the problem at its earliest evolution steps indubitably leads to its better understanding and facilitates clinical research with enormous benefits for society and its individuals.

Currently, the diagnostic practice is still dominated by the model of consolidated centralized laboratories with automated analytical processes that are able to handle large numbers of samples at reasonably low costs. Nevertheless, the substantial and continuous growth of healthcare costs and the new demands advanced by the demographic (ageing) transformation asks for a major change of this strategy.

Relevance for the Electronic Components and Systems (ECS) industry

PoCT systems cannot exist without smart electronic solutions, except for the simplest cases of purely chemical dipstick technologies.

The key enabling components of current PoCT devices must include smart and friendly interfaces, sensors, controllers and communication systems as well as data processing and storage.

These ECS based components have to interact in a most smart and efficient way with the bio-chemical modules of PoCT systems, such as reagents and reaction cells and with the sample control/delivery system, enhancing further the role of electronics and demanding a fruitful multidisciplinary interaction at all the levels of development and utilization.

The potential of ECS industry to contribute to the development of new, and the improvement of existing PoCT solutions is enormous. What is still partly overlooked, is the major interaction with the biomedical field, which should move more towards a kind of "supply and demand" scheme. Often the development of powerful and sophisticated engineering tools does not lead to a significant market success, if any, because they do not align with established medical workflows.

Enabling technology platforms

PoCT systems are typically divided in two categories: portable devices and desktop solutions. The ultimate configuration for a small portable system is a wearable device, communicating with the patient via smartphone.

The *emerging Lab on Chip (LoC) solutions*, *embedding multiple sensor platforms, microfluidics* and simple processing/storage elements is currently the most promising basis for the realization and development of accurate, versatile and user-friendly portable and wearable PoCT devices. In LoC the inspection of various patient parameters is performed directly by molecular testing or indirectly by detecting the modulation of physical signals from optical, magnetic or other functional labels.

Currently, the development of various LoC techniques is driven by desktop solutions, even though their *miniaturization* represents a significant trend in that area. One of the challenges for the ECS community is the gradual downscaling of LoC to wearable or stripe like systems, alongside with the continuous improvement of their accuracy and versatility. Reconfigurable LoC systems, able to switch on demand to the detection of, for example, an emergent virus or microbe, may represent a powerful, if not unique defense for a society with a continuous increasing density of population.
Considering larger PoCT systems, the so called desktop solutions, the efforts are mainly concentrating on their incremental improvement, addressing both accuracy and versatility (multiple analyte detection). Both hardware and software development is crucial and significantly open to the ECS community.

It is expected that wearable solutions will represent in the middle term the preferred choice for screening pathologies (first entry tests, high volumes), still leaving room for conventional diagnosis with complicated desktop devices. In the long term, the anticipated high performance (sensitivity/specificity) of wearable solutions are expected to increasingly replace desktop-based tests.

Links:

- MADIA (Magnetic Diagnostic Assays) – project website http://www.madia-project.eu/
- BIOCBx **(**A miniature Bio-photonics Companion Diagnostics) – project website http://biocdx.eu/

Further Reading:

- S.K. Vashist, "Point-of-Care Diagnostics: Recent Advances and Trends," Biosensors (Basel). 2017 Dec; 7(4): 62.

3.11 Remote sensing and monitoring

Measurements at a distance: the missing link to chronic monitoring

Remote sensing comprises several sensing mechanisms for the continuous monitoring of vital signs. They all operate without physical contact to the subject, hence the term noncontact sensing that is sometimes used.

Remote sensing is a concept that comprises multiple sensing techniques, some of which have gained increased interest recently.

Societal impact

The field of remote sensing holds great promise for lifelong and chronic monitoring of vital signs. Key to achieving that goal is the invisible and completely unobtrusive integration into everyday objects, such as bed sheets, office/car chairs, couch or PC screen. In this case, the strength is not in the quality of the acquired signals, but the longitudinal nature, with the potential to reveal slowly changing patterns - possibly symptoms from underlying physiological changes. The analysis of such datasets, currently largely unexplored, will provide new insights into normal versus pathological patterns of changes over very long periods of time.

Another area where remote sensing could play an important role, is in monitoring of patients that cannot withstand continuous skin contact, such as neonates.

Relevance for the Electronic Components and Systems (ECS) industry

Remote sensing and monitoring holds a great promise in the prevention and very early detection of pathological symptoms. Remote sensing and monitoring has the potential to become embedded into everyday life objects, such as furniture, TV sets, etc. It is targeting the entire population.

Technological challenges are foreseen in

- Miniaturization and integration;
- Distributed data analytics and intelligence;
- Data infrastructure.

Enabling technology platforms

Several distinct techniques are being explored for the implementation of remote sensing, where each technique has a unique set of properties and matching use cases.

- Sensing of *ballistic forces* relies on motion created by the heart and blood flow, which can be captured remotely with force sensors or accelerometers integrated in bed or chair. The method is very sensitive to the presence of other forces and vibrations.
- *Optical sensing* techniques can be used for remote reflective photoplethysmography, since well-perfused areas of facial skin changes tone on every heartbeat. Standard RGB cameras can be used for this purpose, and ambient light can act as light source. Novel hyperspectral cameras can improve the sensitivity of the measurement. In theory, heart rate, respiration rate and even blood oxygen levels could be measured in this way. Technical challenges are found in low light conditions, darker skin tones and under conditions of motion.
- *Capacitive sensing* techniques can capture the body's electrical activity through non-conductive layers (e.g. clothing, bed sheets or seat cover). It allows for remote measurement of ECG and bio-impedance from which heart rate, heart rate variability and respiration rate and (relative) depth can be derived. The distance between the measurement electrodes and patient should be small, so approaches can be utilized in which arrays of electrodes are applied such that pairs of electrodes can be chosen to optimize signal quality.
- *Radar sensing* techniques use electromagnetic waves to remotely measure tiny chest displacements. A beating heart, as well as normal respiratory activity, can cause chest displacements that can be measured with radar techniques from a large distance (10's of meters) and through walls. Obviously, displacements of the user cause big artefacts in the recorded signal.
- Terahertz technologies may also play a role in remote sensing for healthcare applications.

As multiple techniques exist, each with their unique set of advantages and disadvantages, it is likely that the deployment of remote monitoring system will be multi-modal, with fusing techniques to smart analytics to unify the data into usable information. All remote sensing techniques are very sensitive to artefacts, which calls for smart algorithms to continuously quantify signal quality, preferably close to the source (edge computing).

Another challenge is related to the power source of the sensors. The furniture in which sensors are envisioned to be embedded into, is typically not connected to mains power. As a consequence, the sensors might have to be powered from a battery, ideally with a single battery over the lifetime of the sensor. This calls for novel ultra-low power sensing, processing and wireless transmission techniques.

A final challenge is the integration itself. For example, integration of capacitive sensors into bedsheets comes with a washability challenge, integration of radar sensing into a TV set comes with a challenge of antenna integration, etc.

Further reading

- Christoph Brüser et al., "Ambient and Unobtrusive Cardiorespiratory Monitoring Techniques", IEEE Reviews in Biomedical Engineering, Vol 8, Mar 2015 Mar pp 30 – 43.
- Marco Altini et al., "Vital-sign monitoring and spatial tracking of multiple people using a contactless radar-based sensor", Nature Electronics, June 2019, pp 252 - 262.

3.12 E-health
Enabling tailored care in the right place

According to World Health Organization (WHO), E-health is defined as the use of information and communication technologies (ICT) for health purposes. As such it is also acknowledged that digital technologies have the potential to play an important role in improving public health.

E-health covers a wide scope of applications, ranging from ambulatory monitoring, coaching and even treatment of diseases. A characteristic of E-health is that it enables the shift of standard care that would normally take place in a hospital setting to an environment that is more trusted and comfortable for the patient.

The essence of E-health is that it should enable patients to gain more control over their own health. When patients take an active role in their own care process, they become less dependent on measurements or treatment from a doctor, hospital or any other organization, which leads to better outcomes.

Some examples of successfully implemented E-health applications are:

E-consults: patients get in contact with their health practitioner through a secure video connection. By using such solutions, the patient is not required to be physically present at the hospital.

Tele-monitoring: by combining the ambulatory systems described in Section 3.9 with a secure way of sharing the data with the health institutions it becomes possible to treat patients with chronic diseases such as heart failure or COPD. The patient is responsible for taking their own measurements. As long as the measured values remain within boundaries as set by the specialist, there is no need for the patients to return to the hospital on a regular basis. When measured values go beyond the set thresholds, the treating physician is notified and contacts the patient. This way of working leads to reduction of control visits, ambulance trips and nursing days.

Medication dispensers: in the form of a device that takes care of automatic administration of medicines at the right moment, combinations and dose. This contributes to the reduction of health risks associated with medication errors, especially when related to complex medication schedules.

e-Mental Health: the patient is enabled to get directly in contact with his/her coach or psychologist through an app during episodes of depression or fear. In addition, the app also keeps records of the usage of the phone, activity and locations. By combining these inputs with questions to the patients, an algorithm learns to recognize patterns of situations under which patients are at higher risks.

Ambulatory physiotherapy: by combining virtual reality with apps, physiotherapists can prescribe VR treatment sessions to their patients. The app provides patients with exercises to help them recover in their own environment and when suitable for them. An example is the treatment of cervical problems, where a VR headset is used to monitor and slowly increase the range of motion of an injured neck or shoulders during several sessions.

Societal impact

The biggest positive effect of E-health applications is expected to be in the following areas:

- **Time and costs saving**: this can be achieved by allowing patients to plan their own consults, while it is no longer required for them to be physically present at the hospital.
- **Insights in own health**: by making use of portals to manage the health records, patients get more engaged with their own treatment. Besides this, it allows patients to selectively share their data with the different caregivers, which leads to faster and more tailored treatments.

- **Living longer at home**: E-health enables people to live longer and independently at home, which in due time leads to costs savings.
- **Less administrative tasks**: E-health can help in reducing de administrative burden to the caregivers, allowing more time for contact with patients and easier sharing of electronic records among specialists.

Relevance for the Electronic Components and Systems (ECS) industry

The relevance of E-health for the ECS industry is very similar to the one of the ambulatory monitoring setting described in Section 3.9, especially because the same type of sensors and technologies are used to gather, process and transfer data.

The ECS industry is a key player in the enabling and upscaling of E-health applications. The biggest challenge nowadays for E-health applications is reaching such a level of interoperability that patient and different care givers involved in the chain can work in an optimized way. The ECS industry should work in close collaboration with the different stakeholders in the health care system on several layers:

- **Governance**: arranging the proper agreements upfront. E-health is not limited to the delivery of a system/sensor. Most applications deliver a service in the form of software where several health institutions may be involved in the chain of care.
- **Processes**: moving care from the hospital setting to ambulatory settings also asks for a different way of working, e.g., the co-development of new standards or guidelines for specific diseases.
- **Information**: adapting a standardized way of sharing information among caregivers.
- **Applications**: the development of the solutions that help in reducing costs while at the same time improve user-friendliness.
- **Infrastructure**: some E-health applications might require infrastructural adaptions to either the hospital centres or the E-health site. Examples are secure internet connections in the case of teleconsulting or new water systems and electricity for home dialysis.
- **Data protection**: ensuring the availability, exclusivity and integrity of all sorts of information collected, processed and transferred by the E-health application.
- **Guidelines and legislations**: proactively monitor developments in international standards and changes in legislations in order to reduce the time required to develop E-health applications.

Enabling technology platforms

The enabling technology platforms for E-health are almost identical to the ones described in Section 3.9, with extra emphasis on data security technology and frameworks to evaluate the efficacy and acceptance of these types of applications.

Links:

- www.luscii.com
- https://www.cardiologiecentra.nl/en/patienten-2/our-care/hartwacht/
- https://www.lifeline.philips.com/pill-dispenser/health-mdp.html
- https://www.ginger.io/
- https://inmotionvr.com/

Further reading:

- Kummervold, Per, et al. "E-health trends in Europe 2005-2007: a population-based survey." Journal of medical Internet research 10.4 (2008): e42.
- Barbabella, Francesco, et al. "How can E-health improve care for people with multimorbidity in Europe?" Copenhagen: World Health Organization, Regional Office for Europe, 2017.

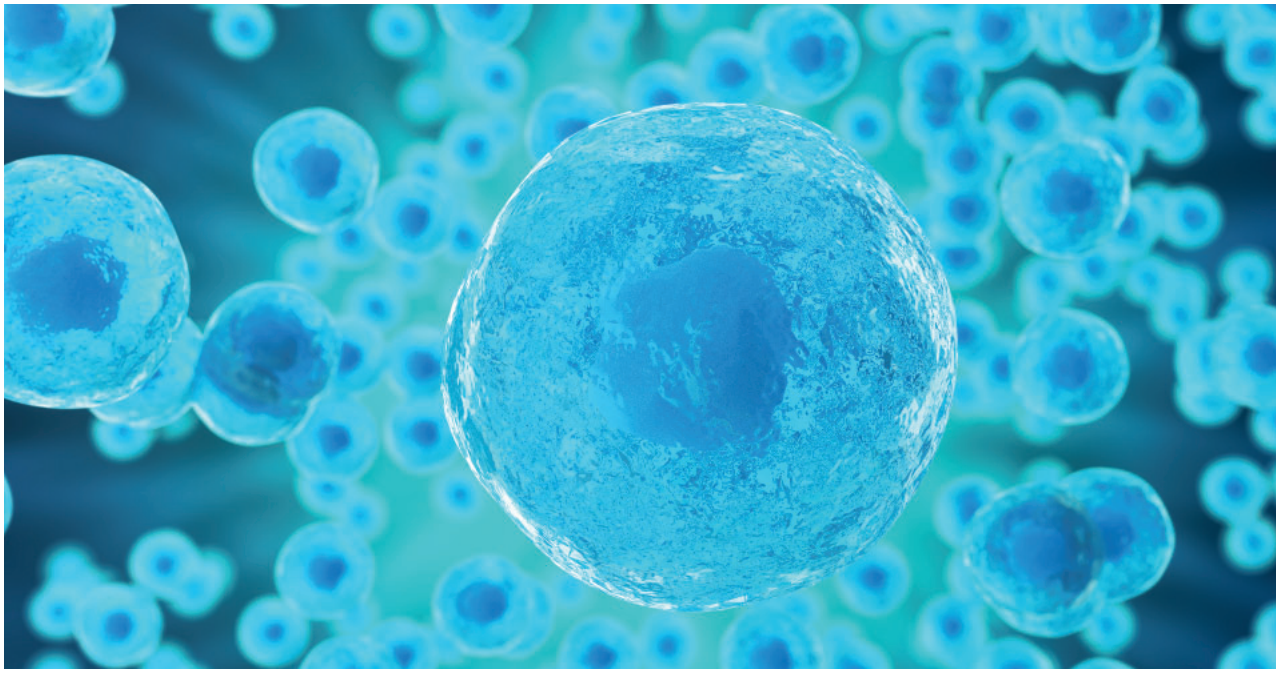
3.13 Advanced therapies using genes, cells and tissues

Scalable manufacturing brings personalized cures and treatments to those in need

Advanced therapy medicinal products (ATMPs) are medicines for human use that are based on genes, tissues or cells. They offer ground-breaking new opportunities for the treatment of disease and injury. ATMPs embrace gene therapy medicines, somatic-cell therapy medicines, tissue-engineered medicines. Gene therapy medicines contain genes that lead to a therapeutic, prophylactic or diagnostic effect and are injected into the body. Somatic-cell therapy medicines contain cells or tissues that have been manipulated to change their biological characteristics or cells or tissues not intended to be used for the same essential functions in the body. Tissue-engineered medicines contain cells or tissues that have been modified so they can be used to repair, regenerate or replace human tissue. ATMPs are exciting new areas of medicine that are just starting to gain regulatory approval. They cover a wide range of individual treatments from CAR T cell cancer therapies (e.g. Kymriah against leukemia and Yescarta against lymphoma), gene therapy (e.g. Zolgensma against spinal muscular atrophy) to regenerative medicine for rare genetic diseases, degenerative disorders such as Parkinson's or other defect disorders (e.g. Carticel for repairing cartilage defects). In all its diversity, mastering the entire manufacturing process from source to patient is key for ATMPs.

Societal impact

ATMPs jump into the gap where classical medicine alternatives are scarce, of low effectiveness or simply non-existent. Autologous treatments with cells obtained from the patient him/herself and re-injected after therapeutic modification offer new avenues to more effective treatments and even cure of diseases (however at a cost of $400k to $2M per patient). Tissue engineering can improve effectiveness of organ and tissue transplantations or replace it by generated tissue, overcoming today's shortage of donor material (about 20% of patients on the liver transplant waitlist die or become too sick to be transplanted). Today, broad adoption of ATMPs is hampered by its cost, not bearable by public health systems and thus by far not reaching all those in need. Automation of ATMP processes are critical to broader adoption and require significant efforts to develop appropriate, safe and scalable platforms and processes.



Relevance for the Electronic Components and Systems (ECS) industry

ATMP biomanufacturing must be transformed from artisanal manufacturing towards high yield/high quality production yet keeping the promise of personalized treatment. The ECS industry can enable ATMP 4.0 by leveraging its expertise on Process Analytical Technology (PAT) for pharmaceutical manufacturing and its efforts towards Industry 4.0. ATMP 4.0 needs to address the inherent variability of the biological cell, gene and tissue material with technology. The convergence of size between biological components and the ECS technologies (nanometer to micrometer) is of great interest for automated systems, possibly decentralized at bedside, and compatible with the scarcity of resources.

The ECS industry can contribute to ATMP 4.0 with

- Microfabrication technologies for *embedded microfluidics* (materials such as silicon or polymer and compatible with biological systems) for production, sorting and manipulation of cells and cell culturing in scaffolds;
- Miniaturized sensor and actuator components for bioprocess monitoring and control;
- *Real-time embedded process control and monitoring* platforms (energy efficient, secure and connected);
- AI-support through efficient (edge-)AI computing hardware / software.

Enabling technology platforms

Essential capabilities for ATMP 4.0 relate to *embedded process control and monitoring* and *embedded microfluidics*. The ECS industry can contribute here with open technology platforms for manufacturing and assembly of *embedded microfluidics* devices, ideally on a foundry service base. Additionally, it can drive standardization of the physical interfaces and testing. Equally important, it can establish systems control, interconnectivity and data standards and contribute the necessary sensors and actuators, embedded systems, and edge AI hardware and software enabling *embedded process control and monitoring*.

Synergies exist with other domains. Organ-on-chip, point of care diagnostics, bioelectronic medicines and smart drug delivery also draw on sensors and actuators and miniaturized microfluidic devices. ATMPs may also contain one or more medical device as an integral part of the therapy administration (combined ATMPs).

Links:

- European Medicines Agency (EMA) – overview ATMP - https://www.ema.europa.eu/en/human-regulatory/overview/advanced-therapy-medicinal-products-overview.
- Alliance for Regenerative Medicine (ARM) - Annual Report 2019 – https://alliancerm.org/sector-report/2019-annual-report/.
- The three obstacles stopping cell therapy becoming mainstream – labiotech, July 13, 2020 - https://www.labiotech.eu/in-depth/cell-therapy-obstacles-widespread-use/
- Raising the bar in manufacturing cell therapy products – imec, white paper 2018 - https://www.imec-int.com/en/expertise/lifesciences/cell-and-gene-therapy
- OrganTrans – Organoids transplantation – project web site https://organtrans.eu

Further Reading:

- Elverum, Whitman – Delivering cellular and gene therapies to patients: solutions for realizing the potential of the next generation of medicine, Nature Gene Therapy, 25 April 2019 (open access).
- Iancu, Kandalaft – Challenges and advantages of cell therapy manufacturing under GMP within the hospital setting, Current Opinion in Biotechnology, 11 July 2020 (open access).
- Puleo, Davis, Smith – Enabling Technology in Cell-Based Therapies: Scale-Up, Scale-Out, or Program In-Place, SLAS Technology 2018, Vol. 23(4) 299-300 and entire volume 23(4).
- Ramos, Moroni – Tissue Engineering and Regenerative Medicine 2019: The Role of Biofabrication – A Year in Review, Tissue Engineering Part C: Methods, Vol. 26 (2), 3 Feb 2020 (open access).

4 Projects connected to the Health.E Lighthouse

The objective of the Health.E Lighthouse initiative is to accelerate innovation in ECS-based healthcare. This is being pursued by reaching out to European initiatives and communities that are active in this field. A continuous exchange and cooperation between these initiatives will help in creating an ecosystem that will reduce fragmentation and duplication of R&D efforts and that will stimulate the development of open technology platforms.
A list of projects associated with the Health.E Lighthouse is presented below. This list is not exhaustive or definitive, since this initiative is open to every project or consortium in the field that is willing to join.

Moore4Medical	Development of open technology platforms for six emerging medical domains. url:
ASTONISH Advancing Smart Optical Imaging and Sensing for Health	Imaging and sensing technologies for monitoring, diagnosis and treatment applications. http://www.astonish-project.eu/
POSITION II	Open technology platforms for the next generation smart catheters and implants. http://position-2.eu/
SCOTT Secure Connected Trustable Things	Solutions for wireless, end-to-end secure, trustworthy connectivity and interoperability. https://scottproject.eu/
EnSO Energy for Smart Objects	Micro energy sources for smart health, society and mobility. http://enso-ecsel.eu/
InForMed	An integrated pilot line for (micro-fabricated) medical devices. http://informed-project.eu/

Projects connected to the Health.E Lighthouse

VOSTARS

Augmented Reality Glasses for Surgical Guidance.
https://www.vostars.eu/

SOLUS

Smart optical and ultrasound diagnostics of breast cancer.
http://www.solus-project.eu/

ORCHID
organ-on-chip in development

Creating a roadmap for organ-on-chip technology and building a network of all relevant stakeholders.
https://h2020-orchid.eu/

MADiA
MAgnetic Diagnostic Assay for neurodegenerative diseases

Magnetic Diagnostic Assays for early diagnosis of Alzheimer's and Parkinson's diseases.
http://www.madia-project.eu/

BIOCDx

A miniature Bio-photonics Companion Diagnostics platform for reliable cancer diagnosis and treatment monitoring.
http://biocdx.eu/

MedPhab
Photonic Medical Devices

hotonics Solutions at Pilot Scale for Accelerated Medical Device Development
https://medphab.eu/

Projects connected to the Health.E Lighthouse

IMPETUS

PPilot line for paper based electrochemical test strips dedicated to quantitative biosensing in liquids
http://www.project-impetus.com/

PIX4life

Pilot Line in Photonics
https://pix4life.eu/

Penta

ULIMPIA
ULTRA-SOUND BODY PATCHES

A platform for smart ultrasound body patches.
http://ulimpia-project.eu/

5 List of workshop participants

The list of emerging medical domains identified in this White Paper was compiled and discussed during a "Vision Workshop", which took place online on August 26, 2020. Participants were the HELoS project partners, HEALTH.E Lighthouse representatives, project owners and other stakeholders in the ECS/medical domain. These stakeholders included representatives from electronic, medical and pharmaceutical industry, RTOs, academia, SMEs and the European Commission. A complete list is presented below.

AARTS	Jos	MAASTRICHT UNIVERSITY	NL	RES
AGUAR FERNANDEZ	Maria Pilar	EC DG RTD	EC	EC
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BOISSEAU	Patrick	MEDTECH EUROPE	BE	CO
CHARBIT	Françoise	CEA	FR	RES-RTO
CHICHKOV	Anton	ECSEL JU OFFICE	BE	ECSEL
COURTNEY	Patrick	SILA	CH	CO
DALLA MORA	Alberto	POLITECNICO MILANO	IT	RES
DE COLVENAER	Bert	ECSEL JU OFFICE	BE	ECSEL
DEDIU	Valentin	CNR	IT	RES
DEKKER	Ronald	PHILIPS	NL	CO
DELMAS	Dominique	VALOTEC	FR	CO
EBERLE	Wolfgang	IMEC	BE	RES-RTO
FERRARI	Vincenzo	UNIVERSITY OF PISA	IT	RES
FIRTAT	Bogdan	IMT	RO	RES-RTO
FOSTER	Alun	ECSEL JU OFFICE	BE	ECSEL
FURJES	Péter	MFA	HU	RES-RTO
GAIO	Nikolas	BI/OND	NL	CO
GALVIN	Paul	TYNDALL	IE	RES-RTO
GARCIA VAN DER WESTEN	Roberto	IMEC	NL	RES-RTO
GRAEF	Mart	TU DELFT	NL	RES
GRAF	Thomas	SIEMENS HEALTHINEERS	GE	CO
GRALKA	Anna	TU DELFT	NL	RES
GRUNDLEHNER	Bernard	IMEC	NL	RES-RTO
GYORVARY	Erika	CSEM	CH	RES-RTO
HAINBERGER	Rainer	AIT	AT	RES-RTO
HENNEKEN	Vincent	PHILIPS	NL	CO
HILTUNEN	Jussi	VTT	FI	RES-RTO
HOFSINK	Robert	PHILIPS	NL	CO
HOLSTE	Dirk	AIT	AT	RES-RTO
HUIBERTS	Hans	PHILIPS	NL	CO
JUNG	Erik	FRAUNHOFER IZM	GE	RES-RTO
LAPLATINE	Loïc	CEA LETI	FR	RES-RTO
LYMBERIS	Andreas	EC DG CONNECT	EC	EC
MALONEY	Colette	EC DG CONNECT	EC	EC
MARRON BRIGNONNE	Lucile	SURGIQUAL	FR	CO
MASTRANGELI	Massimo	TU DELFT	NL	RES
MOLDOVAN	Carmen	IMT	RO	RES-RTO
NOWAK	Anna-Zuzanna	ECSEL JU OFFICE	BE	ECSEL
PAGGETTI	Cristiano	ORTHOKEY	IT	CO
PAOLETTI	Samantha	CSEM	CH	RES-RTO
PERING	Christiane	BAYER	GE	CO

PERKO	Hannes	AIT	AT	RES-RTO
PFALZ	Birgit	BAYER	GE	CO
REIS	Lurdes	BAYER	GE	CO
RYDZ	Alexandra	FRAUNHOFER IZM	GE	RES-RTO
SALOT	Raphaël	CEA LETI	FR	RES-RTO
SWAVING	Sieger	PHILIPS	NL	CO
TARONI	Paola	POLITECNICO MILANO	IT	RES
VAN DEN BRAND	Jeroen	TNO	NL	RES-RTO
VANDENBERGHE	Patrick	ECSEL JU OFFICE	BE	ECSEL
VERPLANCK	Nicolas	CEA LETI	FR	RES-RTO
WEBSTER	Carlo	TYNDALL	IE	RES-RTO
ZANDBERGEN	Peter	PHILIPS	NL	CO
ZERGIOTI	Ioanna	NATIONAL TECHNICAL UNIVERSITY AT	GH	RENS RES
VAN VELTHOVEN	Charlotte			NL

More information: www.health-lighthouse.eu