ECS for European Leadership
in Emerging Medical Domains

White paper for policymakers
May 2022

Health.E
Moore for Medical

ECSEL Joint Undertaking
Electronic Components and Systems for European Leadership
ECS for European Leadership in Emerging Medical Domains

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White paper for policymakers, detailing the top five prioritization of the emerging medical domains, addressing per emerging domain a conceptual explanation, societal and economic impact, and additions needed for the Strategic Research Agenda for European leadership
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1 Introduction

Changing healthcare
Healthcare constitutes one of the major challenges that are facing modern society. Due to demographic and global trends such as an ageing population, environmental changes and the increasing risk of pandemics, new solutions are needed that can be made available at affordable costs. At the same time, the nature of healthcare is changing. It is becoming more and more decentralized, personalized and focused on prevention rather than curing. These changes in healthcare are causing a fading of the borders between medtech, pharma and the electronic components and systems (ECS) industry. At the interface between these communities, new medical domains are developing that offer diagnosis and treatment solutions that address the needs in healthcare.

Opportunities for the ECS industry
Many of these new medical domains offer attractive opportunities for the ECS industry as they rely on digital instruments, advanced electronic sensors and photonics, (Bio)MEMS, and the high volume, high quality low cost production capabilities of the ECS industry.

The Health.E Lighthouse organized a series of three workshops with participants from the ECS and medtech industries, RTOs, projects connected to the Lighthouse, and other stakeholders, such as policymakers and healthcare organizations. The objective of the first workshop was to generate an inventory of emerging medical domains relevant to the ECS community. This resulted in the following un-prioritized list:

- 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

After the identification of these domains, the challenge was to devise a strategy for the development of these areas. This was done in the second workshop, where the role of open technology platforms (OTP) for innovation in electronic medical devices was analyzed. The “lessons learned” were shared with the community of stakeholders in the third workshop.

Innovation in electronic medical devices
Despite the great opportunities for industry and the promise for society, the speed of innovation in electronic medical devices is still slow compared to the speed of innovation in the consumer domain. This is only in part 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, resources are being wasted on the development of expensive point solutions, as much work is done in uncoordinated parallel efforts. 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 technology platforms have accelerated the pace of innovation, reduced risk and lowered costs. There is no reason, apart from convention and habit, why open technology platforms could not be implemented for medical devices.

1 These emerging domains are discussed in detail in the Health.E whitepaper “Emerging Medical Domains for the ECS industry” https://www.health-lighthouse.eu/publications
“Moore for medical”

The current practice with respect to the manufacturing of medical devices is somewhat reminiscent of the situation in microelectronics in the early seventies. Each medical device is developed as a dedicated instrument for a specific application. As the sophistication and complexity of these devices grow, the development costs will increase exponentially, and in due time innovation by the creation of point solutions will no longer be sustainable.

This problem can be alleviated by the implementation into the healthcare domain of the lessons learnt in the microelectronics industry. The complexity of a medical device is increasingly determined by its electronic content, a development that is very similar to what happened in the communication industry some decades ago (with the advent of smartphones) and in the car industry more recently. Electronic components and systems will play the same role as enablers and drivers of innovation in the medical and pharmaceutical industries and in the healthcare domain in general.

This paradigm change in the healthcare domain can be achieved by a basic change in development strategy and methodology. In the conventional development model, new medical devices are dedicated point solutions designed from scratch, using unique components and a unique architecture. In the new development model, a novel medical device is designed as an integrated smart system, incorporating ECS-based components and embedded software. Both the hardware and software subsystems are embodiments of generic technologies, based on standard semiconductor processes (available from foundries), standard design tools and commercially available (or even open source) software solutions.

**ECS for European Leadership in Emerging Medical Domains**

In this white paper, the five emerging medical domains that have the highest relevance for the European ECS industry will be discussed. In the following chapter these emerging domains are presented, while also suggestions are made for research and innovation topics that might result in open technology platforms that will help securing Europe’s leadership in this societally and economically relevant field that up till now remains largely unexplored.

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2 The Health.E lighthouse white paper “Open Technology Platforms for Emerging Medical Domains” discusses the advantages and challenges related to OTPs for medical devices. https://www.health-lighthouse.eu/publications
2 Prioritized emerging medical domains

Thirteen emerging medical domains were identified in the white paper “Emerging Medical Domains for the ECS industry”, published by the Health.E Lighthouse. After a prioritization according to their relevance for the ECS industry, five domains have been selected for discussion in this document. They are presented in this chapter in arbitrary order.

Recommendations to the strategic research agenda are listed per prioritized emerging medical domain, although it should be stressed that many of the recommendations, e.g. on data security, are relevant for multiple domains.

2.1 Bioelectronic medicines

Towards an electrical cure for chronic diseases

For many years, active implantable devices have been used to treat chronic conditions with minimal side effects. 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.

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 originate from 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 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 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 on 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.
Recommendations for the strategic research agenda

Soft encapsulation technology
In contrast to present electronic implantable devices that rely on heavy titanium casings, the next generation of smart implantable devices will have to be small and lightweight, suitable for implantation deep inside the human body. Polymer encapsulation is explored in several EU initiatives, but further action is needed to fully validate the technology and to bring it as an open technology format to a high TRL level.

Power delivery and storage
Bioelectronic medicines will need a form of energy storage that is inherently safe to the body, has a small form factor and a high power density. Presently, there are no commercially available energy storage elements that satisfy all these requirements. Also, the charging of implants from a power source outside the human body is not trivial, especially for deep implants where inductive or RF charging is not a viable option. Currently, ultrasound powering is explored to effectively supply power to and provide communication with deep implants. Although encouraging results have been demonstrated, the technology is still far from being a commercially available OTP offering. Biofuel cells are an attractive power source alternative, but still require some form of local storage to accommodate peak power consumption.
2.2 Ambulatory and remote sensing and monitoring

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. The status of these parameters play an important role in the onset of chronic diseases and therefore, also their cure and prevention.

Recent technological developments 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.

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

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. Ambulatory and remote sensing and 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 costs of hospitalization and sick leave. More importantly, it greatly reduces the social and physiological burden of being hospitalized. 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 and remote monitoring can play an important role in accelerating 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 ECS industry

The prospect of the deployment of ambulatory and remote sensing and 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. ECS based solutions are 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)).

Recommendations for the strategic research agenda

Data security

The protection of personal data is one of the major challenges for (wireless) medical monitoring devices, especially if these are used in the home environment.

Today, lightweight cryptography and key management ensures security in the resource constrained sensor nodes within the edge. The e-Passport is the unique worldwide standardized e-ID document and can be applied to health
applications for identity management and authentication. When transitioning between the edge and the cloud, the traditional cryptographic tools for securing the data in transit (e.g., transport layer security (TLS)) and storage (symmetric disk encryption) are not sufficient anymore. Several technologies have been proposed to ensure end-to-end (E2E) security and privacy of medical data. However, an open platform that combines the required E2E security with the low power requirements is still missing and could be the objective of a dedicated EU initiative.

Wearable ultrasound
So far, wearable monitoring devices can only monitor parameters accessible at a person’s skin, e.g. electrical potentials, light reflection and absorption, humidity, movement, etc. With the development of MEMS ultrasound devices, it has become possible to develop wearable devices (“patches”) that can also monitor processes deep inside the body. Affordable 3D ultrasound transducers, small, lightweight, and high-capacity batteries, power efficient edge computing, ultrasound compatible adhesives are just a few of the innovations that could be topics of new EU initiatives.

Sensors
Remote sensing comprises several sensing mechanisms for the continuous monitoring of vital signs. They all operate without physical contact to the subject. It is sometimes also referred to as “the next step after ambulatory monitoring.” To make remote sensing the solution for lifelong and chronic monitoring of vital signs, a continuous effort is needed to push sensor technology towards the limits of what is technologically and physically possible. These sensors include:

- Sensing of ballistic forces;
- Optical sensing techniques;
- Capacitive sensing;
- Radar sensing;
- Terahertz technologies.
2.3 Portable ultrasound

Ultrasound diagnostics and monitoring everywhere and by anybody
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.

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 first-line caregivers 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 home fetal monitoring.

With the development of MEMS ultrasound devices, it has also become possible to develop wearable devices (“patches”) that can also monitor processes deep inside the body.

Relevance for the 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, ultrasound diagnostics presents 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.

Recommendations for the strategic research agenda
Affordable 3D ultrasound
The MEMS ultrasound benchmark in the ECSEL JU project POSITION-II has shown that MEMS ultrasound transducers are reaching a level of technical maturity comparable to standard piezo transducers. Furthermore, these transducers are already offered as an open technology platform by several manufacturers. It is expected that the combination of 3D ultrasound acquisition combined with AI will eliminate the need for skilled sonographers and will bring ultrasound imaging and diagnostics to first line caregivers and even consumers. However, in contrast to optical sensors, where the pixels can be scaled down to micron size dimensions, the dimensions of an ultrasound transducer will always remain large (cm range), since the dimensions are directly coupled to wavelength and penetration depth. When these transducers are made monolithically, the costs might be prohibitive. This calls for the development of alternative technologies, where a large aperture is achieved by a combination of so-called sparse matrices and advanced assembly techniques.
Ultrasound compatible adhesives
Since high frequency ultrasound does not propagate through air, in clinical settings an acoustic gel is used to couple the ultrasound from the transducer into the body. In the clinic optimal performance is required, and the use of a wet gel is acceptable. However, in a first line care setting or home environment the use of a wet gel is less desirable. Dry solutions, consisting of an ultrasound conducting adhesive type film in combination with an advanced acoustic matching layer stack (window) on the transducer have already been demonstrated in research. For personal and wearable ultrasound to become a practical reality, these devices must be developed to the level of commodity products. This will require the availability of open technology platforms.

Optimized edge AI technology
The concept of low-cost portable, personal, or even wearable ultrasound can only be realized by a combination of 3D ultrasound acquisition and optimized edge AI to extract from the 3D data the relevant clinical information without the need of a skilled sonographer. Optimized architectures are needed to minimize the computational power consumption in the portable and wearable applications, and to limit the data traffic between the application, the hub and the cloud.
2.4 Point-of-care diagnostics and wound monitoring

Near patient diagnostics: accurate, fast and friendly
Point of care testing represents a reasonably young but continuously expanding emerging domain based on two simple concepts: perform frequent but accurate medical tests and perform them close to the patient. Both approaches lead to a better diagnostic efficiency and to a considerable reduction of diagnostic costs. Point of care methodology encompasses different approaches from the self-monitoring of glucose or pregnancy to more professional testing of infectious diseases or cardiac problems.

A point of care modality that has especially high potential for social and economic impact is “smart wound monitoring”, i.e. the merger of highly miniaturized sensors, electronics, 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.

Societal impact
Early diagnosis is a key factor for the successful treatment of both modest and challenging medical conditions of patients. 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. Currently, the diagnostic practice is still dominated by the model of consolidated centralized laboratories with automated analytical processes that can 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.
In the special case of chronic wound monitoring, the economic price of prolonged cost of 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 and curtail social and economic activities. 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.

**Relevance for the ECS industry**

The key enabling components of current point of care devices includes smart and friendly interfaces, sensors and communication systems, as well as data processing and storage. These ECS based components must interact in a smart and efficient way with the bio-chemical modules of point of care systems, such as reagents and reaction cells and with the sample control/delivery system.

The European ECS industry has the tools and expertise required to make point of care systems and smart wound dressings a reality. 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.

**Recommendations for the strategic research agenda**

**Miniaturization**

Smart Lab-on-Chip (LoC) solutions, embedding multiple sensor platforms, microfluidics and simple processing/storage elements are currently the most promising basis for the realization and development of accurate, versatile, and user-friendly portable and wearable point of care devices. Currently, the development of various LoC techniques is driven by desktop solutions. However, their miniaturization to portable or even wearable devices represents a significant opportunity for the ECS community. LoC miniaturization, together with the continuous improvement in accuracy and versatility, will be crucial in opening this huge market to the ECS industry.

**Dressing integration platforms**

Although technology platforms for the (roll-to-roll) manufacturing of smart body patches are readily available from several vendors, there are presently no advanced manufacturing technologies for the reliable integration of microelectronic technologies with foam- and polymer-based dressing materials. Collaborative project initiatives in this direction should address topics such as:

- Biodegradable materials;
- Incineration compatible assembly of electronics (e.g., a bare silicon die is incineration compatible, but an epoxy packaged device is not);
- Encapsulation technologies to protect the electronics from bodily fluids;
- Complete end-of-life strategy.

**Incinerable power sources**

One of the great hurdles in the development of smart wound dressings for the treatment of e.g., chronic wounds is that in most cases these dressings after use are labelled as clinical waste, which cannot be recycled or disposed of in a traditional manner but needs to be incinerated. This will require the selection and development of special materials and substrates that can be disposed of in that manner in an environmentally friendly way. Technology platforms are needed to create solutions to power these dressings remotely, and for batteries that have a reasonable capacity, are low-cost and are still incinerable.
2.5 Smart drug delivery

*Improve patient adherence and help to move healthcare from hospital to home*
Recent years have seen significant increase in the prevalence of chronic diseases such as diabetes and autoimmune conditions, and the very high cost of the drugs 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 the 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 ECS industry**

The 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 sensorised 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. 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.

**Recommendations for the strategic research agenda**

**Miniaturized micro-pumps**

Manufacturable, low cost and easy to use micro-pumps are not only an enabling component for smart drug delivery devices, but also for organ-on-chip. In the ECSEL JU project Moore4Medical, miniature silicon based micro-pumps are being developed, tested, and even transferred to a production level. Although these pumps have an excellent performance, their technology is cumbersome and difficult to scale up to large volumes. Furthermore, they require individual assembly of a piezo ceramic actuator and a high driving voltage. The development of an open technology platform for low-cost high performance micro-pumps will benefit more than one emerging medical domain.

**Environmentally friendly materials**

Smart drug delivery devices will sometimes be used on a daily base and for a large part will be disposables. This implies that they not only need to be low-cost, but they also call for the development of new materials platforms for e.g., containers and microfluidics that will meet stringent environmental and clinical disposal standards.
3 Conclusion

Within the scope of the Health.E Lighthouse Initiative, an inventory was made of emerging medical domains that can be served by the ECS industry. Open technology platforms play a crucial role for the development and manufacturing of innovative ECS-based medical devices. The application of best practices and methodologies from the microelectronics industry in the medical domain will give a boost to innovation in healthcare.

The Health.E Lighthouse organised three workshops with stakeholders, to generate a vision (identification of emerging medical domains), to develop a strategy (based upon open technology platforms) and to disseminate these insights, respectively. The results have been made available to the public in three white papers, including the present one.

For five emerging medical domains which were considered to be of particular importance for the ECS community, a number of recommendations for policymakers and stakeholders have been generated, which are presented in this document. These recommendations may serve as input for the construction of a European strategic research agenda for the healthcare domain and as a reference for cooperative initiatives across the value chain.

The recommendations given are not exhaustive. It is expected that many new opportunities for innovation will emerge as the increasing availability of ECS-based open technology platforms will revolutionize the healthcare domain.