Photonics21 Strategic Research and Innovation Agenda (SRIA) –

Main socio-economic challenges addressed (~1 page)

The trend of the European population to age increasingly is still unbroken: the number of people today older than 65 relative to those in the working-age is assumed to double by 2045. Accordingly, age-related diseases like Type 2 Diabetes, many cancer subtypes like breast cancer in females and prostate cancer in males as well as lung cancer for both sexes[1], dementia and macular degeneration are on the rise. However, there are not only serious diseases but also less severe conditions that afflict patients like infections of the gastrointestinal system or urinary tract infections, where new methods could help to decrease the burden.

Traditionally care only sets in once a disease is diagnosed. Well-being could strongly be improved and suffering reduced if we would change this paradigm into the prevention of diseases, early risk assessment or, at least diagnosis before the onset of symptoms. Photonic tools and methods can help identifying the underlying mechanisms for the big diseases which affect millions, e.g. Alzheimer's and Parkinson disease, or finding ways for early detection of, e.g., pancreas, lung or colorectal cancer, or understanding how major global pathogens cause infections on a molecular, cellular, tissue and organism level. Early intervention starts with diagnosis and therapy in utero, at birth and beyond for conditions where the social burden is increasing as the society ages, for example, premature birth and congenital malformations. Here, a major trend is P4 Medicine (Predictive, Preventive, Personalised and Participatory), for which the instant diagnosis of major diseases is imperative.

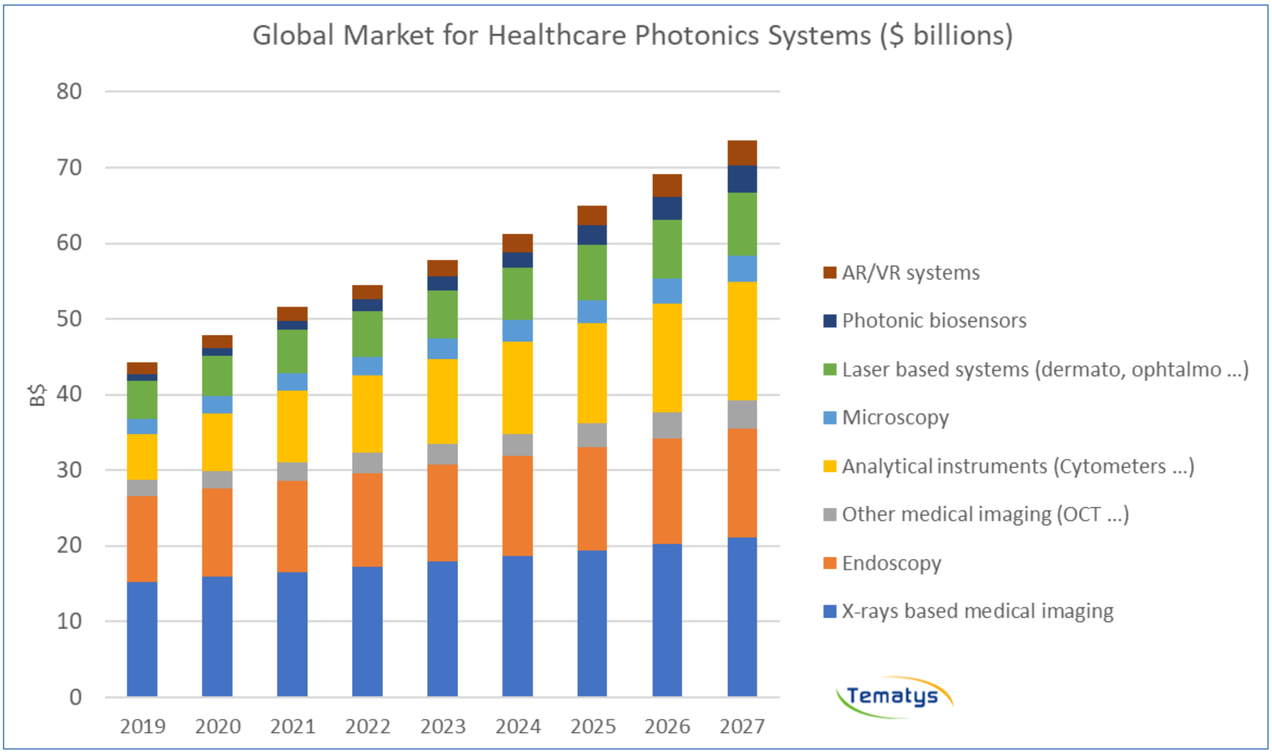
In addition to these central themes, further issues also have to be addressed. One is that our healthcare systems already struggle to keep up with the ever-increasing costs, a fight that will become more difficult due to our ageing society. Healthcare spending already accounts for nearly 10 % of our GDP, amounting to roughly €1 trillion per annum. Saving costs has led to the trend of outsourcing the production of drugs to countries outside the European Union, a trend that needs to be reversed as recently the Covid-19 pandemic has demonstrated. Europe has to strive for sovereignty, which certainly also concerns photonics-based bio- and med-tech products. Costs could also be saved and, at the same time the well-being of European citizens improved if the digital transformation would also be further expedited with regard to patient care. Not only that treatment could be more effective and faster if patients' data would be interchanged between different health care facilities and practices, but the data could help to develop better healthcare solutions, provided that privacy and data security is appropriately taken care of. Last but not least, medical technology also must become greener, e.g., disposables must be avoided where possible and measures to assure saving power must be taken.

European industry is currently among the global leaders in Biophotonics. This market is more mature now and is growing at a rate of about 7% with a total market volume of

[1] (see e.g. http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/incidence-invasive#heading-One)

$87.2 billion in 2019[2]. Photonics systems for Healthcare accounted for a total of $44.1 billion in 2019[3] and are assumed to reach more than $73 billion worldwide by 2027, making it not only one of the largest markets within photonics, but also one of the more rapidly expanding sectors globally, a tendency which will be accelerated by the current crisis. With its rich innovation landscape formed by traditional companies, start-ups, universities and research institutions, Europe has a unique opportunity to secure a prominent role and lead the corresponding markets if the challenges are met accordingly in the next few years.

The market of Photonics systems for Healthcare is illustrated below:



Global Market of Healthcare Photonics Systems

(AR: Augmented Reality; VR: Virtual Reality; See-through imaging: mainly X-Ray & Photoacoustic imaging, Surface imaging: OCT, Ophthalmoscope …) - Source: Tematys

Major photonics research & innovation challenges (~2 pages)

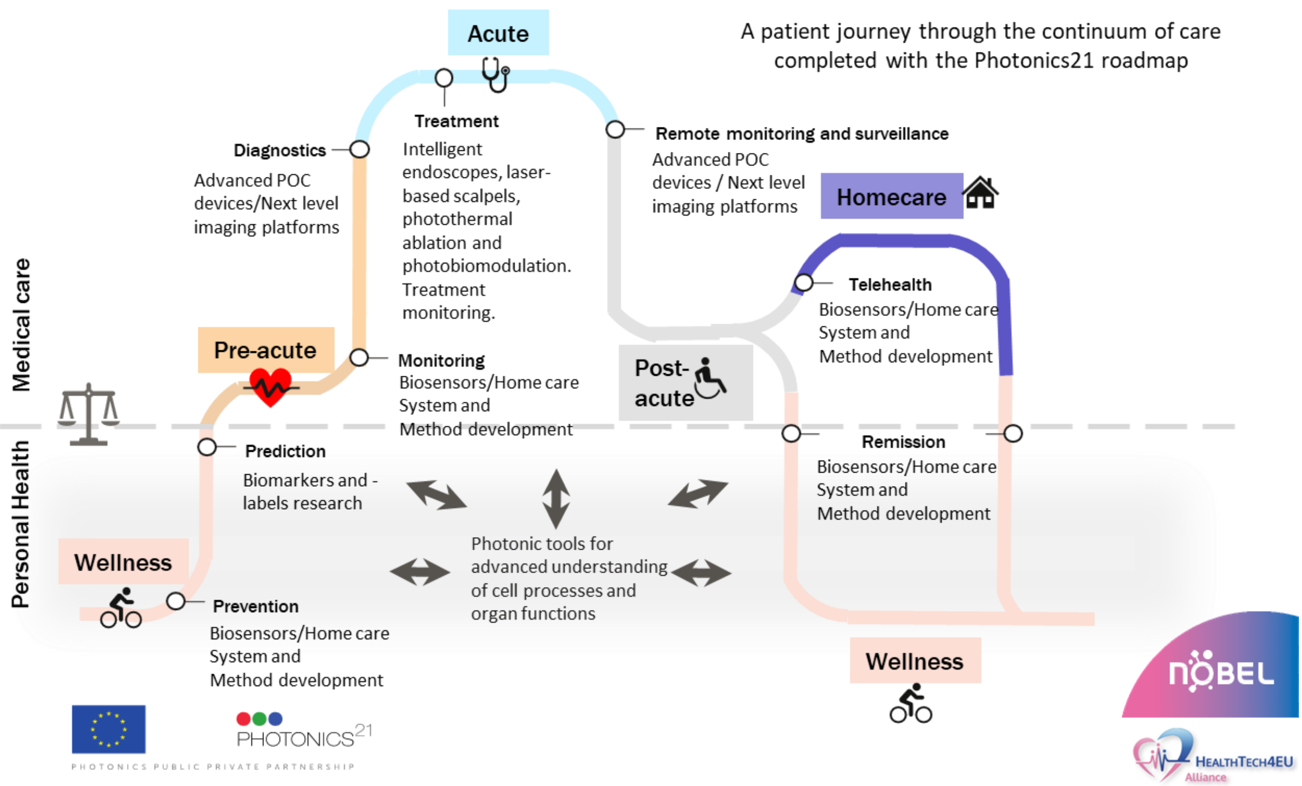
Work Group 3 decided to align its major photonics research & innovation challenges along the continuum of care as it was introduced by the EU project NOBEL and HealthTech4EU:

Accordingly, our goal is to provide photonic tools and methods that aim to support at all stages of a disease, starting with increasing wellness by helping to prevent and to predict those, ideally before their onset. For the pre-acute phase, mobile biosensors and home care systems shall be developed that are able to monitor vital parameters and support diagnostics at the onset of the acute phase. Diagnostics itself requires more advanced equipment, that is point-of-care devices as well as imaging platforms depending on the nature of the disease. In the acute phase, photonic tools and methods need to be (further) developed that support treatment including the monitoring of the

[2] Including spectacle and contact lenses. The figure is extracted from ref 3 below. Note that excluding lenses and X-ray based systems, the rest of the market is growing at a faster rate of about 10%.

[3] Photonics21 – European Technology Platform, VDI Technologiezentrum & Tematys: Market Data and Industry Report 2020.

treatment success. In the post-acute phase such monitoring must be able to be carried out remotely, which means that telehealth will play an important role if the disease could not be cured completely. If the curation is complete, it makes nevertheless sense to further use further/newly developed mobile sensors and home care equipment to accompany remission and help to keep a healthy lifestyle to prevent reoccurrence. An overarching theme is to better understand disease mechanisms and how to detect and interfere with them on a molecular and cellular level. Such findings can improve care at all possible disease states and, eventually, allow to cure diseases before their onset.



In particular in the field of prevention and prediction, sensors have great potential not only to improve and preserve well-being, but also to prevent the onset and outbreak of diseases. Sensor technology needs to be taken to the next levels by miniaturization (photonic integrated circuits), combination of multiple bands (UV-VIS-IR-THz) and techniques in tandem. Corresponding mobile or stationary equipment could not only serve to allow non-invasive and fast personalized diagnostics, but also to scan the environment and surroundings, as well as food and water for potential contaminants, pollutants and microbes. Such surveillance could certainly be also extended to schools, hospitals, workplaces etc. In particular for cardiovascular diseases, e.g. for atrial fibrillation, wearables like watches already prove their value and their usefulness could even be much more extended in the future. In particular in combination with medical databases and artificial intelligence-based methods, data recorded by mobile or stationary sensors could not only be used for surveillance of the medical status, but also to detect the onset of diseases long before their outbreak Overall, such methods might also be useful to remind us to take on and to keep a healthy lifestyle. The photonics parts of such instruments may not only be focused on gaining averaged data like classical point-of-care equipment, but may include imaging solutions, e.g., for in-vivo non-invasive assessment of tissues or organs like the eye. The latter is known to offer easy access for photonic methods and can be seen as window or gateway to body health. This offers a cornucopia of possibilities with high potentials that are still largely unused, not only for acute, but also for systemic diseases. Overall, multi-spectral diagnostic sensor technologies, embedded in hand-helds or even mobile phones, or in stationary forms, combined with AI algorithms for data/image processing have a high potential for a wide range of diseases.

Concerning prediction, we often still lack suitable probes and biomarkers, not only for cancer, but also for many other diseases like cardiovascular, neurodegenerative and liver diseases. Efforts have to be made to improve this situation and enable the use of additional, yet unknown probes. While label-free methods may be preferable, where endogenous markers are missing, label development may be necessary. Towards personalized medicine, it may be necessary to boost bioinformatics and investigations of human-specific metabolic processes.

In the acute phase, when diagnostics is needed, the ability of light-based methods to measure precisely could help to improving diagnostic accuracy in general, leading to a lower rate of false positive diagnoses, which would avoid referrals and unnecessary treatments. At the same time a lower rate of false negative diagnoses would result with fewer undetected and left untreated diseases. Optical imaging of 'difficult to reach' parts of the body, e.g. pancreas, liver, brain via minimally invasive techniques would be desirable. Potentially cellular-scale resolution should be reached, which could be ultimately the gold-standard for diagnosis. This will also help targeting some very difficult to detect and treat diseases, e.g. pancreatic cancer. New imaging technologies like X-ray imaging driven by femtosecond laser or quantum imaging with entangled photons may allow to detect cancerous tissue more easily and more quickly. In addition to imaging, advanced gas sensors used for breath analysis may allow the immediate diagnosis for various diseases such as cancer, infectious diseases, COPD, asthma, etc. The immediate detection of the host response may be enabled by smart based POC cell sensors.

For treatment photonics technologies offer widespread possibilities for treatment monitoring and upgrading endoscopes. Intelligent endoscopes, i.e. spectroscopic endoscopes combined with AI spectral interpretation could be used in the future for fast and reliable diagnosis of cancer combined with light-based ablation for treatment. Endoscopic treatment could, e.g., replace open chest surgery and provide the surgeon with real time feedback. Overall, lasers could replace scalpels and could allow robotic surgeries, flanked by photothermal ablation and photobiomodulation. For both methods it is important to continue to work on the optical dose deposit. In addition, photonic methods can also be used to assist in the fabrication of implants/scaffolds as well as in tissue growth for organ replacement.

An overarching theme is the advanced understanding of cell processes and organ functions. For this the development of new photonic tools would be helpful, in particular of new microscopic technologies which are able to image with higher resolution and higher frame rates. With regard to method development some gaps would need to be closed to, e.g., better understand tissue optics for biomarker detection and simulation thereof to better predict their optical response.

Data evaluation must be performed objectively, by artificial intelligence-based solutions and corresponding software solutions need to be developed. Applying 'explainable' AI to optical sensors/imaging data might be useful, so that clinicians can understand why the AI makes certain decisions and can override those if necessary. Accordingly, there may be a need for a framework for allowing simple descriptions of optical features, e.g., time- and frequency domain spikes that clinicians can understand.

In Biophotonics, as in all medical technologies related fields, the translation of a proof-of-concept to a final product is very challenging. European regulations (MDR) have considerably changed in the last few years and became very complex. The proof-of-concept must have the potential to be developed further into a product which is not only capable of passing clinical trials but also of fitting into a doctor's workflow and gaining their acceptance. Otherwise, the corresponding procedure will fail to be reimbursed. All these steps must also be considered in the face of potentially competing technologies. The whole value chain of a new medical device should be accounted for from the first phases of development. Accordingly, technologists have to work hand with clinicians, patients, and regulatory experts in the same environment in order to avoid that promising technologies arrive too late on the market, or in a form not acceptable for the user. Cost efficiency is also important, i.e., technologies must have a potential of cost reduction using technologies of scale.

Cooperation needs with Horizon Europe Missions or partnerships (~0.5-1 page)

Among the Horizon Europe Missions, the EU Mission: Cancer is at the heart of this working groups interests, since this mission is about "improving the lives of more than 3 million people by 2030 through prevention, cure and for those affected by cancer including their families, to live longer and better." Accordingly, Photonics21 has established links to this mission and cooperates with it towards its goals. Photonics tools and procedures play an important role in diagnostics, monitoring and treatment of many different forms of cancer, and will most likely continue to do so also in the future. Specifically, early diagnosis is key for successful treatment of most cancers and here the sensitivity and specificity of photonics-based diagnostic tools can offer game-changing solutions

Among other partnerships there are several with overlapping goals, among which the Innovative Health Initiative (IHI) is the most prominent one. IHI's "core goals are to translate health research and innovation into tangible benefits for patients and society, and ensure that Europe remains at the cutting edge of interdisciplinary, sustainable, patient-centric health research." Correspondingly, we strive at common calls, to contribute with technical developments in the first place, but also to overcome challenges such as regulatory hurdles, standardisation reimbursement issues, and standard protocols.

Due to the increasing convergence of technical solutions, with topics that range from big data to robotics, electronics, biomaterials, fiber and nanomaterials which are all involved in the fabrication of sensors and wearables, for example, a close and structured collaboration with all these stakeholders and the corresponding European Technology Platforms (ETPs) and initiatives is essential. The HealthTech4EU initiative of which we are part of and which also establishes links to IHI is a result of this insight.

While not neglecting the central role of more fundamental, but application-oriented research in developing break-through solutions for diagnostics and new treatments, a challenge that still needs to be addressed on the European level is the faster translation of latest health technologies into the market/health care. On a national level, a corresponding initiative is, e.g., the infrastructure Leibniz Center for Photonics in Infectious Diseases. This infrastructure provides an ideal approach to efficiently and quickly develop the potential of photonic technologies for routine clinical processes. On the European level pilot lines could take over a similar function. Some of these, like MedPhab, "Europe's first Pilot Line dedicated to manufacturing, testing, validation, and upscaling of new photonic technologies for medical diagnostics" will also "accelerate the commercialization of measurement, monitoring, and diagnostic devices and treatment instruments based on photonics technologies". Further Pilot lines like Phabulous (Pilot-line providing highly advanced & robust manufacturing technology for optical free-form micro-structures) and MIRPhab (A single-access point to the best miniaturized Mid-IR technology provided by a consortium of leading companies in the field of photonics), as well as initiatives like PhotonHub, need to be included as well as academic institutions, RTOs, start-up incubators and large industrial actors to create and provide an innovation-friendly ecosystem, with which photonic solutions can be translated quickly into products for the benefit of Europe's citizens.

Proposed roadmap for 2025 - 2030

	2025-2027	**2028-2030**
Photonics Research (R) Challenges, TRL up to 5	**New markers and biolabels, advanced understanding of cell processes and organ functions**	**Sensor technology miniaturization (photonic integrated circuits), combination of multiple bands (UV-VIS-IR-THz) and techniques in tandem**
Photonics Innovation (I) Challenges, TRL starting from 5	**Advanced Treatment and Monitoring systems and methods**	**Next generation advanced Imaging and POC systems and methods**
Joint actions required with other Horizon Europe Missions or partnerships	**Potential collaborations with Mission on Cancer and Innovative Health Initiative**	**Potential collaborations with Mission on Cancer and Innovative Health Initiative**