Dutch CardioVascular Alliance

Transforming Cardiovascular Health: Technology for a Brighter Future
Purpose

Among the Dutch population, 1.7 million inhabitants suffer from cardiovascular disease. Living with cardiovascular disease can severely impact a patient’s life, including emotional distress and behavioral changes, often leading to common issues like depression and anxiety, which can worsen heart disease symptoms. The cost of providing care to cardiovascular patients is 8.6 billion Euros each year, and it is projected to increase by approximately 3% per year in the coming years. In addition, we are currently experiencing a period characterized by increased demands for healthcare services, coupled with limited resources and workforce capacity. In order to uphold a high standard of cardiovascular care in the present day, it is crucial to minimize costs and staff requirements. A new strategy of improved, but more efficient healthcare delivery is necessary to reduce the burden of cardiovascular disease and lower healthcare costs.

The application of technological innovations presents the possibility of addressing these major challenges. Therefore, the Dutch CardioVascular Alliance (DCVA) and 4TU.Health explored a wide range of technology domains and developments that are important for the future of cardiovascular health, resulting in this Cardiovascular Technology Agenda. The agenda aims to (1) form a basis for connecting the world of technological possibilities with the clinical challenges identified in cardiovascular practice, and (2) accelerate and achieve collaboration between DCVA partners, especially universities of technology and clinical professionals.

Now is the time to connect the world of technological advancements to the challenges that are identified in clinical practice. To achieve this, multidisciplinary teams are required to advance validation and implementation in practice. We need to implement impact driven projects rather than technology driven projects. Clinicians identify the unmet clinical need for their patients, but lack the expertise of advanced technologies, whereas technical developers have the expertise, but often lack the knowledge to translate it to a clinical application in the field of cardiovascular disease. Collaboration is essential for innovation, validation and implementation of technology to transform healthcare.

DCVA aims to build a bridge between these two worlds and expertise, specifically by stimulating funding for further collaborative development and clinical implementation of smart and innovative technologies for the diagnosis, treatment, and monitoring of cardiovascular patients. In this way, technology will be a major contributor to the ambition of the DCVA, which is to reduce the growing burden of cardiovascular disease by 25% by 2030.
Medical technology covers the development and application of innovative tools, devices, software and systems, designed to enhance healthcare delivery, diagnosis, treatment, and disease management. In the context of the Cardiovascular Technology Agenda, cardiovascular technology refers to (bio-)medical technologies that are relevant for conditions and diseases related to the cardiovascular system. The agenda explores the possibilities of eight medical technology categories:

1. Digital Health Technologies within the cardiovascular field (e.g., e-health, lifestyle-apps, telemedicine, mobile phones, smartphones, tablets, wearable devices, smartwatches, personal health sensors, chatbots/language processing).

2. Imaging, signal recording and monitoring technologies within the cardiovascular field (e.g., MRI, CT, Ultrasound, ECG, PPG, AI development to improve medical imaging and signal processing).

3. Robotics in Healthcare (e.g., surgery support, soft robotics to support damaged hearts pump function, home robots for patient care).

4. (Implantable) Device technologies within the cardiovascular field (e.g., implantable subcutaneous string defibrillators, assist devices, intravascular devices).

5. Biomaterials/Nanomaterials within the cardiovascular field (e.g., nanomaterials for drug delivery, biomaterials for regenerative therapies, devices and preservation).

6. Biotechnology within the cardiovascular field (e.g., cell therapies, gene therapies, (m)RNA therapeutics, gene editing techniques, tissue engineered models, organ-on-chip, organoids, bioprinting, regenerative medicine).

7. Computational modeling technology for human digital twins of health and disease (e.g., patient specific models to improve diagnostic and therapeutic management, in silico clinical trials for device evaluation).

8. Big data and AI within the cardiovascular field (e.g., big data to support detection & prevention of cardiovascular disease, decision support, workflow optimalization, disease management).

**Background and rationale**

Improving health and establishing a cost-effective healthcare system are significant national challenges. Technological innovation plays a crucial role in addressing these challenges by enabling personalized care that caters to individual preferences and capabilities (self-management). Moreover, technology is essential for ensuring the sustainability and affordability of healthcare by reducing the demand for care and partially substituting the need for care personnel. This can be achieved through the development of technologies that prevent existing conditions from worsening or becoming chronic, as well as those that enhance the effectiveness of diagnosis, treatment, and follow-up. By supporting patient self-management, empowerment in their own healthcare and streamlining care procedures for professionals, medical technology contributes to a reduced reliance on healthcare personnel. Medical technologies and healthcare innovation drive improvements in processes and technology, fostering greater
integration between people and technology. The primary purpose of medical technology in healthcare innovations is to assist individuals. Notably, medical technologies have made significant contributions to the advancement of cardiovascular care throughout history. For instance, the Implantable Cardioverter-Defibrillator (ICD) continuously monitors the heart's rhythm and administers electric shocks if life-threatening arrhythmias are detected, thereby preventing sudden cardiac death in high-risk patients. Another example is the Transcatheter Aortic Valve Replacement (TAVR), which offers a minimally invasive alternative to open-heart surgery for individuals with severe aortic valve stenosis. TAVR involves deploying a replacement valve through a catheter, providing a less invasive option for patients at high risk or deemed ineligible for traditional surgical valve replacement. Lastly, wearables like smartwatches and fitness trackers provide continuous monitoring, empowering individuals in managing their cardiovascular health and enabling remote monitoring by healthcare professionals. These examples demonstrate how medical technologies have significantly advanced the diagnosis, treatment, and management of cardiovascular diseases, leading to improved patient outcomes and quality of life.

In addition, for discovery of new medicines and development of new therapies we are mostly dependent on animal models and conventional in vitro models. Although these models have broadened and deepened our insights into cardiac development and disease, discovery of new drugs and novel therapeutic approaches have been lagging. There is a clear and urgent need to create and implement innovative experimental models that accurately mimic the human heart with the potential to include patient-to-patient variations. Previously, it has been shown 3D human stem cell-based cardiac tissues, cardiac organoids and microfluidic organ-on-chip models have the potential to (partially) mimic organization and function of the (developing) human heart. A higher predictability of human-based testing models for disease modelling and drug discovery will ultimately lead to dramatically reduced attrition rates and time-to-market in the process of drug development.

Innovation, whether through new treatments, test models, devices, or processes, equips clinicians, healthcare organizations, and patients with the necessary tools to prioritize the needs of patients, staff, and themselves. The utilization of (bio)medical technologies enables the early detection, better understanding, better monitoring, and prompt treatment of risk factors and signs of cardiovascular diseases, thereby preventing damage and deterioration. This reduces the burden of cardiovascular diseases and ensures that care for individuals with such conditions remains adequately staffed in the future. Additionally, the inclusion of ethical, legal, sociological, economic, and behavioral-psychological considerations as integral parts of the development of these medical technologies fosters societal support.

The Cardiovascular (Biomedical) Technology Agenda focuses not only on pure technical advancements, such as devices and software, but also encompasses technology in a multidisciplinary approach. This includes (micro) engineering, chemical and biological technologies for development and advancement of innovative technologies, including organ-on-chip, tissue engineering, biomaterials and nanotechnologies technologies, which fall within the agenda's scope. However, a vital criterion for technological development within this agenda is its patient-centric approach, targeting specific problems that future cardiovascular patients may encounter. As such, the Technology Agenda will not only identify technological opportunities, but also the ‘receiving’ clinical needs.
Objectives

The main objectives of this agenda are:

- Identify and address gaps between cardiovascular science/technology and the clinical needs within the field to advance cardiovascular care.
- Raise awareness about the significance of technology in cardiovascular research and healthcare, leading to accelerated (research) outcomes.
- Develop a cardiovascular research roadmap that establishes connections between technological possibilities and clinical practice challenges. The roadmap aims to bridge the gap between clinical practice, technology, and their respective expertise to enhance prevention, diagnosis, treatment, and the overall quality of life for cardiovascular patients.
- Encourage collaborations, foster better networking, and facilitate technology transfer between Dutch Technical Universities or research groups with proven technical expertise and other research institutes (e.g. cardiovascular research groups/institutes in Dutch Universities and Medical Centers).
- Define themes and opportunities for funding cardiovascular technical research projects.

Methods

The Technology Agenda was developed by collecting and consolidating information from various sources. A survey was conducted to acquire knowledge in two main areas. Firstly, the survey aimed to understand the currently available technologies and recent technological advancements in the Netherlands that could contribute to addressing cardiovascular challenges. Secondly, from a clinical perspective, the survey gathered information regarding the most critical needs and how technology could revolutionize cardiovascular care, thereby reducing the burden of cardiovascular disease. The survey provided insights into the expertise in (bio)medical technology development in the Netherlands and included questions about the cardiovascular clinical needs where technology could add value.
A comprehensive analysis was conducted to examine the survey results and the results were compared to the following additional sources:

- The Research Agenda for cardiovascular diseases, developed in 2015 through collaboration between the Dutch Heart Foundation, physicians, patients, and researchers. This agenda identified five top priorities.
- The ‘DCVA Cardiovasculaire kennishiaten agenda’, which consolidated and prioritized knowledge gaps identified by various professional associations associated with DCVA (NVVC, NVIVG, HartVaatHAG, NVvV, NVT, NVN, NVvR, and NVHVV).
- The themes being addressed by different DCVA research consortia, which provide valuable information for understanding opportunities to connect technological developments.
- The Knowledge and Innovation Agenda (KIA) and the related Knowledge and Innovation Covenant (KIC), which encompass several key technologies. Key technologies are future-oriented technologies with high anticipated impact. The technical universities have identified 13 key technologies as the foundation for the “Breedgedragen programma” MedTechNL. Key technologies are well-suited to support new innovations and integrate them into the medical domain. The Cardiovascular Technology Agenda should also establish links to the Key Enabling Technologies (KET) 3.0 - Priority Technologies.
- The European Research Area network on cardiovascular diseases (ERA-CVD) and the Strategic Research Agenda for Cardiovascular Disease (SRV-CVD) highlighted 15 research domains.

**Important (disease) areas for technological innovation**

As a result of the survey, we have stated the important (disease) areas within the realm of cardiovascular health where technological innovations can play a pivotal role and hold immense promise. The ensuing discourse underscores the symbiotic relationship between technology and cardiovascular care, charting a course toward more precise, efficient, and patient-centric treatments.

**Heart failure**

Heart failure is a chronic cardiac condition that worsens over time, impairing the heart’s ability to provide the body with the required amount of blood. This deficiency leads to an insufficient cardiac output, which fails to match the body’s metabolic demands, resulting in a significant decline in the quality of life for affected patients. The importance of innovative technology in the management of heart failure cannot be overstated. It plays a pivotal role in offering advanced treatment modalities, enhancing our comprehension of the condition through monitoring and management utilizing sensors and remote systems, enabling the delivery of personalized care via precision medicine and genetic testing, facilitating ongoing support via telemedicine, empowering patients through educational resources and self-management tools, driving groundbreaking research and innovation, and ultimately, improving the diagnosis, treatment, and outcomes for individuals grappling with this challenging condition.

**(Ischemic) stroke**

A stroke occurs when blood flow to the brain is blocked, causing brain cells to rapidly die without prompt treatment. Innovative technologies aid in early stroke detection and treatment. New technology is crucial for stroke care due to faster and more accurate diagnosis with advanced imaging techniques like CT scans and MRI, combined with patient-specific computational models. Timely interventions are enabled by telemedicine and mobile applications, even in underserved areas. Integration of robotic devices, virtual reality, and wearable sensors...
in rehabilitation enhances personalized experiences. Technology supports stroke prevention through vital sign tracking and risk identification. Furthermore, the fast and efficient treatment of stroke will benefit from new intravascular devices. Furthermore, these advancements and cutting-edge experimental models will drive research and innovation, improving diagnostics, interventions, rehabilitation, and prevention. Ultimately, new technology improves patient care, outcomes, and reduces stroke burden.

Atherosclerosis
Atherosclerosis is a common condition where plaque builds up inside arteries, causing them to narrow and reduce blood flow to vital organs. It can lead to various diseases such as coronary artery disease and peripheral artery disease (e.g. critical limb ischemia). New (bio)technology is crucial for improved detection, enhanced (personalized) treatment options, genetic testing, preventive measures, and supporting research and development. Advanced imaging enables early and accurate detection, aiding timely intervention. Patient-specific plaque models will aid in the improved selection of treatment strategies. Innovations in endovascular therapies and stents improve outcomes. Wearable devices and monitoring systems assist in preventive measures. Technological advancements drive research, leading to deeper insights and targeted therapies. Overall, technology improves detection, treatment, prevention, and research, benefiting patient outcomes and cardiovascular health.

Aneurysm
An aneurysm is a significant widening of a blood vessel that can occur in several places in the body (cerebral, thoracic, abdominal, peripheral), leading to an abnormal bulge in vessel wall that can be life-threatening if it ruptures. Many aneurysms go undetected without symptoms. New technology is crucial as it enables accurate diagnosis through advanced imaging, facilitating effective treatment planning. It provides improved treatment options e.g., minimally invasive surgical techniques, resulting in better outcomes and shorter recovery times. New innovative approaches to study and to treat small intracranial aneurysms – the majority of the aneurysms that are currently diagnosed and extremely difficult to treat – need to be developed. Technology enables monitoring and surveillance, allowing prompt intervention. It also drives research, improving diagnosis, personalized treatment, and research in aneurysm management, enhancing patient outcomes and reducing the risk of rupture.

Cardiac arrhythmias
Cardiac arrhythmias refer to an abnormal heart rhythm that can cause inadequate pump function. While medication can help manage arrhythmias, new technology can be crucial as it enables accurate diagnosis through advanced diagnostic tools, such as ECG devices and implantable monitors. It also offers improved treatment options, including catheter ablation and implantable devices, while enabling continuous monitoring and remote management through wearable devices and remote monitoring systems. Innovative human experimental models may increase our understanding of underlying mechanisms, which may lead to better treatment options. Additionally, new technology supports risk prediction and personalized treatment strategies, enhancing patient outcomes and overall management of cardiac arrhythmias.

Cardiovascular risk management
Early detection, management, and treatment of cardiovascular diseases are crucial for public health improvement. New technology is crucial for cardiovascular risk management as it can create genetic profiles, enables more
accurate assessment of risk factors, facilitates personalized monitoring and management, supports predictive modeling for individual risk profiling, and drives research and innovation in the field. These advancements enhance risk assessment, empower individuals in their health management, enable tailored preventive strategies, and contribute to improved patient outcomes and population-level cardiovascular health, while also addressing disparities between the social and medical domains, complex multifaceted issues such as poverty, socio-economic status and reducing barriers to healthcare access.

**Technological themes**

From the survey we have gathered several technological themes that are important in the field of cardiovascular health. The survey's findings spotlight the intersection of cutting-edge technology and the intricate landscape of cardiovascular diseases.

**Personalized medical solutions**

Personalized medicine harnesses a subject's own data to individualize their own care, from diagnosis through treatment selection and monitoring. Technological approaches to precision medicine will harness population-wide data, including genetic profiles, to identify individualized treatment strategies. This includes technology for e-health that make it possible to read health and medical information remotely (e.g., in case of AEDs) and makes this data usable and accessible within the healthcare system. Other examples are aimed at further developing telemonitoring (e.g., patients with heart failure, arrhythmias or stroke) that contributes to improving treatment and lower healthcare costs because fewer hospital visits are necessary and physicians can detect changes in diet, lifestyle and health status more quickly.

**New and/or improved imaging and diagnostic techniques**

Medical imaging technology has revolutionized health care over the past 30 years and currently continues to evolve, presenting health care workers with new applications in diagnosing and treating diseases. With new technologies it is possible to identify even more accurately new cardiovascular injuries, conditions, and diseases in their early stages. Because of its ability to offer quicker and more reliable information, new techniques for diagnostic imaging have drastically improved patient outcomes and helped doctors achieve better results. Examples of these new techniques are new generation multi-energy CT and photon counting CT.

In addition to better techniques for diagnosing cardiovascular disease, new imaging techniques can also contribute to the improvement of treatment. By developing new imaging techniques, procedures will become safer, more efficient and more effective, leading to improved patient outcomes. Examples of new imaging technologies for the treatment of cardiovascular disease can be image guided robotics for surgery, multimodal/multi-source tools and the development of faster and cheaper imaging techniques with automated analysis using artificial intelligence.

**Human Disease Models**

Cardiovascular models, including in vitro and ex vivo disease platforms, and in silico/computational models continue to play an essential role in understanding the etiology, disease pathogenesis, pathophysiology, progression, underlying mechanisms of cardiovascular disease (CVD) and recently also for validation of treatment. Human disease models (e.g., based on patient-derived or genetically modified induced pluripotent stem cells)
offer valuable tools in disease modelling, drug discovery and safety, and therapeutic interventions, however the difference between the human condition and the complexity of physiology, pathophysiology along with genetic and environmental factors, have made it rather difficult to recapitulate the complexities of cardiovascular conditions with just a single experimental model. Therefore, the bioengineering and tissue engineering field have been implementing extensive efforts to develop in vitro and in silico models for more physiologically and clinically relevant readouts for CVD. Emergence of human disease models, both in vitro, ex vivo and in silico will complement preclinical assessment and can fine-tune decision making steps in drug discovery, safety pharmacology, development pipelines and to personalized medical solutions. In addition, these human disease models also serve as an important tool in medical device design, as they can stimulate better prediction of product safety and efficacy, virtual physiologic patients for testing medical products and clinical trial simulation that reveal interactions between therapeutic effects, patients’ characteristics and disease variables.

**Advanced Computational techniques and Data**

Potential benefits of precision or personalized medicine in cardiovascular disease (CVD) include more accurate geno- and phenotyping of individual patients with the same condition or presentation, using technological innovations to guide diagnosis, treatment and monitoring. The future development of precision medicine depends on a vast exchange of data as well as harmonized integrative analysis of large-scale clinical health and sample data. Approaches to realizing this potential include advanced computational techniques, e.g., in silico models, computational fluid dynamics, digital twins, real-world data and artificial intelligence (AI). To date, digital devices and services play already an important role in assisting both providers and patients, from data collection to clinical communications to decision support in disease management and beyond. The emerging advanced computation techniques is being touted as an exciting and promising approach that can further advance efforts in medical discoveries and improve clinician and public health outcomes.

Data plays a key role in advanced computational techniques and focus on improved data gathering and sharing is very important with the increasing amounts of health data available. Access to health data is essential for improving the performance of existing medical devices or in-vitro diagnostic medical devices and to develop new and innovative technologies. Additionally, health data can provide insights to patient populations more targeted research. Improved infrastructure for the usage and storage of these data is essential.

Computational models are boosting the capacity to enable learning and discovering new knowledge, new hypothesis generation and testing, and experiments and comparisons, as they can reduce the complexity of large data sets. They are poised to play a key role in formulating highly personalized treatment and interventions in the future.

Precision or personalized CV medicine can be delivered, not only by data, but also by inductive and deductive reasoning built in model systems. Working with model systems (in silico, digital, etc.) are uniquely positioned to address the wide variety of patient characteristics. Models will be used to simulate and contribute to evaluation of effectiveness and safety of novel CVD-innovations and in addition it will contribute to predict outcomes and guide clinical decision support.
Given the significant potential for advanced computational techniques to empower cardiovascular research, fuller understanding of its scope will beneficially be combined with the development of novel advanced computational techniques. Despite the growing popularity of computational-modelling approaches, there are many hurdles to overcome for their clinical routine implementation in the future.

Role of the DCVA
We are currently experiencing a period characterized by increased demands for healthcare services, coupled with limited resources and workforce capacity. In order to uphold a high standard of cardiovascular care in the present day, it is crucial to minimize costs and staff requirements. Technological solutions that promote self-management or enhance work efficiency are considered viable options to address this imbalance between supply and demand. The DCVA aims to foster collaboration between the technological field and clinical medicine. This collaboration encompasses various stages, including identifying medical needs, assessing the value of new technologies, validating their efficacy in patients, and implementing them into clinical practice. The primary goal of the DCVA is to reduce the burden of cardiovascular disease by 25% by the year 2030. Therefore, our programs within the DCVA are specifically designed to maximize impact in the aforementioned disease areas and themes. This can be accomplished through various means, such as moderately reducing disease burden across large patient populations or significantly reducing it within a more targeted group.

The present moment underscores the importance of linking the realm of technological potential with the cardiovascular challenges discerned in clinical practice. To accomplish this, the advancement of validation and practical implementation requires the collaboration of multidisciplinary teams. While clinicians proficiently identify unmet clinical needs for their patients, there is a deficiency in expertise concerning advanced technologies. Conversely, (bio)technical developers possess the necessary expertise, but often lack the knowledge to translate it into clinical applications. The aim of this DCVA (Biomedical) Technology Agenda is to establish a bridge between these two domains of expertise. In order to foster this bridging, the DCVA emphasizes its holistic approach in the execution of its activities. Within the overarching framework of the DCVA mission, a fundamental principle is the constant examination of how the technological domain can contribute to the advancement of solutions, as delineated in its explorations and consortia initiatives, as well as through programs and projects such as Check@Home. The integration of technology is viewed as an integral aspect of the DCVA mission, ultimately serving as a catalyst for the realization of its ambitious goals in the field of cardiovascular health and care.

In addition, the DCVA recommends to develop an open research funding program with a focus on promoting collaboration, sustainability, and inclusivity within the technological aspects of cardiovascular research. This call will be tailored to encourage collaboration among a wide array of researchers, ranging from large research groups to small teams and mid-career scientists. In addition, the industry plays a crucial role in achieving a significant impact on society and driving change in healthcare. Implementation of new innovations through public-private collaborations is of utmost importance. All parties are invited to contribute their expertise and innovative ideas to enhance cardiovascular health. By creating an open platform for the emergence of the most promising projects, our aim is to attract researchers and technical experts who might not currently be engaged in collaborative endeavors. Our objective is to cultivate an environment that nurtures interdisciplinary approaches and propels the discovery of groundbreaking solutions.