Editorial

Patient customized engineering for smart cardiovascular therapy

As research trends move towards the use of personalized medicine, many projects are focused on genetic, molecular, biological and pharmacological approaches. One of the most apparent aims of personalized medicine is to analyze and image patient-related biological processes at the cellular and molecular level and use the information provided to influence these processes therapeutically. However, personalization strategies and a correspondingly improved patient orientation also present major opportunities relative to the field of medical engineering.

This is where the Aachen-based medical engineering network “innovating medical technology in.nrw” comes in: according to the guiding principle “Patient Customized Engineering” (PaCE), customized solutions and therapies are being developed, adapted to specific diseases and problems of the individual patients.

The development of medical components, devices and systems “tailored” to an individual pathological requirement in a specific patient is carried out, more at the anatomical and physiological, than at the pharmacological level. This approach reveals an enormous amount of untapped potential for improvement of interaction between technical systems and recipient organisms.

Based on this idea, a total of six research and development (R&D) projects and one coordinating project, including 40 partners in the Aachen-based network, are completing these projects to establish a new generation of medical devices and systems. All these projects have a focus on the particularly relevant field of cardiovascular disease which is still the leading cause of death in Germany.

In the following a short introduction of each project is given.

Occurring with a frequency of 30%, cardiovascular emergencies rank first in emergency assistance operations. With cardiovascular emergencies, fast diagnosis, treatment, and therapy are vital. As the number of emergency admissions and the shortage of emergency doctors simultaneously increase, the use of tele-medicine in the rescue service is becoming increasingly more important. The development of a telemedical rescue assistance system (TemRas) for Emergency Medical Services (EMS) aims to address this problem [2]. Real-time broadcast of all vital signs together with voice and image communication, from the scene to the so called ‘tele-emergency physician’ enables this person to directly support the emergency team on-site. The system is going to be implemented in five rescue service areas in Aachen, Cologne, Düren, Euskirchen and Heinsberg for a 1-year trial period.

Heart failure is a chronic disease with the highest mortality rate for elderly people [6]. Often, the treatment simply aims to prevent complications, that makes the diagnosis and treatment of concomitant diseases critically important. Therefore, early detection of exacerbation of the clinical pattern is a key. With this in mind, individualized nightly tele-monitoring for outpatient therapy in heart failure is developed. Use of external sensors allows the timely diagnosis of exacerbation of heart failure and improves the early detection of concomitant diseases like hypertension, atrial fibrillation and sleep apnea. To enable this, the sleep time of patients is used to monitor the vital parameters more intensively and more comfortably at home.

Surgical interventions are increasingly being replaced by image-guided procedures with minimal trauma (interventional therapy). For example, in the hepato-biliary field, an artificial shunt may be created between the portal and the hepatic venous system. These highly complex surgical interventions are associated with severe complications and high mortality rates. HyTher aims to generate and improve image-guided surgical procedures [5]. The accuracy and, thereby, the safety of complex image-guided procedures is enhanced, with concurrent reduction of radiation exposure and duration of the intervention. The project is focused on image data fusion of interventional ultrasound and pre-interventional 3-D C-arm CT (=hybrid therapy). Furthermore, the generation of patient-specific, adaptable 3-D models and a navigation platform for the electromagnetic navigation of instruments combined with the realization and integration of correcting algorithms for the respiratory support are central issues.

Delayed or deficient endothelialization and induction of coagulation and immunological reactions restrict the applicability of current cardiovascular implants. In the “PATIM” project the biologizing of cardiovascular implants is accelerated [3]. Vascular prostheses, heart valves, and other synthetic structures are provided with functional groups to attract the body’s own cells and bind them at the surface. Furthermore, the implants can be cultured “in vitro” from the patient’s own cells (tissue engineering). In addition to the generation of implants, the imaging and subsequent monitoring of the patients for clinical application is also considered. Here, the reaction of the synthetic implants to the body, and the reaction of the vital implants themselves, are crucial. Thus, existing imaging markers need to be integrated in the generation of biologized implants, and molecular imaging methods with magnetic resonance tomography – positron emission tomography (MRT-PET) are developed to monitor the processes at the implant and in its proximity.

Interventional procedures all require image guidance to allow device navigation inside the vascular system. Up until now, catheters and guide wires have only been suitable for use under fluoroscopy. The project “MiGi” aims to close this gap [1]. The development of a novel guide wire should facilitate the application of alternative imaging techniques (MRI and ultrasound) during medical interventions. These methods may be advantageous in some applications, for example, for displaying the area surrounding the region of intervention. Furthermore, the radiation exposure for patient and medical staff can be reduced or even avoided. Using new materials (fiber composite plastics) and flexible manufacturing technologies, the goal of this project is to develop thin guide wires with variable material properties that meet the requirements of MRI and ultrasound with respect to visibility and patient safety.

The project I³-Assist is focused on the development of a highly integrated modular system of life-supporting functional units [7]. This system can be used as a heart-lung machine (HLM), but also as an extracorporeal life assist (ECLA/ECMO). Thanks to this new technology, a direct and seamless change between HLM and ECLA, as well as between ECLA and HML, is made possible. This system can be specifically adapted to the requirements of the patient. Due to the high degree of individualization, it can be modified to suit humans of all ages and weight classes. Consequently, the system provides different treatment options enabling treatment of the oldest and the youngest patients affected by a variety of concomitant diseases. The I³-Assist system is compact, which means, it can easily be carried around with the patient for transport inside the hospital, but also for transport between different hospitals.

The time to market of future innovative medical devices is predicted to become even longer than it is today due to the increasing complexity. In addition the requirements on quality assurance in research and the entitlements to transferable results gain strongly in importance. That is where the documentation of biomedical research comes in: the laboratory notebooks, that are widespread as personal paperbacks. While many industrial laboratories have already changed to electronic documentation systems, the academia lags behind. Little is known on the underlying reasons and the potential of electronic notebooks (ELN) in supporting the biomedical researcher. Therefore, a survey was conducted on the acceptance of ELN including 101 researchers from various sites and disciplines in order to develop a statistical model to predict the probable user acceptance before implementing an ELN [4].

Last but not least: an active and prospective coordinating entity is crucial for the vitality and efficiency of a cluster. Here it is called “Cluster Development”, not only delivering coordination, cooperation, and other services to improve the cluster, but also further develop it to a more efficient stage. Besides the integration of a variety of aspects and partners, the coordination of cluster partners to initiate new cooperations and to offer new services for the region is a key task. Here, the R&D work of the involved scientists is combined with the transfer of knowledge, technology, and know-how in order to improve the innovative power of the cluster.

**Recommended actions**

Through this initiative and other activities, Germany and in particular North Rhine-Westphalia has attained a pioneering role in the development of patient customized engineering (PaCE). However, further efforts must be made in science, economics and health policymaking, to maintain and enhance this level nationally and internationally: broadening of the research base, translation of the results into economically meaningful implementations in standard care contexts. Then the investment in patient customized engineering will have resulted in sustainable progress that patients will benefit from. The priority actions necessary to achieve the above-mentioned objectives include all stations in the value-added chain of medical technology innovation, also including the users and caregivers:

- Interdisciplinary training and education for increased interdisciplinary cooperation between clinicians, engineers and scientists.
- Development of suitable clinical study models and procedures for patient customized engineering based on
individualized study protocols and the fundamentally changed supply paths. In addition, it is increasingly important internationally to attract clinical partners for feasibility studies and clinical trials.

– Development of benefit analyses and concepts to prove the benefit of patient customized engineering compared to the current gold standard. Last but not least, this promotes acceptance by clinicians and patients. In addition, it is necessary to promote the financing of patient customized engineering by healthcare insurers in primary care by means of health economics assessment.

– Development of appropriate approval procedures for individualized medical devices, especially those in the highest risk category.

– Need to establish and test new business models, in companies as well as across sectors by service providers, so as to reflect the changing supply situation for patient customized engineering.

– Resolution of the economic dilemma between mass production and customization by promoting the development and introduction of new production processes as part of overall care.

– Innovative concepts of automation and quality assurance in production, especially of the biologic component, are required to tap the great potential of “bioimplant”.

– Creating a legal environment for clinical and paramedical professions regarding the application of patient customized engineering with respect to security and safety for data, users and patients.

– Further development of adaptation to the patient by developing appropriate modeling and simulation methods, i.e., taking into account morphological specifics by means of preoperative imaging.

– Creation of international acceptance to accommodate patient customized engineering. This includes also partnerships in science, medicine, and business, in particular with regard to the global market.

In conclusion, our preliminary results and achievements out of these cluster activities are encouraging that “Patient Customized Engineering – PaCE” represents a significant optimization strategy with high levels of innovation, moving in the direction of improved patient care. The trend of personalization may have the potential to usher in a new era of medical engineering. Many research collaborations are already established and initial success stories are emerging. Now it is important to secure the foreseeable progress and to firmly and sustainably maintain the implementation of innovative products and treatments.

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