telerehabilitation. Monitoring cardiovascular risk factors seems to be particularly appealing for the use of telemedicine. This includes health applications to improve lifestyle and adherence to pharmacotherapy by surveillance, education, psychological support and interactive motivational tools i.e. to improve physical activity, healthy nutrition and smoking cessation with the final goals of reducing metabolic risk factors and improving cardiovascular health. Telerehabilitation may be a support or, in the case of a lack of adequate cardiac rehabilitation programs, a substitute as a home-based program in particular in areas where cardiac rehabilitation programs are not available for patients within a reasonable distance. This is of particular interest in areas with a low level of development and low population density.

This article is complemented by a statement of Paul Dendale who is a Board member of the European Association of Cardiovascular Prevention and Rehabilitation and presents a comprehensive view about potential shortcomings but also great opportunities for telerehabilitation to be applied in the near future.

The contribution by Friedrich Köhler and colleagues presents results on feasibility and perception of telemedical care by patients and physicians. This has been studied in the framework of the Telemedical Interventional Monitoring in Heart Failure (TIM-HF) trial with the objective of proving the superiority of remote patient monitoring compared to usual guideline-based care in terms of total mortality, heart failure-hospitalization, quality of life and other markers of cardiovascular health. Two telemedical centers, located in two German regions, provided physician-led medical support for 24 h/day, 7 days a week, according to defined standard operating procedures. Patients were enrolled from 165 practices in cardiology, internal medicine or general medicine, and followed for at least 12 months with several outpatient visits. Results are encouraging, showing the feasibility of telemedical care and positive perception by patients and physicians.

Conclusions

eHealth and telemedicine are excellent examples of innovative technology. They will rapidly evolve and become an important component of today's medical care. They have the potential to reduce healthcare costs by reducing the burden of disease, the risk of complications, hospitalizations, recurrent events and premature death and to improve quality of life. eHealth and telemedicine have a particular potential in cardiovascular disease prevention but also in the long-term care management of patients with cardiovascular disease. An important challenge for those involved in these new technologies will be to keep the main focus on patients' individual needs and not to be overwhelmed by the enormous speed of progress in technology and informatics and to continue to carefully evaluate the evidence behind the practice.

Conflict of interest

The author declares that there is no conflict of interest.

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Electronics for better healthcare

Bernhard Wolf and Karolin Herzog

Abstract

Microelectronics and microsystem technology have changed our daily lives considerably in the past 50 years. Countless everyday objects contain microelectronic components. In healthcare up to the present, however, it has not been possible

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to make major alterations in introducing electronics and information technology that would lead to innovative improvements and greater transparency. This paper describes initial steps in diagnostics and oncological therapy including telematic healthcare systems which can, for example, assist patients with cardiovascular diseases and shows, through these areas, how electronics and microsystems technology can contribute to better healthcare.

Keywords
Medical diagnostics, diagnostic and therapeutic chip system, telematic healthcare, microelectronics, microsystem technology

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Introduction

From imaging diagnostics to sensor chips

About 30 years ago, we started introducing quantitative methods and systems into tumor histopathology and tumor therapy using image-analytical and electron-beam-micro-analytical techniques.[1,2] With the dawn of the computer age, it became clear that it would become increasingly possible to integrate quantitative diagnostic systems in doctors' decision-making processes.

Having obtained so much data from these studies we developed, in collaboration with semiconductor manufacturers, chip-based methods for tumor diagnostics and telemedical therapy. These methods are now being tested in clinical research projects and gaining acceptance in the field of drug research, rehabilitation and in the assistance of cardiovascular or psychosomatic diseases.[3,4]

Microelectronic chip systems for marker-free analysis and diagnostics

The basic principle of such multiparametric sensor chips is that cell and tissue material is cultivated on the chips using conventional technology, supplying the cultures with nutrients by fluidic systems and subjecting them to microscopy and sensor-based microphysiologic observation.[5] By this method, the cells, tumor sections and model tumors can be tested with chemotherapeutic drugs to determine their chemosensitivity. Compared to other methods, this procedure has the advantage that the cell and tissue material can be examined in a label-free way in its physiological environment. Thereby, longer testing is feasible in order to identify possible resistance patterns. Previous methods often neglecting parallel, dynamic and non-linear signaling patterns of cells—requiring individual tests—were unable to do this.[6,7]

Figure 1 shows the basic setup of such a test system, indicating how the signal parameters of the cells couple into the chip. This fundamental principle applies for further developments of the system and permits on-line and real-time analysis of cellular signal behavior.

Based on present knowledge, it can be assumed that no more than 20% of cancer patients suffering from the most common tumors (breast, lung, stomach, colon) respond to conventional chemotherapy.[8] A predictive test based on our research (see Figure 2) could help in the decision-making process between patient and oncologist and it could disburden the healthcare system from the costs of futile therapies.

The chip devices are mainly operated in incubators ensuring physiologic temperature and sterility. Our test systems are based on modular setups with chip-based stations for the observation of the cultures under a microscope. A handheld system for cell-biological analysis, for example, in connection with 'bed-side' or emergency applications (see Figure 3) allows the doctor to offer individual, personalized treatment in combination with databases.

From a single-chip system to a high-content analysis robot

Despite the plethora of data and knowledge gained in the past years through molecular-biological research, no major breakthroughs have been made in the search for new drugs. This consideration alone should be an incentive to turn the search for new drugs to other systems and switch from deterministic screening to functional metabolism research.

For this reason, from our cell-chip systems which were originally developed for diagnostic purposes, we developed robot-based platforms based on sensor multiwell plates which can be employed for drug search. That's how the concept of parallelization was introduced for the first time into the analysis and functional diagnostics of metabolic changes in tumor cells. Today these systems are able to monitor in real time in 24–96 parallel samples under microscope visualization and under close to physiologic conditions. Microscope

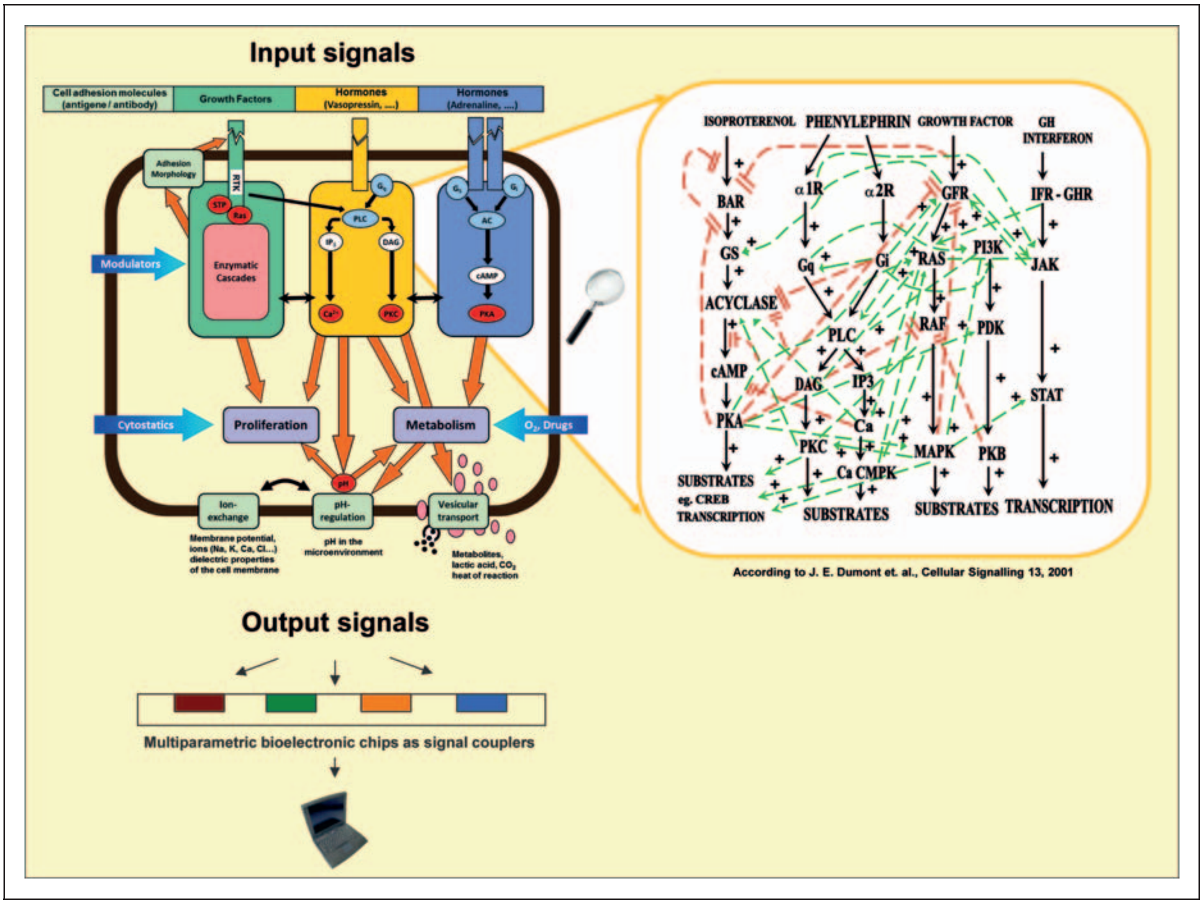

Figure 1. Schematic course of mitogen signal transfer in a cell and multiparametric bioelectronic chips as an interface for signal reading.

control is not only limited to imaging but also includes several microscope-based analytical methods.[9]

From cell chip to 'Doctor in the Bag'

Having developed various analytical chip systems for the experiments with living cells, we also employed them for different analytical purposes. In cooperation with partners, these efforts resulted in a series of medical measuring devices which were able to communicate, for example, with mobile and conventional phones. In a project called 'Doctor in the Bag' and a follow-up venture, 'COgnitive MEdical Systems®' (COMES® is a realization and a registered trademark of Heinz Nixdorf-Lehrstuhl für Medizinische Elektronik of the Technische Universität München), it became possible to connect blood pressure measuring devices, spirometers, glucose measuring devices, electrocardiogram (ECG) sticks and other devices to measure relevant medical parameters in doctors' practices and hospitals via a mobile phone, in one single system (COMES®-Platform).[10,11]

Cardiovascular diseases like chronic heart failure can be especially assisted by such a 'telematics companion'. This disease is one of the most frequent causes of death in Western industrialized countries which consequently entails enormous costs. Therefore, ever more systems are, and will be, required in the future which allow the medical self-determination and emancipation of a patient. Heart failure is a disorder of heart functionality. In most cases a circulatory disturbance of the heart leads to this disease. As a consequence the patient must expect a significant reduction of his physical work capacity according to the degree of severity. Based on this physical limitation as well as psychological and social subsequent problems and their alternating interactions, both life expectancy and life quality of the affected patients are compromised by heart failure.

The COMES®-Platform mentioned above, will be available for this practical application and is being extended continuously by us.[12] Figure 4 shows some of the devices and their link to the COMES®-Database which is specialized for this purpose.[13]

After having collected a multitude of physiological data (such as blood pressure, ECG, glucose, weight, activity and more) from the patient, the multi-modal sensor platform will transmit them to the COMES®-Database. The measurements collected in the real environment are automatically sent via smartphone. This happens directly and safely.

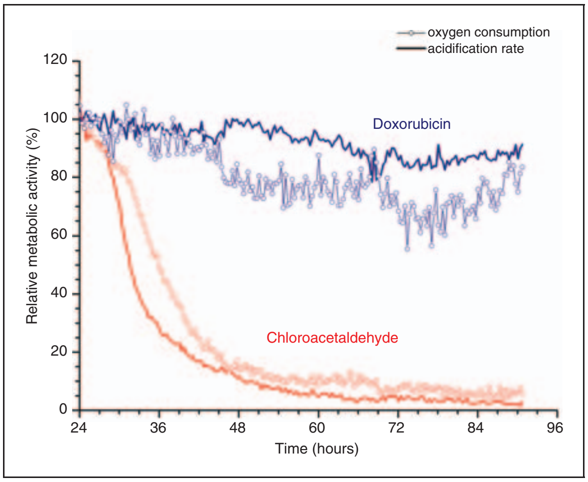

Figure 2. Measuring the chemosensitivity of a human mammary carcinoma tissue sample. Adding the metabolite chloracetaldehyde (CAA), formed from ifosfamide or cyclophosphamide, results in a substantial decrease of the acidification activity and oxygen consumption in this sample, while only little effect of doxorubicin can be seen here. By means of statistical tests including controls, it is possible to assess the degree of sensitivity that must be expected and to personalize the therapy for this patient accordingly.

The written data on the COMES®-Database is linked to Expert-Software. This purposefully developed COMES®-Expert-System (Figure 5) and special Expert-Software will also provide intelligent feedback and intervention management. Messages can automatically be sent for medication control or recommendations to the patient. Depending on the individual indication, user-specified limits can be set which create a definable callback, rather like notifying the patient or ringing up the doctor.[13] In the current project stage the callback, particularly the feedback, is realized by a traffic light system, which allows a three-stage evaluation of the measured values. In the COMES®-Portal the users (patients, family members or treating doctors) can access both a statistical listing of the data, graphics and algorithmically calculated trends. With this detailed information an accurate profile of the user's current health status can be drawn, as needed.[14]

Furthermore, a classification algorithm is developed especially to predict the patient's risk for those who suffer from chronic heart failure connected with psychosomatic illness. The developed model is using Rapid-I's Rapid Miner toolset and automatically executed from scripts.[12]

In the case at hand with heart failure patients with depression, the COMES®-Platform proves to be an eminent tool, as not only necessary physiological data can be collected but also supporting therapy measures

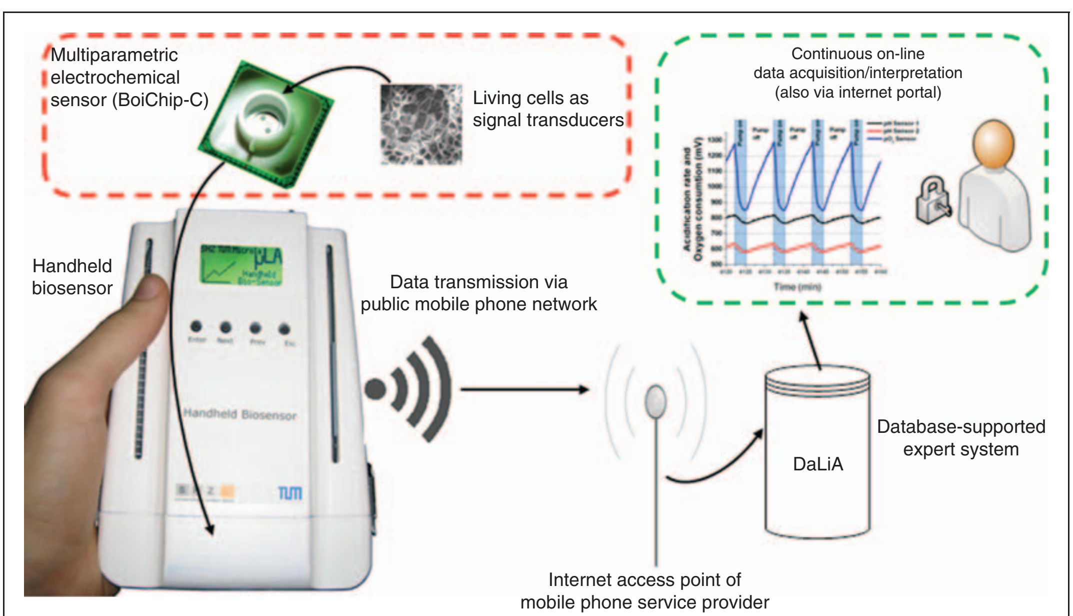

Figure 3. Handheld lab-on-a-chip (μLa) for mobile cell-biological assays, e.g. for bedside monitoring of side-effects of medication or individualized treatments.

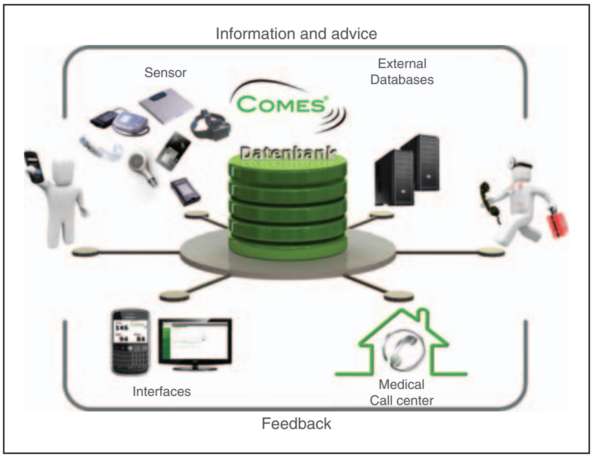

Figure 4. Mobile medical measuring devices combined with telecommunication systems and a database COMES®.
COMES®: COgnitive MEdical Systems.

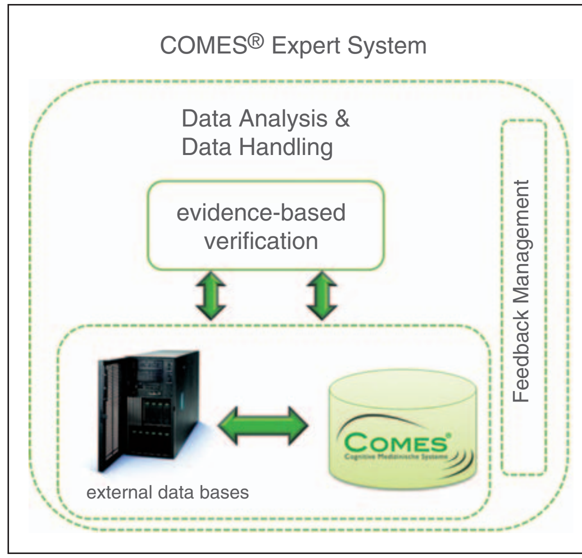

Figure 5. Composition of the COMES®-Expert System included in the platform.
COMES®: COgnitive MEdical Systems.

can be provided as feedback. A study in progress will clarify if there is a connection between chronic heart failure and psychosomatic illness.[12]

Using such a system, personalized data can be transmitted to the treating doctor or medical provider practically anywhere in the world, either to give treatment recommendations directly over the mobile phone or to provide medical care via a medical portal (Figures 4 and 5). Today telemedical portals based on sensor-based personalized medical measuring devices are already able to automatically detect critical health conditions early and, under some circumstances, predict them (asthma, cardiovascular diseases, glucose) in order to initiate medical intervention or recommend what to do.

If these systems are combined with evidence-based medical information technology, the individual comes one step closer to controlling her or his own medical information.

Individualization of the patients through telematic and personalized healthcare systems

The state-of-the-art combination of modern body sensors, fluidic actuators and telematic control systems permits setting up of therapeutic systems, whether extra-corporal, partially or fully implanted, allowing the majority of patients to live self-determined lives with their illness.

Through these personalized therapies, as seen for example with COMES®, we notice that the compliance of patients, compared to conventional treatment methods, is clearly elevated. Through regular feedback to the user his acceptance, as well as his readiness for an active contribution to therapeutic measures, has largely increased. These results lead to the conclusion, that sensor-supported telematic assistance systems provide a considerable contribution to more self-responsibility regarding individual health and medical autonomy. COMES® represents a multimodal sensor platform which collects and transports not only a large amount of physiological data, but also those for telematic controllable biomedical agents. The collected data through this electronic assistance give important awareness of the development and introduction of individualized therapy- and assistance concepts, as well as innovative physical, non-medical feedback therapies.

Microsystems for bioelectronic diagnosis and treatment

The previously described approaches show that microelectronic systems have a future in personalized medicine. Unfortunately, in the past, too much focus was put on giant equipment imaging devices. Although their significance in many cases is undisputed, no systemic permeation in the public health system is given. On the one hand, with their high costs these systems tend to spiral general healthcare costs because the investments have to be justified by use. On the other hand, they show no real relevance in general healthcare today.[15] Doctors' diminishing anamnesis training has led to the current bizarre situation that giant equipment imaging devices are employed which can show findings but interpretation depends essentially on the treating doctor's experience and still too little on evidence-based interpretation systems. Just as in the case of histopathological diagnostics, trainable image-analysis systems with intuitive user guidance are lacking, so that actual medical progress is also questioned by others. In this context, we would like to quote an expert in relation to one of our early research projects on quantification of histopathological preparations by means of electron microscopy and numerical image analysis: 'The trained eye of a pathologist can see more than 10 computers' (Personal Communication). In individual cases this may actually be true if the eye really is trained, despite the double-digit number of known misdiagnoses in tumor diagnostics.

In internal medicine and general practitioners' practice, it is however undisputed that greater use of giant equipment cannot improve the present healthcare cost structure rather than the selective use of small, mobile measuring devices directly linked to intuitive evidence-based databases. A simple mobile phone with a good camera can permit making dermatological findings at home, giving nutritional advice and ensuring contact with the patient. Combined with sensor and actuator systems, this mutates into a real theranostic (therapy and diagnostic) system which like all microsystems can set in motion an enormous efficiency potential in the technical as well as the medical world.

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Conflict of interest

The authors declare that there are no conflicts of interest.

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