Medical Progress Requires Interdisciplinary Cooperation

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Summary

Medicine has been strongly connected with natural sciences and technology since the very beginning. Diagnostic and therapeutic instruments have long been helping physicians to heal patients. Many ancient civilizations developed tools to improve surgical procedures and the diagnosis of disease. Today, minimally invasive procedures are the clinical state of the art and a variety of implants improve patients' quality of life. Every day we benefit from the progress in medicine and the improvements of the supporting sciences. Today we face two major demands: the growing costs of health care and an aging population in developed countries. Both factors require a continuous development of new, more effective and less expensive health care procedures. As was true in the past, this challenge requires a close cooperation between physicians, scientists and engineers. In this contribution, two examples show that interdisciplinary cooperation is a necessary prerequisite for the successful development of new therapeutic systems. As the first example, the development of the fractally coated pacemaker electrode is presented, which resulted in a significant improvement in sensitivity and pacing thresholds. Secondly, the introduction of the hybrid concept in coronary stent development has allowed simultaneous optimization of mechanical properties and biocompatibility. Thus, both developments improved the safety and cost-effectiveness of the medical procedure.

Key Words

Medical progress, biomedical engineering, interdisciplinary cooperation, fractal pacemaker electrode, stent

Introduction

The aim of biomedical engineering is to provide the physician with effective medical devices supporting his treatment of diseases according to the basic principle "technology helping to heal". Today, biomedical engineering is an established subject area. However, for a proper understanding of its basic principle, it is necessary to keep its origins in mind. It was the attitude of outstanding scientists like Walter Brattain, who focussed on both theoretical work, for achieving a fundamental physical understanding, and possible technological applications based on the acquired knowledge. Together with John Bardeen and William Shockley, who met each other at Bell Telephone Laboratories and who contributed significantly to the theory of semiconductors, he was awarded the Nobel Prize in 1956 for the invention of the transistor. This led to a breakthrough in the development of electronic devices, and has revolutionized our daily lives.

Walter Brattain was also interested very early in another application of theoretical physics. In close cooperation with the physician Philip N. Sawyer, he developed the electronic theory on interactions between metallic implants and the human body and applied the electronic theory it to device technology [1]. Based on experiments on thrombus formation in the vicinity of metals with different positions in the electromotive series, he stated the hypothesis that an electronic charge transfer is essential for triggering the coagulation cascade.

The importance of interdisciplinary cooperation may even become clearer when one looks at the issues surrounding modern life expectancy, which has nearly doubled during the last 100 years. Undoubtedly, the healing process of the patient ultimately depends upon the expertise of the physician in attendance. However, his success relies significantly on the development of effective technical equipment, which in turn requires close interaction between medicine and technology. In the beginning, the physician has to define the problem to be solved by the medical device. In the second step,

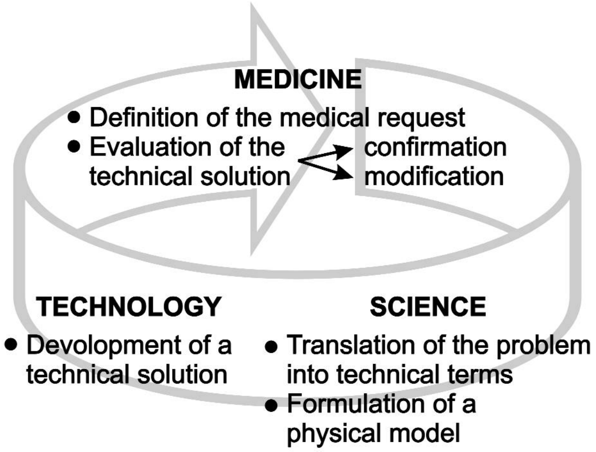

Figure 1. Development and improvement of medical devices based on interdisciplinary cooperation between medicine, science, and technology.

the medical condition to be addressed must be translated into technical terms based on a fundamental understanding of the physical processes involved. When a technical solution is found and device prototypes have been refined and passed appropriate laboratory tests, clinical trials are the next step. Clinical results either confirm the development or influence modifications for improvement. Thus, development of advanced medical devices necessitates close interaction between physicians, researchers and engineers to approach the goal of effective therapy based on clinical experience supported by medical devices "tailor-made" to address the specific disease state (Figure 1).

In the following, two representative examples will be given to demonstrate how success in treatment of cardiac diseases can be achieved by close cooperation between medicine, biomedical research, and technology. In both examples, the interface between the implant and the human body plays the dominant role. The surface of an implant is in the focus of both examples desirable and undesirable interactions between the implant and the human body are determined by the physical processes at their interface. In both cases the technological solution will be a hybrid concept: the implants consist of a bulk material matching the mechanical requirements of their environment and a surface coating for improvement of its specific functionality at the tissue-implant interface. However, the medical requirements for interaction between the body and the implant surface in these examples are completely different, resulting in completely different technical solutions.

The first example is an electrode necessary for modern cardiac pacemakers. The function of the electrode is to deliver stimulation impulses from the pacemaker to the heart tissue and support the pacemaker with detected electric signals of the time-resolved information on the condition of the heart. To support the functionality of the pacemaker, the electrode tip must have an electrically active coating that decreases the energy necessary to stimulate the heart and increases the detected electrical signals.

The second example is taken from interventional cardiology. A major challenge in the development of coronary stents applied in narrowed coronary arteries for restoring the lumen of the vessel is to reduce the rate of acute and subacute occlusion, which is mainly caused by unwanted interactions between the surface of the stent, circulating blood, and the vessel wall. In this application, the clinical requirements for the coating are to hinder the triggering of the coagulation cascade and prevent the bulk material of the stent from corrosion.

The Fractally Coated Pacemaker Electrode

A significant disadvantage of conventional cardiac pacemaker electrodes is polarization. When a pacing pulse is delivered, an electrical polarization occurs at the electrode's interface to the myocardium due to capacitive effects. A considerable loss of energy results, which limits the lifetime of the implant. In addition, the polarization artifacts (i.e., large artificial potentials after a stimulus) prevent the measurement of the cardiac potentials after the stimulus, which can be used to monitor pacing success, among other things.

To create a better resource for targeted development of pacemaker electrodes, a physical model of the entire stimulation system was developed. This model helps to translate medical challenges into specific technical requirements for the electrode. Thus, the medical requirement to reduce energy loss and improve sensing properties leads to — in technical terms — an electrode with the largest possible active surface area with the smallest geometrical dimensions [2].

In the natural organism, transport processes exist that are similar to the mechanism of charge transfer through the pacemaker electrode/myocardium interface. For example, the lungs, which must exchange a large volume of gas between liquid and gaseous solutions, provide an elegant solution to this problem through the highly ramified structure of the bronchial tree. One vessel branches into smaller ones, which subdivide into even smaller vessels. This multi-level, self-repeating, fractal structure leads to an enormous augmentation of the pulmonary active surface area. Thus, the biological system in nature reveals the powerful advantage of a large, active, fractal structure. For enhanced electrotherapy, a fractal structure minimizes the resistance of the charge transport through the phase boundary during stimulation and subsequent sensing [2, 3].

Maximizing the active surface area is most effectively realized by a hybrid construction of the electrode. The electrode tip is coated with fractal layers, guaranteeing the desired surface enlargement (Figure 2). The coating must meet specific requirements, such as long-term stability, biocompatibility, and adherence to the substrate. Renowned in implant technology for excellent tissue compatibility, iridium and titanium were chosen as materials for the coating and the substrate, respectively.

For enlarging the active surface, a thin-film coating process was developed through which layers with fractal surface structures are deposited. A layer of iridium is deposited on the substrate by DC-sputtering in a diffusion-limited process. High-energy argon ions knock atomized particles off a target, and these displaced grains of iridium are deposited on the electrode tips. With close control of the process parameters, a fractal layer of iridium grows on the tips of the electrodes.

The existence of fractals on the electrode surface is proven using microscopy at different resolutions. Methods of electron microscopy, as well as atomic force microscopy and scanning tunneling microscopy, document the existence of hemispherical structures on the electrode surface. The presence of these particle spheres is illustrated at different levels of magnification, even down to a level approaching atomic dimensions. The self-repeating character of this surface structure, apparent over a wide range of magnitudes, functions to increase the active surface by approximately 1000 times without increasing the geometrical dimension. Unlike standard uncoated electrodes, fractal electrodes exhibit extremely low impedance values over a large frequency range. Furthermore, the coating possesses excellent, long-term stability under electrochemical loads.

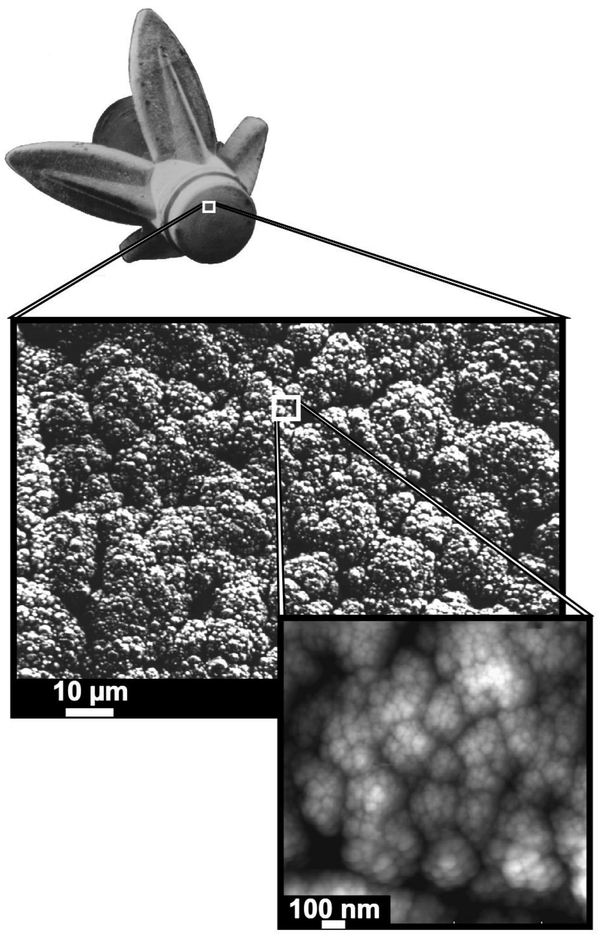

Figure 2. Scanning electron micrograph (middle) and scanning tunneling micrograph (bottom) of the electrode's fractally coated surface (top). The difference in resolution between the micrographs is two orders of magnitude.

Today, fractally coated electrodes are in clinical use worldwide. With their coating and the resulting large active surfaces, they are distinguished by energy-conserving pacing properties clinically proven by low threshold values. The fractally coated surface of the electrodes is also the basis for excellent sensing properties. These electrodes can sense much smaller cardiac potentials than can be detected by conventional, uncoated electrodes. Completely new possibilities for therapy and diagnosis result from this exclusive, fractal characteristic. Fractally coated electrodes exhibit no afterpotentials. Therefore, it is possible to measure cardiac potentials and to conduct efficacy control directly following a pacing pulse. By evaluating these signals, a wealth of information about the myocardial state

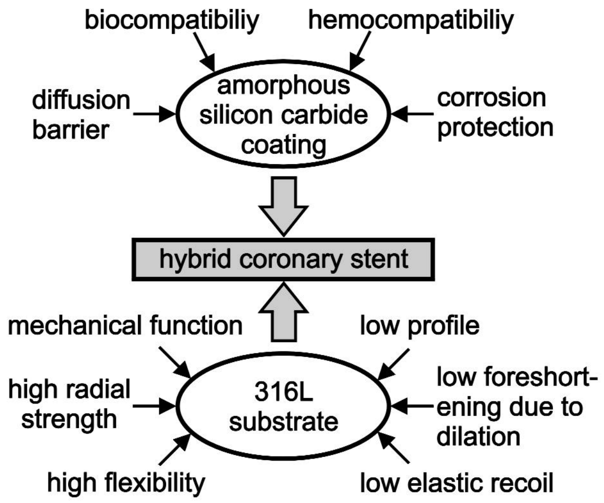

Figure 3. Schematic of the hybrid coronary stent design. A delicate balance of disparate materials is necessary to match the requirements of both the substrate and the surface to the clinical application.

becomes accessible [3]. Given these ever-growing applications, it is apparent that fractally coated electrodes are blazing new trails in the field of cardiac electrotherapy.

The Hybrid Coronary Stent

Obstruction of the coronary arteries (stenosis) due to arteriosclerosis depletes the supply of oxygen in the myocardium (ischemia). Consequently, acute stenosis very often leads to myocardial infarction. As an alternative to an invasive bypass-operation, percutaneous transluminal coronary angioplasty (PTCA) has become a widespread, minimally invasive technique for correcting stenosis. A balloon catheter is advanced through the arterial system to the diseased, constricted section of the vessel, and dilated.

To reduce the risk of repeat stenosis (restenosis) after dilatation, a coronary stent is applied at the atherosclerotic lesion site. The coronary stent is advanced to the previously PTCA-dilated site and expanded to the size of the vessel. The stent then functions as a long-term scaffolding support.

The main risk associated with implanting metal stents in blood vessels is the tendency to induce blood clotting at the stent surface. Consequently, long-term anticoagulation of the stented patient has been required to combat acute closure of the stent with thrombus. However, systemic anticoagulation leads to the risk of bleeding complications. The task of biomedical engineering has been to improve stents by tailoring materials to achieve the desired hemocompatibility, X-ray visibility, and mechanical properties. To this end, a hybrid design was again developed, this time combining a bulk material and a hemocompatible surface coating [4]. This design is configured to guarantee the necessary mechanical properties and reduce coagulation at the surface of the implant (Figure 3) [5].

The intention of this issue of "Progress in Biomedical Research" is to illuminate in detail the development of the hybrid coronary stent as a result of interdisciplinary cooperation of physicians, scientists and engineers.

In the first section, medical indications in interventional cardiology will be presented together with an overview of stent development to describe the state of the art in this field. Following a contribution on the physiologic interactions occurring at the phase boundary between components of the blood and the stent surface, the medical requirements of the "ideal stent" will be summarized from the physician's point of view.

The second section is concerned with construction, production and evaluation of the stent body. First, it is shown how the geometrical design of a coronary stent is optimized to the desired mechanical properties through the use of finite element methods. Then the laser cutting process used for structuring small tubes is described. Following the laser cutting process, the mechanical properties of the stents have to be evaluated. The second section concludes with the presentation of suitable measurement methods and a quantitative comparison of different stent designs.

The interactions between the implant surface and the human body are the focus of the third section. Starting with a description of the relevant electrochemical aspects of biocompatibility, a physical model of the processes at the phase boundary is established, resulting in the coating of the stent surface with silicon carbide (a-SiC:H). After a presentation of the coating process, the efficacy of a-SiC:H in hindering thrombus formation is evaluated on a molecular level by AFM (Atomic Force Microscopy).

After formulation of the requirements of the "ideal stent" by physicians, the construction of a corresponding stent body by engineers, and the production of an antithrombogenic surface coating based on a physical model made by scientists, the cycle of development is closed by clinical evaluation of the hybrid concept.

Initial clinical results impressively confirm the strategy of the hybrid concept, consisting of an optimized stent body and an antithrombogenic a-SiC:H coating, and also validated the principle of interdisciplinary cooperation between medicine, science, and engineering.

Conclusion

Successful treatment of patients is determined by the expertise and the skills of the physician. However, the physician is supported by diagnostic and therapeutic devices. Expertise, skills and technology must complement one another. Additional progress in health care requires a continuous and close cooperation between medicine, science, and technology.

This progress normally follows a clear sequence: daily clinical practice allows the physician to define needs from a clinical perspective. These needs must be translated into technical terms, which requires a fundamental understanding of the physical processes involved. Based on these technical requirements, a technological solution is developed. Finally, the resulting product must be evaluated in vitro and in vivo. Then, the loop closes again when the clinical results lead to new clinical experiences, which stimulate the next step.

This closed loop characterizes the cooperation of physicians, scientists and engineers that is the basis for a successful progress in health care. Without the clinical evaluation and the experience of the physician, the scientists and engineers could not accurately define the clinical scenario and requirements of the new device. Without the support of scientists and engineers, physicians would not have the advanced technology available to adapt for use in specific medical therapies. This issue of "Progress in Biomedical Engineering" is intended to raise awareness of the importance of the link between the disciplines involved in advancing the technology of health care. However, even the greatest advances in technology must not overshadow the importance and responsibility of the physician in the quality of life of the patient.

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