



D UNIVERSITÄT BERN

**Master Biomedical Engineering** 

# Annual Report 2016



# MASTER OF SCIENCE IN BIOMEDICAL ENGINEERING

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# Introduction

At end of spring 2016, we became suddenly aware that we were approaching the 10th birthday of our Master's program and I am very glad we took the initiative to celebrate that event properly in November. We welcomed some 120 students and teachers for an enjoyable anniversary with a welcome address by our vice-rector for research, Prof. Daniel Candinas, a retrospective by the founder of our BME program, Prof. Lutz Nolte, and two insights into outstanding research projects by Prof. Marcel Jacomet and Prof. Stefan Weber.

In terms of content and number of starting students, our BME program experiences a period of stability. The succession of lecturers who leave our universities remains always a challenge, but gives opportunities to young researchers to participate in our educational effort and to refresh the content of our courses. The proximity of the program to the local hospital network and the economy remains a major focus. The trip to MEDICA, the world forum for medicine in Düsseldorf, was rescheduled in the 2016 academic calendar and encountered a frank success among the students. The study direction attended the Master Messe in Zürich-Oerlikon for the second time and the need for additional information about our program in the universities of applied sciences in Switzerland was clearly recognized.

The Biomedical Engineering Day 2016 attracted some 280 participants and 15 companies to join our 3 core research

institutes. It was a pleasure to discover numerous alumni of the program as presenters of the invited companies. We received a very encouraging feedback about our efforts to cultivate this relationship between our students and research partners. The clinic of hand surgery led by Prof. Esther Vögelin offered a live surgery of a metacarpal fracture brilliantly executed by Dr. Carsten Surke in the OR and professionally moderated by Dr. Bettina Personeni in the auditorium. The keynote lecture was delivered by Prof. Rothen-Rüthisauser, from the Adolphe Merkle Institute, on the exciting opportunities and challenges of nanomaterials for life sciences. I would like to thank all the participants for this exceptional edition of the BME Day!

As usual, I wish to emphasize the remarkable performance of both internal and external teachers, who represent the heart of our master's program. I would also like to reiterate my thanks to the study coordination, Mrs Ulla Jakob, Alexandra Neuenschwander-Salazar and Julia Spyra for continuously ensuring an excellent service to the students and lecturers of the program. I am truly proud to present our 2016 activities in this report and wish you an enjoyable reading.

Philippe Zysset Program Director



# Organization

# Management



Ph. Zysset Program Director



V. M. Koch Deputy Program Director

# Administration



U. Jakob-Burger Study Coordinator



A. Neuenschwander Salazar



J. Spyra Study Coordinator

Study Coordinator



M. Reyes Master Thesis Coordinator

# Structure of Courses in the Master's Program

Since the start of the Master's Program Biomedical Engineering in March 2006, the constant effort to improve the quality of our curriculum has resulted in substantial changes of the course structure over the past years. The first curriculum consisted of a number of individual courses that were either mandatory or elective, but their coherence with regards to contents was in most cases not expressed by a defined structure. However, two major modules (formerly called "focus areas") already existed.

As of Fall Semester 2009, all courses were grouped in a strictly modular way in order to enhance both the clarity and the complexity of the curricular structure. A main idea was to guide the students through their studies in a better way by adding an elective part to the major modules, which formerly had consisted exclusively of mandatory courses. Besides, the curriculum was expanded by a number of new specialized courses as well as an additional major module called "Image-Guided Therapy".

Adaptations in the legal framework of the master's program are now offering more flexibility in the design of courses and modules, thus providing the basis for a second fundamental restructuration of the curriculum as of Fall Semester 2013. In particular, a new module called "Complementary Skills" is replacing the former module "Unrestricted Electives". In addition, the list of mandatory courses in both basic and major modules was revised.

# The Curriculum

# Duration of Studies and Part-Time Professional Occupation

The full-time study program takes 4 semesters, which corresponds to 120 ECTS points, one ECTS point being defined as 25-30 hours of student workload. It can be extended to a maximum of 6 semesters. When a student decides to complete the studies in parallel to a part-time professional occupation, further extension is possible on request. To support regular part-time work, mandatory courses take place (with rare exceptions) on only 3 days per week.

# **Basic Modules**

The basic modules provide the students with the necessary background to be able to fully understand the highly complex subject matter in the specialized courses. All students with an engineering background (for all other students, individual study plans are set up which may contain certain variations) have to complete all courses in the Basic Modules Human Medicine, Applied Mathematics, and Biomedical Engineering. In the first semester, all courses belong to this group, whereas in the second and third semester, the courses from the basic modules make up for approximately 30%.

### **Major Modules**

The choice of one of three major modules Biomechanical Systems, Electronic Implants, or Image-Guided Therapy after the first semester constitutes the first opportunity for specialization.

Approximately one third of the major modules consist of mandatory courses. In the elective part of the major module, the student is allowed to select every course from the list of courses in the master's program, giving rise to a high degree of diversity and flexibility and allowing for numerous course combinations. However, this freedom makes it somewhat difficult for the student to make reasonable choices regarding professional prospects.

This is why the responsible lecturers developed a recommended study plan to guide the students through the course selection process and to avoid organizational problems such as overlapping courses. If a student follows the recommended path, he or she can be sure to establish a sound professional profile.

# Module "Complementary Skills"

Apart from the rapid development of technology itself, today's biomedical engineers are increasingly challenged by complementary issues like ethical aspects, project planning, quality assurance and product safety, legal regulations and intellectual property rights, as well as marketing aspects. Language competence in English is of paramount importance both in an industrial and academic environment. This situation has been accounted for by the introduction of a new module called "Complementary Skills" where students are required to complete two mandatory courses (Innovation Management; Regulatory Affairs and Patents) as well as 2 ECTS from the electives courses (Ethics in Biomedical Engineering; Scientific Writing in Biomedical Engineering; Introduction to Epidemiology and Health Technology Assessment). If a student selects more than 2 ECTS from the elective part, the additional points can be credited in the student's major module.

### **Master's Thesis**

The last semester is dedicated to a master's thesis project on an individually suited topic in an academic research group at the University of Bern or the Bern University of Applied Sciences or, for particular cases, in an industrial research and development environment. As a rule, all 90 ECTS points from the course program have to be completed, thus ensuring that the student is able to fully concentrate on the challenges imposed by exciting research activities. The master's thesis includes the thesis paper, a thesis presentation and defense as well as a one-page abstract for publication in the Annual Report of the master's program.



# **List of Courses**

- Applied Biomaterials
- Basics of Applied Molecular Biology
- Basics in Physiology for Biomedical Engineering
- Biological Principles of Human Medicine
- Biomaterials
- Biomedical Sensors
- Biomedical Acoustics
- Biomedical Instrumentation
- Biomedical Laser Applications
- Biomedical Signal Processing and Analysis
- BioMicrofluidics
- C++ Programming I
- C++ Programming II
- Cardiovascular Technology
- Clinical Applications of Image-Guided Therapy
- Computer Assisted Surgery
- Computer Graphics
- Computer Vision
- Continuum Mechanics
- Cutting Edge Microscopy
- Design of Biomechanical Systems
- Engineering Mechanics
- Ethics in Biomedical Engineering
- Finite Element Analysis I
- Finite Element Analysis II
- Fluid Mechanics
- Functional Anatomy of the Locomotor Apparatus
- Image-Guided Therapy Lab
- Innovation Management
- Intelligent Implants and Surgical Instruments
- Introduction to Clinical Epidemiology and Health Technology Assessment

- Introduction to Digital Logic
- Introduction to Medical Statistics
- Introduction to Signal and Image Processing
- Introductory Anatomy and Histology for Biomedical Engineers
- Low Power Microelectronics
- Machine Learning
- Measurement Technologies in Biomechanics
- Medical Image Analysis
- Medical Image Analysis Lab
- Medical Robotics
- Microsystems Engineering
- Modeling and Simulation
- Molecular and Cellular Biology Practical
- Numerical Methods
- Ophthalmic Technologies
- Osteology
- Principles of Medical Imaging
- Programming of Microcontrollers
- Regenerative Dentistry for Biomedical Engineering
- Regulatory Affairs and Patents
- Rehabilitation Technology
- Scientific Writing in Biomedical Engineering
- Technology and Diabetes Management
- Tissue Biomechanics
- Tissue Biomechanics Lab
- Tissue Engineering
- Tissue Engineering Practical Course
- Wireless Communication for Medical Devices

# **Major Modules**

# **Biomechanical Systems**



Prof. Dr. Philippe Zysset

The cardiovascular and musculoskeletal systems are the transport and structural bases for our physical activities. Their health has a profound influence on our quality of life. Cardiovascular diseases, musculoskeletal injuries and pathologies are the most costly ailments facing our health care systems, both in terms of direct medical costs and compensation payments related to loss-of-work.

In this module, students will gain a comprehensive understanding of the multi-scale organisation of the cardiovascular and musculoskeletal systems, combining knowledge from the cell, tissue, organ to the body level. They will learn how to apply engineering, biological and medical theory and methods to resolve complex problems in biomechanics and mechano-biology. Students will learn to draw connections between tissue morphology and mechanical response, and vice versa. Students will also gain the required expertise to apply their knowledge in relevant, practice-oriented problem solving in the fields of cardiology, vessel surgery, orthopaedics, dentistry, rehabilitation and sports sciences.

The mandatory courses in this module provide the student with fundamental knowledge of fluid and solid mechanics, tissue engineering, tissue biomechanics and finite element analysis. This provides an overview of the functional adaptation of the cardiovascular or musculoskeletal system to the demands of daily living, and the necessary conditions for its repair and regeneration. This major module requires a prior knowledge of mechanics, numerical methods and related engineering sciences, as many of the mandatory and elective courses build upon these foundations. Elective courses allow the students to extend their competence in a chosen direction, gaining knowledge in analytical methodologies, medical device design, minimally invasive surgery or rehabilitation.

Knowledge gained during the coursework highlights the multidisciplinary nature of this study focus area, encompassing the cell to body, the idea to application and the lab bench top to the hospital bedside. This knowledge is applied during the final thesis project, a project often with a link to a final diagnostic or therapeutic application. Examples of recent master thesis projects include the design of intra-cardiac energy harvesting, the development of a flow sensitive magnetic resonance imaging sequence, the estimation of yield properties of human trabecular bone or the investigation of cell-surface markers around biomaterials.

Career prospects are numerous. Many students proceed to further post-graduate education and research, pursuing doctoral research in the fields of biomechanics, tissue engineering or development of biomaterials. Most of the major companies in the fields of cardiovascular engineering, orthopaedics, dentistry, rehabilitation engineering and pharmaceuticals are strongly represented within the Swiss Medical Technology industry and, despite the strong Swiss franc, have an ongoing demand for graduates of this major module. At the interface between biomedical engineering and clinical applications, graduates may also pursue careers related to the evaluation and validation of contemporary health technology, a cornerstone for future policies on the adoption of these new methods in the highly competitive health care domain.



High speed optical and thermal images of orthogonal cutting experiments on compact bone at two distinct cutting depths.

# **Major Modules**

# **Electronic Implants**



Prof. Dr. Volker M. Koch

Electronic implants are devices like cardiac pacemakers and cochlear implants. Due to miniaturization and other developments, many new applications become feasible and this exciting area is growing rapidly. For example, cochlear implants provide already approximately more than 320'000 people worldwide a sense of sound. These people were previously profoundly deaf or severely hard of hearing. Recently, researchers demonstrated that electronic retinal implants allow the blind to read large words.

There are many more applications for electronic implants beyond treating heart problems, hearing loss or blindness. For example, there are electronic implants that treat obesity, depression, incontinence, hydrocephalus, pain, paraplegia, and joint diseases.

In this module, students will learn about the basics of electronic implants. This includes: signal processing and analysis, low-power microelectronics, wireless communications, and MEMS technology. Application-oriented elective courses are also taught, e.g., diabetes management, biomedical acoustics, and biomedical sensors.

Since the development and manufacturing of electronic implants is highly complex and since it involves many different disciplines, it is not the goal of this major that students are able to develop an electronic implant on their own but rather to be able to work successfully in a project team that develops electronic implants.

Students may already apply their knowledge as a parttime assistant in a laboratory and/or during their master's projects. After finishing the degree program, a wide variety of career paths are available, ranging from research and development to project and product management. Many companies in Switzerland work in this field and "traditional" implants manufacturers have recently become interested in electronic implants, e.g., to measure forces in knee implants.



Prototype of a lead- and batteryless cardiac pacemaker (courtesy of the Group for Translational Electrophysiology. Deptartment of Cardiology, Bern University Hospital & ARTORG Center for Biomedical Engineering Research).

# Image-Guided Therapy



Prof. Dr. Stefan Weber

Image-Guided Therapy refers to the concept of guiding medical procedures and interventions through perceiving and viewing of medical image data, possibly extended by using stereotactic tracking systems. Medical imaging typically relates to a great variety of modalities ranging from 2D fluoroscopy and ultrasound to 3D computed tomography and magnet-resonance imaging, possibly extended to complex 4D time series and enhanced with functional information (PET, SPECT). Guidance is realized by determination of the spatial instrument-to-patient relationship and by suitable visualization of tracking and medical image data. Image guidance is very often accompanied by other surgical technologies such as surgical robotics, sensor enhanced instrument systems as well as information and communication technology.

Students of the IGT module will study the clinical and technical fundamentals of image-guided therapy systems. They will develop an understanding of currently applied clinical standards as well as an overview of latest advancements in research (check out the recently introduced course on Clinical applications of IGT as well as the IGT Lab). Successful students will be enabled to develop novel clinic-technological applications for complex medical procedures as well as improve existing approaches. This will be the basement for successful careers both in the industrial and academic sector.

Mandatory courses of this module are concerned with the fundamentals of Signal and Image Processing and Medical Image Analysis. Furthermore, fundamental aspects of stereotactic image guidance, tracking, patient-to-image registration and basic clinical applications are taught in the course Computer-Assisted Surgery. Recent trends and fundamental aspects in surgical robot technology, minimally invasive procedures and its applications within IGT are introduced in the course Medical Robotics. Additional elective courses extend students competencies in related areas such as computer graphics, pattern recognition, machine learning, and regulatory affairs.



The world's first robotic cochlear implantation, Inselspital Bern, July 2016 (© ARTORG Center).

# **Evaluation of Courses in the Academic Year 2015/2016**

Like in the previous years, a centralized evaluation was performed in the Master's program in Fall Semester 2015 and Spring Semester 2016 according to the guidelines of the University of Bern. Both semesters were considered, leading to 43 course evaluations involving more than 1000 forms in total. The results regarding all forms (see below) reveal that the students are very satisfied with the course program and that the courses are interesting and demanding at the same time.



1: very poor 2: poor 3: good 4: excellent



1: far too narrow/narrow 3: just right 5: far too high/wide

# Faculty

# **University of Bern**

Christiane Albrecht, Prof. Dr. Philippe Büchler, Prof. Dr. Dario Cazzoli, Dr. Roch-Philippe Charles, Prof. Dr. Bruno da Costa, Dr. Marcel Egger, Prof. Dr. Matthias Egger, Prof. Dr. Tobias Erlanger, Dr. Favaro Prof. Dr., Paolo Christian Fernandez Palomo, Dr. Martin Frenz, Prof. Dr. Benjamin Gantenbein, Prof. Dr. Amiq Gazdhar, Dr. Kate Gerber, Dr. Nicolas Gerber, Dr. Olivier Guenat, Prof. Dr. Wilhelm Hofstetter, Prof. Dr. Doris Kopp Jan Kucera, Prof. Dr. Glenn Lurman, Dr. Ange Maguy, Dr. Ghislain Maguer, Dr. Ines Margues, Dr. **Beatrice Minder** Stavroula Mougiakakou, PD Dr. Tobias Nef, Prof. Dr. Thomas Nevian, Prof. Dr. Lutz Nolte, Prof. Dr. Dominik Obrist, Prof. Dr. Mauricio Reyes, Prof. Dr. Steffen Schumann, Dr. Walter Martin Senn, Prof. Dr. Marc Stadelmann Jürg Streit, Prof. Dr. Raphael Sznitman, Prof. Dr. Stefan Andreas Tschanz, Dr. Prabitha Urwyler, Dr. **Benjamin Voumard** Stefan Weber, Prof. Dr. Tom Williamson, Dr. Wilhelm Wimmer, Dr. Guoyan Zheng, Prof. Dr. Matthias Zwicker, Prof. Dr. Philippe Zysset, Prof. Dr.

# Bern University Hospital (Inselspital) and School of Dental Medicine

Daniel Aeberli, PD Dr. Sufian Ahmad, Dr. Tommy Baumann, Dr. Dieter Bosshardt, Prof. Dr. Marco-Domenico Caversaccio, Prof. Dr. Vivianne Chappuis, Dr. Sigrun Eick, Prof. Dr. Jens Fichtner, Dr. Michael Fix, PD Dr. Simon Flury, Dr. Pjotr Fudalej, PD Dr. Andreas Häberlin, Dr. Tim Joda, Dr. Joannis Katsoulis, PD Dr. Martin Kompis, Prof. Dr. Kurt Laederach, Prof. Dr. Kurt Lippuner, Prof. Dr. Dobrila Nesic, PD Dr. Thomas Pilgrim, Prof. Dr. Lorenz Räber, PD Dr. Christoph Andreas Ramseier, Dr. Thiago Saads Carvalho, Dr. Christophe Von Garnier, Prof. Dr.

# Bern University of Applied Sciences

Norman Urs Baier, Prof. Dr. Heiner Baur, Prof. Dr. Daniel Debrunner, Prof. Bertrand Dutoit, Prof. Dr. Josef Götte, Prof. Dr. Kenneth James Hunt, Prof. Dr. Marcel Jacomet, Prof. Dr. Björn Jensen, Prof. Dr. Jörn Justiz, Prof. Dr. Theo Kluter, Prof Dr. Volker M. Koch, Prof. Dr. Martin Kucera, Prof. Alexander Mack, Dr. Christoph Meier, Prof. Thomas Niederhauser, Dr. Heinrich Schwarzenbach, Prof. Andreas Stahel, Prof. Dr. Jasmin Wandel, Prof. Dr.

# Partner Institutions and Industry

Daniel Baumgartner, Dr. Marc Bohner. Dr. Mathias Bonmarin, Dr. Jürgen Burger, Prof. Dr. Philippe Cattin, Prof. Dr. Alessandro Cianfoni, Dr. Barbara Cvikl, PD Dr. Emmanuel de Haller, Dr. Nicolas Alexander Diehm, Prof. Dr. Nicola Döbelin, Dr. Alex Dommann, Prof. Dr. Patrick Dubach, Dr. David Eglin, Dr. Lukas Eschbach, Dr. Marie-Noëlle Giraud, PD Dr. Reinhard Gruber, Prof. Dr. Janosch Häberli, Dr. Daniel Haschtmann, Dr. Bernd Heinlein, Prof. Dr. Philippe Henle, Dr. Roman Heuberger, Dr. Ulrich Hofer, Dr. Thomas Imwinkelried, Dr. Herbert Keppner, Prof. Dr. Jens Kowal, PD Dr. Beat Lechmann Reto Lerf, Dr. Lukas Lichtensteiger, Dr. Reto Luginbühl, Dr. Simon Milligan, Dr. Walter Moser, Dr. Richard Nyffeler, PD Dr. Yves Pauchard, Dr. Matthias Peterhans, Dr. Jorge Sague, Dr. Barbara Rothen-Rutishauser, Prof. Dr. Birgit Schäfer, PD Dr. Matthias Schwenkglenks, PD Dr. Jivko Stoyanov, PD Dr. Tim Vanbellingen, Dr. Jürgen Vogt, Dr. André Weber, Dr.

# **Statistics**



# Number of New Students and Graduates per Year



# **Profession after Graduation**





# 10 Years Master Biomedical Engineering – a Retrospect

On November 10, 2016, students, lecturers and alumni met in the auditorium Ettore Rossi at the Inselspital in Bern to celebrate the 10th birthday of the Master's Program in Biomedical Engineering. Talks were given on research projects carried out at the University of Bern and the Bern University of Applied Sciences. The former and current program directors shared their reflections and ideas covering both past and future developments. The evening was completed by an informal get-together with a delicious buffet, piano music and interesting conversations.



A considerable number of students, alumni and lecturers joined us to celebrate the 10th birthday of the BME master's program. Photo: Adrian Moser

Looking back, 19 hopeful students gathered at the beginning of summer semester 2006 in a small lecture hall at the Institute for Surgical Technology and Biomechanics (ISTB) in Bern-Wankdorf to attend the very first lecture in the new Master's program Biomedical Engineering.



Daniel Candinas, Philippe Zysset, Lutz Nolte, Lukas Rohr, Volker Koch and Stefan Weber (from left to right) are listening attentively the talk of Marcel Jacomet, Bern University of Applied Sciences who presents a research project he conducted in collaboration with the ARTORG center. Photo: Adrian Moser

A lot of preparatory work had preceded this day: the curriculum had to be developed, the regulations had to be set up and got through the administrative processes involved, lecturers had to be recruited, the existence of this new program had to be made public, the financing had to be secured and, among many other little things, the program director Prof. Lutz Nolte (who happens to be a trained civil engineer) organized the construction and equipment of two brand new lecture halls at the ISTB in Stauffacherstrasse.

In the early years of the program, practically all courses took place there. Students will remember the days in 2008 when parades of Dutch football fans making noise with toy trumpets and kettledrums passed the lecture hall's windows. They were on their way to the Wankdorf stadium where the Dutch team played the qualifying round in the European Football Championship.



Alumni from the first class in 2006: Prabitha Urwyler, Elisa Munafo and Alois Pfenniger. Photo: Adrian Moser

However, the history of the master's program reaches back to the beginning of the millennium when Lutz Nolte, director of the ISTB, perceived the need for welltrained medical engineering professionals in the blooming Medtech industry in Switzerland. Nevertheless, only a very limited number of corresponding education options existed at the time. Besides, over the years he had employed a number of highly motivated and skilled engineers with a degree from a university of applied sciences. Repeatedly, he had to experience that these valuable employees left after few years because they had no opportunity to pursue a successful career in an academic environment. Consequently, he developed the idea of establishing a master's program in biomedical engineering which should also be open to engineering graduates from universities of applied sciences. Therefore, it seemed a natural choice to set up this new study program in collaboration with the Department of Engineering and Information Technology of the Bern University of Applied Sciences (BFH-TI). In Jürgen Burger, a research project partner of Lutz Nolte's and professor of Biomedical Engineering in the micro and medical technology program at BFH-TI, he found an enthusiastic colleague who pursued the task to find official support and lecturers at BFH-TI. At the same time, Lutz Nolte convinced the Faculty of Medicine that it was of great value to offer such a study program.



Philippe Zysset (left) and Lutz Nolte, current and former program director of the BME master's program.

Both of them succeeded and the official collaboration between these institutions could be established. The basic concept was set up for the new master's program: for the first time in Switzerland, graduates from a university of applied sciences were accepted to university level master studies without additional requirements, thus also allowing them to continue their education towards a PhD degree. Moreover, the program was the first Master of Science program in Biomedical Engineering in Switzerland, followed one semester later by the corresponding program at ETHZ.



Daniel Debrunner (left) and Andreas Stahel, lecturers in the BME master's program right from the start.

Like today, the program was organized as a specialized master's program (120 ECTS points) admitting graduates from various engineering fields, physics, computer science as well as outstanding candidates possessing a degree in natural sciences or medicine. It contained a number of basic courses, elective courses, and two specializations, formerly called focus areas. The focus area "Musculoskeletal System" was affiliated to the Faculty of Medicine of the University of Bern, whereas the focus area "Microsensor and Actuator Technology" was offered by BFH-TI. The concept to have a full-time study program where presence is required on three days per week only – thus enabling students to have a regular part-time professional occupation – also dates back to the very beginning.



Following the official program, a delicious buffet was served in the foyer of the Ettore Rossi auditorium. Photo: Adrian Moser

The level of perfection in matters of organization and equipment, however, left room for improvement at the time: as the construction of the "big" lecture hall was not quite finished during the first weeks in 2006, students had to sit on simple chairs without a desk, balancing all material on their knees. Registration for courses and exams was done by signing in to lists which were displayed in the lecture hall, and it was more the rule than the exception that the communication of exam dates and timetables was a last-minute affair. It was only due to the competence and tireless commitment of our program coordinator Ulla Jakob that in this and all other aspects of the development and organization of the master's program we could always provide high-quality service to our students.



Piano Man Alper Akcöltekin, PhD student at the ISTB, provided the musical entertainment. Photo: Adrian Moser

However, not so slowly but surely the program underwent substantial improvements during the last 10 years. In 2008, it experienced a tremendous push due to the founding of the ARTORG Center for Biomedical Engineering Research at the Faculty of Medicine. All of a sudden, a number of biomedical engineering specialists were available to teach in the program. As a consequence, the list of specialized courses could be augmented significantly. A third specialization (now referred to as "Major Module") called "Image-Guided Therapy" was established in 2009 and is now affiliated to the groups of Prof. Stefan Weber at ARTORG.



All would-be surgeons could enjoy themselves at the BME Club's photo booth. Photo: Juan Ansó

In addition, the focus area "Microsensor and Actuator Technology" was restructured by Volker Koch, succeeding Jürgen Burger as professor of Biomedical Engineering and as BFH-TI representative in the master's program. The new specialization had its focus mainly on electronics in biomedical implants and was consequently renamed to "Electronic Implants". At the same time, the curriculum was given the modularized structure it has today.

All these changes occurred just at the right moment when the number of students substantially increased as of 2009. The program had already outgrown the lecture halls at ISTB with a maximum of 40 seats. As a consequence, most courses took place at different locations in the center of Bern.



Dobrila Nesic, lecturer of the Tissue Engineering course, meets Christian Szücs, her very first master student. Photo: Adrian Moser

The process of constantly expanding and enriching the study program did by no means end at this point. Philippe Zysset, newly appointed professor of biomechanics at the ISTB, replaced Lutz Nolte as program director in 2012. In 2013, the specialization "Musculoskeletal System" was redefined and renamed to "Biomechanical Systems", thus including the topics of fluid mechanics and microfluidics covered by research groups at ARTORG. In addition, the new module "Complementary Skills" was introduced, designed to familiarize the students with non-engineering knowledge and skills that are important to a biomedical engineer such as management, legal and quality issues, ethical aspects, epidemiology and scientific English. An important breakthrough came in 2014 when the basic courses in Anatomy and Physiology that had previously been taught in German could be offered in English. Since then, the master's program has been a 100% English program, which was a major achievement considering the fact that in 2006, 40% of all courses had been held in German. Almost every year, new elective courses broaden the scope of the program.



Julia Spyra, organizer of the BME birthday party, shares a hilarious moment with Tobias Nef and Alexandra Neuenschwander (from behind). Photo: Adrian Moser

Still, the improvement of the curriculum has not come to an end. The next goal is to take better account of the fact that our students come from various fields of study, leading to a certain imbalance concerning the students' previous knowledge in many courses. To deal with the situation, a number of elective "bridge courses" intended to convey basic knowledge in programming, electrical engineering, engineering mechanics and biomaterials are in the process of planning. In view of the rapid pace at which research and development in biomedical engineering is evolving, it is to be expected that the Master's Program in Biomedical Engineering will continue to develop over the next 10 years and beyond.

# **Graduation Ceremony**

Like all students who successfully finished the BME Master, we were invited to receive our merited diploma at the Casino Hall in Bern. Not only biomedical engineers attended the ceremony but the entire medical faculty. For us, engineers, we were only a small representation of the audience and we had time before coming on stage to remember these two previous years.

Everything started with the introduction day where we received information about the BME program. We needed the first weeks to get used to the different classroom locations. The main building, UniS, and the Chemie building did not have any secrets after a while. Having colleagues speaking German, French and other languages with the common denominator of English was a real enrichment opportunity. After the first semester of general lectures, the second semester, more specifically, allowed us to study deeply in our field of interest. This was also the occasion to learn how to move in the city of Bern, between the ISTB situated in Wankdorf, the Inselspital, the ARTORG center, the DKF, the anatomy and physic building, etc.

Suddenly the row before us stands up and goes in the direction of the stage. We follow the movement and walk on the stage. We receive our diploma, so fast in comparison with all the efforts of these last years and go back to our chairs. The following aperitif is the time to discuss with our friends and family. We are ready for our future, as biomedical engineers!

Benjamin Voumard



Our alumni 2016

Top (from left to right): Samuel Mosimann, Benjamin Voumard, Tobias Stöckli, Stefan Funariu, Stefan Stucki, Mirko Betto, Sandro Burn, Alexander Grundmann, André Schwery, Flurin Feuerstein, Adrian Zurbuchen (PhD) Bottom (from left to right): Sarah Zbinden, Jan Beerstecher, Daniel Zolliker, Adrian Sallaz, Sebastian Spicher, Felix Wassmer, Sören Miethke, Barbara Esch, Rico Fausch, Wilhelm Wimmer (PhD)

# **RMS** Award



The RMS Award stands for the Robert Mathys Foundation Award that honors the student with the best grade average over the two year master program with a prize of 1000 CHF.

The study direction wishes to thank Dr. Beat Gasser and the executive board of the Robert Mathys Foundation for this contribution to the excellence and visibility of our biomedical engineering field.

RMS Award 2016 Samuel Mosimann receives the Award from Beat Gasser, RMS Foundation.

# **Graduation Profile**



Sebastian Spicher, BME Alumnus (2016)

**Q:** What was your academic and professional background prior to your BME studies?

**A:** After the compulsory school time, I attended the Collège St. Michel in Fribourg and did the Matura. During that time, I spent a year abroad in the States where I went to high school. Then, I decided to continue my studies at the Bern University of Applied Sciences in the field of computer science. As part of my studies I did an internship of 11 months as a software engineer. After receiving my bachelor's degree, I worked for three years as a software engineer.

**Q:** Why did you choose to pursue your Master's studies at the University of Bern / Bern University of Applied Sciences?

**A:** The driving force to pursue my master's studies was mainly that I wanted to change the field in which I was working, as well as my strong interest in image processing which was already part of my bachelor studies. With the Biomedical Engineering Master's program at the University of Bern I was able to combine those two preferences and apply my previous studies to a new field.

**Q:** You continued to work during your studies. How was this experience?

**A:** At the beginning, I was working a 40% part time job. This proved to be too great of a burden and influenced my studies negatively. That is why I decided to reduce my part time job to 20%. I worked in a field not directly related to the biomedical field.

**Q:** What was your career plan after the completion of your degree?

**A:** My goal was to get first experiences in a company in the field of biomedical engineering. With that in mind I sent my application to different companies in the region even though not all of them were actively looking for new employees. In the end I got a job at Ziemer Ophthalmic Systems AG as a software engineer.

**Q:** What is the benefit of the Master studies with regard to your current professional activity?

**A:** At Ziemer Ophthalmic Systems AG all the different engineering fields are actively practiced, be it mechanical, electronical or software engineering. My daily work takes place in a highly interdisciplinary environment. The possibility during the master's studies to attend modules and study with people from different engineering fields has helped me in the beginning.

# **Biomedical Engineering Day 2016**

# The industry, medical doctors, and engineers meet for the Biomedical Engineering Day at the Inselspital in Bern with great success.

On May 27, 2016, the Biomedical Engineering Day took place in the auditorium Ettore Rossi at the Inselspital in Bern. The Master in Biomedical Engineering program of the University of Bern organized this event for the eighth time.



Participants in the auditorium Photo: Adrian Moser

The event is an efficient platform in Switzerland for networking of Master and PhD graduates and Swiss and international medical technology companies. This year's companies introduced themselves through oral presentations and gave insight into their commercial activities and their company philosophies as well as showed their demands on junior employees. Students thus had the opportunity to get to know potential future employers and contact them directly. This was made possible between the sessions in personal conversations and at the exhibitors' booths.



BME students Mirco Gysin and Iwan Paolucci discuss how surgeons place an ablation needle precisely with the CAS-ONE navigation system. Photo: Adrian Moser

The BME Day offered great opportunities for the Bernese biomedical researchers, too. The ARTORG Center for Biomedical Engineering Research and the Institute for Surgical Technologies and Biomechanics as well as the Bern University of Applied Sciences, a partner within the Master program, used the possibility of presenting current research projects to more than 250 participants. Interestingly, Master and PhD students play an important role in many of these projects. Thereby, this event was a demonstration of scientific achievements, too.



BME students gather during break time. Photo: Adrian Moser

Besides company representatives, scientists, researchers, and young academics, many medical doctors participated in this year's event as they had the chance for intensive communication with the biomedical engineers.



ISTB researchers enjoy their discussions. Photo: Adrian Moser

One highlight of the day was the successful live hand surgery by Carsten Surke, Department of Plastic and Hand Surgery, Inselspital Bern. Illustrative explanations in the auditorium were given by Bettina Juon Personeni, from the same department.

# Awards

At the end of the day, four awards for excellent academic achievements in the field of Biomedical Engineering at the University of Bern were presented:

- 1. SICAS Award for the best master's thesis: **Benjamin Voumard** (Intra-Operative Prediction of Bone Quality and Bone-Implant Compound Stability for Dental Implantation)
- 2. SICAS Award for the best PhD thesis: Li Liu (Development and Validation of Computer Assisted Diagnosis, Planning and Navigation Systems for Periacetabular Osteotomy (PAO))
- 3. BME Club Award for the best poster: **Joachim Dehais** (A Computer Vision-Based Smartphone System for Carbohydrate Counting)
- 4. BME Club Award for the best master's thesis abstract: **Jan Beerstecher** (Novel Implant Design for a Long-term Esophageal ECG Recorder)



SICAS Award winners: Benjamin Voumard and Li Liu. Photo: Adrian Moser



BME Club Award winners: Joachim Dehais (left) and Jan Beerstecher (right) with Andreas Stahel and Dobrila Nesic. Photo: Adrian Moser



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# **The Biomedical Engineering Club**

# The BME Club and Its Mission

The BME Club is an alumni club with the mission to provide and promote networking among its interdisciplinary members. We are a constantly growing group of biomedical engineers, scientists, past and present students and medical technology corporates eager to bring together the principles of engineering, biology, and clinical medicine. BME club accomplishes these goals by hosting events such as information sessions on the latest cutting-edge research in different fields of biomedical engineering, attendance of international conferences and organizing visits of various industrial plants and laboratories. BME club is recognized as an official alumni association of the University of Bern under the umbrella organization – Alumni UniBe. A dedicated executive committee follows the principles of our constitution.

We are an enthusiastic and versatile group with diverse activities:

• bi-monthly "Stammtisch" in a local restaurant as an amiable platform to exchange, discuss, brainstorm or simply chat

• visits to Swiss medical and engineering companies

- organization of the annual MEDICA trip
- information on career opportunities (including job offers)

• organization of the annual welcome event for new students of the BME Master program

- organization of an annual alumni gathering
- sponsorship of the poster and abstract awards at the annual BME day
- sponsorship of Travel award
- publish annual BME club Newsletter
- provide access to the Medical Cluster events
- offer joint membership with SSBE (Swiss Society for Biomedical Engineering)

In short, the BME club represents a unique platform for professional, lifelong communication and networking. For further details look up our website at http://www.bmeclub.ch.

# How to Join

Becoming a member is easy! Simply sign up at any BME Club event or visit us at http://www.bmeclub.ch. We are looking forward to welcome you!

## The BME Club Board in 2016



Prabitha Urwyler President



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Carlos Ciller Treasurer



Dobrila Nesic Faculty



Hector Alvarez Marquez Master Students



Fatih Toy Alumni

# Trip to Medica 2016

The 2016 trip to MEDICA was an exhilarating experience filled with good friends, good food, lots of walking and, of course, medical devices. The trip began with dinner in Bern, allowing the group to get to know each other before our excursion. With our stomachs full of Cordon Bleu, we loaded the bus and left for the medical device mecca in Düsseldorf.

MEDICA is the world's leading trade fair for medicine and medical technology, with over 5,000 exhibitors and over 125,000 attendees. Upon arrival, we could feel the draw of the fair throughout the entire city. The trams were loaded to maximum capacity, (so full one even broke down from weight!) and the city bustled with people from all sectors of the medical field. Entering the fair was like walking into a wonderland of medical technology. The amount of vendors and companies showcasing their products seemed endless. With over 15 halls, each with hundreds of companies within, there is no possible way to see everything during the timeframe of the exhibit. There really was something for everyone, with products ranging from MRI machines to sports equipment to companion robots to massaging water beds. Thankfully, the conference is divided into sections of interest so we could easily find the booths most interesting to us.



The group in front of the MEDICA. Photo: Hector Alvarez Marquez

After breaking into smaller groups, we ventured into the fair to explore. Some main product groups we visited included electrical medical equipment, laboratory equipment, surgical & diagnostic tools, physiotherapy technology, but there were many more. The smaller groups enabled us to better interact with the exhibitors, where we could ask guestions about the products and often times discuss with designers about the engineering behind the devices. Throughout the day we had the opportunity to meet with companies from all over the world and gain an impression of just how massive the medical industry is. Examples taught in our studies barely scratch the surface of the things found at MEDICA. The opportunity to touch and use devices on display triggered discussions about how we could improve these devices based on what we've learned, sparking creativity and widening our views about our future possibilities after the Master's program. In the evenings we took advantage of the trip and explored the city. Düsseldorf is a beautiful town with plenty

to see. Between food, coffee shops, and parks, we again found ourselves unable to see it all during the short stay.



Phuong-Ahn Laurence Tran, Marie Anne Larraillet, Pierre-André Friederich are using the device called "Cefaly", used for migraine prevention. Cefaly is an External Trigeminal Nerve Stimulator (e-TNS). An adhesive electrode is placed on the forehead and the Cefaly is connected magnetically to this electrode. Precise micro-pulses are then sent through the electrode to the upper branch of the trigeminal nerve preventing future migraine attacks. Photo: Hector Alvarez Marquez

The timing of the trip added to the ambiance with start of the city's Weihnachtmarkt. The second evening in the city was the first lighting of the central Christmas tree, and offered live music, twinkling lights and Glühwein to keep warm. After the final day, all the small groups came back together for a delicious parting dinner at Füchschen, a local brewery, where we traded stories of the fair and enjoyed food in the local style.



The group picture was taken in Düsseldorf Altstadt, the name of the place is "Em Pöötzke". Photo: Hector Alvarez Marquez

Overall, the MEDICA trip with the BME club was a remarkable experience. While the medical fair in and of itself is a biomedical engineer's dream exhibition, attending with the BME club enhances the experience even more with extra events in the city and great people to share the trip with. I highly recommend attending if you ever get the chance to go, and if you do be sure to check out the physiotherapy hall...they give free massages!

Emily Kathryn Thompson, BME student

# Master's Theses 2016



























































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# **Development of a Leadless Cardiac Dual-Chamber Pacemaker**

Emir Artik

Supervisors: Lukas Bereuter, MSc and Thomas Niederhauser, PhD Institutions: ARTORG Center for Biomedical Engineering Research, Universität Bern Examiners: Lukas Bereuter, MSc and Andreas Häberlin, MD, PhD

### Introduction

Contemporary cardiac dual-chamber pacemakers monitor and control the heart's electric activity by using several implanted leads. Major complications related to these leads are dislodgement, fracture and infections. The surgical re-interventions may cause complications and are costly. Leadless cardiac pacemakers were introduced recently, but they are only single-chamber pacing devices and cannot maintain atrioventricular synchrony. In order to permit more physiologic pacing and to maintain atrioventricular synchrony, two leadless pacemakers may be implanted (one in atrium, one in ventricle) and in order to synchronize, these devices have to communicate with each other. The aim of this project was to characterize the myocardial tissue for galvanic coupled intra body communication. This communication method makes use of the human body (i.e. heart) as a propagation medium for transmitted data and enables communication with a power consumption in the microwatt range. Within this project, the influence of design-specific parameters such as signal carrier frequency, electrode distance, active electrode surface area and device distance have been investigated in order to set requirements for the development of leadless dual-chamber pacemakers.

## **Materials and Methods**

For the electrical characterization of the myocardial tissue, impedance and transfer function measurements were performed on pig hearts both in-vivo and in-vitro, by using an impedance spectroscope (fig.1). Additionally, an existing theoretical model for the simulation of the galvanic coupling intra-body communication was adapted to myocardial tissue. [1]



Fig. 1 Hardware setup for transfer function measurements.

# Results

Based on the measurement results, design-specific requirements have been set for the development of a leadless dual-chamber pacemaker system.

Analysis of a total of 144 transfer function measurements performed on 15 pig hearts allowed the specification of an attenuation range for general heart tissue (fig.2). It was observed that on average, a minimum attenuation of -18dB is obtained at 1MHz. The theoretical model's minimum attenuation is centered around 500 kHz, which is in accordance with the in-vivo measurements.



Fig. 2 Transfer function (mean and standard-deviation) results from 144 measurements (including all in-vivo and in-vitro measurements). This is crucial for characterizing the attenuation range for heart tissue in general.

### Discussion

The carrier signal frequency for the communication should be set to 1MHz for achieving lowest signal damping. Implementing the proposed design-parameters would allow to improve the system's power efficiency, which is mainly achieved by increasing the input impedance and decreasing the signal damping. In particular, continuous communication with a power consumption of <6  $\mu$ W would be possible.

### References

[1] Song, Yong, et al. "The simulation method of the galvanic coupling intrabody communication with different signal transmission paths." *IEEE Transactions on Instrumentation and Measurement* 60.4 (2011): 1257-1266.





# Development of Algorithms for Peripheral Nerve Segmentation using Machine Learning Approaches

# Fabian Balsiger

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# Introduction

Peripheral neuropathy refers to any disorder or damage of the peripheral nervous system. Approximately 2.4 % of the population suffer from peripheral neuropathy and trauma patients yield a prevalence of 2.8 %. Magnetic resonance neurography (MRN) has gained popularity in the past years as a complementary tool to the state-ofthe-art diagnosis for peripheral neuropathies, which is mainly based on neurological examination, biopsies, and electrodiagnostic studies. MRN contributes structural information, allows to image situated nerves, and deeply enables the examination of the surrounding tissue to detect signs of muscle denervation. Therefore, MRN provides significant additional and complementary information to the state-of-the-art diagnosis.

The aim of this thesis was to develop a machine learning-based algorithm to segment peripheral nerves from MRN images, and to investigate the feasibility of modeling peripheral nerves as tubular structures.

# Materials and Methods

We propose a fully automatic segmentation pipeline consisting of five main steps: (i) pre-processing of the images, (ii) registration of the TIRM image to the T2-weighted image, (iii) feature extraction, (iv) voxel-wise tissue classification into peripheral nerve and background using a random forest, and (v) post-processing of the classification, which generates the final segmentation of the peripheral nerves.

Turbo inversion recovery magnitude (TIRM) and T2weighted MRN images of six healthy volunteers (23  $\pm$  1.3 yrs; 5 male) from four anatomical regions upper arm, lower arm, upper leg, and lower leg were used.



Fig. 1 Dice coefficients of the segmentation pipeline, which were evaluated for each anatomical region separately.

# Results

The proposed segmentation pipeline identified and successfully segmented the peripheral nerve with a maximum Dice coefficient of  $0.643 \pm 0.185$  in the upper leg, Fig. 1. However, due to low contrast information presented in the images of the upper arm, lower leg, and lower arm, the Dice coefficients were  $0.366 \pm 0.089$ ,  $0.185 \pm 0.076$ , and  $0.283 \pm 0.125$ , respectively.



Fig. 2 Visualization of the segmented N. ischiadicus from the upper leg (left). Colors represent the distance to the ground truth (right).

# Discussion

The proposed method is able to segment peripheral nerves from the upper leg due to a clearly visible boundary, Fig. 2. Experiments on the upper arm, lower leg, and lower arm resulted in a low segmentation accuracy due to a low contrast between peripheral nerve and its surrounding tissues. The tested vessel enhancement methods showed that using a tubular model might be a too restrictive assumption for the enhancement of peripheral nerves, due to more elliptical shape of the peripheral nerves. Therefore, a new model that incorporates this information has to be evaluated. Moreover, a deeper study of high-resolution MRN images or alteration of MRN sequences should be considered, in order to improve the contrast information between peripheral nerve and its surrounding tissues.

# References

Martyn C. N. and Hughes R. A., Epidemiology of peripheral neuropathy, J Neurol Neurosurg Psychiatry 62(4):310-318, 1997.





# Development and Evaluation of a Tele-Rehabilitation Application for Aphasic patients

# Sarah Blankenberger

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# Introduction

Aphasia is an acquired language impairment caused by a cerebral lesion following a stroke, a traumatic brain injury, a brain tumour or in rare cases of infections or neurodegenerative diseases. This language impairment implies difficulties to speak, understand spoken language, read or write in different forms and degrees. Every year, more than 3000 people will develop aphasia and will then need intensive and individualised therapy'. The introduction of tablet devices allows patients to train independently anytime and anywhere in addition to the standard face-to-face therapy. Tablet based therapies thus promote increased therapy frequency and thereby early recovery. The tablet application created by the ARTORG institute in consultation with speech therapists allows patients to train language related tasks autonomously. Speech therapists can assign exercises to their patient and track their results using the dedicated therapist interface. Although the level of the current exercise is adaptable to each patient, the existing tasks are too easy or do not cover all language domains. The aim of this master thesis was to develop and test the usability of new effective training tasks which are self-motivating and tailored for patients with mild to moderate aphasia.

# **Materials and Methods**

Eleven sub-tasks grouped into three categories (question task, assignment task, word-writing task) were developed in order to address the missing domains in the existing rehabilitation exercises.



Fig. 1 Screenshot of a word-to-word assignment task

The question task category trains language comprehension by presenting either a text, picture, video or audio file followed by a question. The assignment task consists of word-to-word, word-topicture and picture-to-picture classification exercises. The last task category, a word-writing task consists of replicating a word displayed using the built-in keyboard or by handwriting (free style or box writing). A commercial available handwriting recognition engine has been integrated and adapted for our custom needs. The newly developed tasks were evaluated for usability by N=5 aphasic patients and N=10 healthy subjects using the system usability scale<sup>2</sup> (SUS) and a user-tracking system.



Fig. 2 Handwriting recognition in a box writing task

### Results

The new tasks scored a high usability by both groups (SUS score: patients 88.3 ± 6.8, healthy subjects 97.3 ± 2.5).

# Discussion

The high SUS score reveals a good acceptance and integration into the existing application along with a clear and consistent user interface. The patients showed motivation to use these new challenging tasks. Moreover, the integration of handwriting recognition shows potential for new perspectives of training for aphasic persons.

### References

<sup>1</sup>K. Meyer K., S. Anja, A. Marcel, M. Heinrich, N. Krassen. Stroke Events and Case Fatalities in Switzerland Based on Hospital Statistics and Cause of Death Statistics. Swiss Medical Weekly 139(5-6): 65-69, 2009.

<sup>2</sup>J. Brooke. SUS - A quick and dirty usability scale. Usability evaluation in industry, 189(194):4-7, 1996.





# 3D Reconstruction and Simulation of Heart Potentials in the Esophagus

Dominik M. Brügger

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Heart rhythm disorders (arrhythmias), affect an increasing number of people and are associated with an increased risk for ischemic strokes and heart failures. Current clinical practice for the diagnosis of arrhythmias is the 12-lead surface ECG (sECG), or invasive Electrophysiology study (EPS). Currently a method with higher quality than sECG is lacking, whereas being less invasive than EPS. Esophageal ECG (eECG) has proven to feature better signal quality, especially atrial sensitivity is increased. For testing and the development of novel eECG signal processing algorithms a simulator capable to generate "real" eECG signals including the most frequent distortions, is highly desired.

# **Materials and Methods**

Based on data collected during a currently running clinical trial, an algorithm capable to estimate the catheter motion during the measurement period is developed. The catheter position is estimated by using morphological changes of the ECG signal to align multiple heartbeats. Solving this optimization problem in a computational efficient manner is achieved by approximating each time-sample over all channels with a high ordered polynomial, and using precomputed matrices for the optimization with steepest gradient descent algorithm.



Fig. 1 Estimated motion of the measurement catheter, during slowly catheter pulling.

The estimated motion of the catheter is used to generate a motion-compensated reference signal as an input for the simulator.

# Results

The depth profile of the measurement has successfully been reconstructed, and used to create high quality reference signals for the simulator. A simulator capable to generate eECG signals at different positions within the esophagus has been created. Simulation parameters are amongst other things electrode number and spacing, position within the esophagus, and breathing artefacts.



Fig. 2 Simulated esophageal ECG signals. Simulation of a catheter movement of 8cm within 4s, of a catheter with 9 electrodes and 1cm spacing.

# Discussion

Multichannel eECG data has successfully been used to create reference data for an eECG simulator.

The simulator has already proven its usability in the development of the motion estimation and compensation algorithms.

### References

Haeberlin A, Niederhauser T, Marisa T, Goette J, Jacoment M, Mattle D, Roten L, Fuhrer J, Tanner H, Vogel R. The optimal lead insertion depth for esophageal ECG recordings with respect to atrial signal quality. J Electrocardiol. 2013 Mar-Apr;46(2):158-65.

# Acknowledgements

I would like to thank my supervisors Dr. Reto Wildhaber and Dr. Thomas Niederhauser for their encouraging support. All members of the HuCE microLab, Biel are thankfully acknowledged.





# **Reliability Study of Neuro-Stimulation Electrodes Surfaces**

Sébastien Buchwalder

 
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 Examiners:
 Prof. Dr. Herbert Keppner and Dr. Jason Jinyu Ruan

# Introduction

Deep brain stimulation (DBS) has been applied successfully in the past 20 years for the treatment of neurologic disorders refractory to medication. Aleva developed proprietary Neurotherapeutics has neurostimulation platform based on microDBS Technology that enables significantly better therapies for neurological diseases. MEMS technology can be used to make advanced neuro stimulation electrodes. Micro fabrication techniques allow flexibility in design and this is used to develop directional stimulation electrodes. The aim of this project is to study the reliability of different coatings in terms of mechanical stability and to try to determine how stress of the different layers is related to the performance of the product

# Materials and Methods

The devices are fabricated on a silicon wafer carrier by stacks of several layers involving polyimide, dielectrics and metallic conductors. Additionally coatings could be deposited on the electrodes to improve the product lifetime. A method of characterization to test wafers with different coatings was developed. Lab testing was performed to quantify the mechanical stability. Two different approaches were verified: bending and peeling tests. Bending test aim is to provoke a default in the coating by performed an adapted bending test the main to combine the different measures as resistivity of the thin film and the applied force during the test. The peeling test consists of apply a dedicated tape on the coating and remove by traction, in order to test the adhesion of the coating.



Fig. 1 Custom-made bending test setup. Four-point measurements were performed on samples with bending radius from 200 down to 50  $\mu$ m.

# Results

The results obtained with the bending test results on Platinum (Pt) lines with widths of 50, 500 and 1000  $\mu$ m were presented through two aspects. The first aspect was the behavior of the measured resistance of the thin film during the test. The second aspect concerned the evaluation of the optical imaging. The peeling test results were evaluated by microscope imaging.



Fig. 2 Adhesive rupture and complete crack of a Pt over insulating layer line with 50  $\mu$ m width after was performed the bending test with a dedicated tip of 50  $\mu$ m radius.

# Discussion

The bending test permitted to determining the minimum radius of curvature of a patterned Pt line with different widths on a polyimide film can withstand before the breakdown of the electrical line occurred. In addition, the results showed the relevant effect of interlayer of an in-house developed insulating layer between the polyimide foil and the Pt film for established parameters. The peeling test results confirmed that Aleva's coating process has already an excellent mechanical and able to stability adhesion, withstand successfully to an adhesive tape test.

### References

C. Pollo, A. Kaelin-Lang, M. F. Oertel, L. Stieglitz, E. Taub, P. Fuhr, A. M. Lozano, A. Raabe, and M. Schüpbach, "Directional deep brain stimulation: an intraoperative double-blind pilot study.," Brain, May 2014.

### Acknowledgements

The project was supported by Aleva Neurotherapeutics and the important contribution of Dr. Jason Ruan for proposing me this exciting project and for providing me with guidance throughout the project is gratefully acknowledged









# **Radial Flow Sensitive Magnetic Resonance Imaging**

Silvan Duner

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Institution:	Department of Diagnostic, Interventional and Paediatric Radiology,
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Examiners:	Prof. Dr. Dominik Obrist and PD Dr. Bernd Jung



# Introduction

Cardiovascular magnetic resonance imaging gained a growing importance for non-invasive assessments of heart and vascular diseases. It allows the acquisition of the beating heart providing parameters such as ventricular volumes, functional imaging of malperfused myocardial areas as well as blood flow. For this master thesis, a flow sensitive magnetic resonance imaging sequence with radial instead of a Cartesian acquisition trajectory was developed and tested on a Siemens Magnetom Aera 1.5T system.



Fig. 1 3D pathlines in a normal thoracic aorta illustrating the temporal evolution of blood flow in systole.

### **Materials and Methods**

In a first part, an existing Cartesian sequence was modified to realize a radial stack of stars data acquisition. The modification then allowed implementing velocity encoding in all three spatial dimensions. The second part of the development was to add the flow encoding.



Fig. 2 Cartesian vs. stack of stars trajectory that was implemented in the protocol software code

The second part of the development was to add the flow encoding to the previously tested radial sequence.

### Results

The adaptations for radial data acquisition could be tested successfully on the MRI system. A gradient echo image was reconstructed to prove the correct calculation of the radial trajectories. The modified gradients for flow-encoding could be simulated. However, tests on the scanner showed errors in the flow gradient calculations..

# Discussion

Even though the complete radial flow sensitive MRI protocol could not be successfully tested, an important step to the development of a radial 4D-flow sequence could be done. The software code now allows changing the gradients in each spatial direction in a very versatile way. After resolving the calculation issues, the protocol software will be ready to be tested in detail and compared to existing Cartesian 4D flow sequences.

### References

M. Markl, A. Frydrychowicz, S. Kozerke, M. Hope, and O. Wieben. **4D flow MRI**. Journal of Magnetic Resonance Imaging, 36(5):1015–1036, 2012.

# Acknowledgements

The project was supervised by PD Dr. Bernd Jung and the MR-physics team at the Department of Diagnostic, Interventional and Paediatric Radiology, University Hospital of Bern. The support of this research group is highly acknowledged.





# Integration Of Wireless Functional Electrical Simulation In a Recumbent Therapy Trike

# Thomas Falk

Supervisor:	Prof. Dr. Kenneth James Hunt
Institution:	Institute for Rehabilitation and Performance Technology
	Department of Engineering and Information Technology, Bern University of Applied Sciences
Examiners:	Prof. Dr. Kenneth James Hunt and MSc Manuel Bracher

# Background

Spinal cord injury (SCI) is a medical condition that usually causes enormous changes in a person's lifestyle because of a severely reduced exercise capacity and cardiopulmonary fitness compared to able-bodied people.

Functional electrical stimulation (FES) cycling is a well-established kind of rehabilitation exercise for people with SCI, and is associated with a wide range of physiological benefits. However, most currently available devices for FES come in a bulky design and thus are restricted in portability, confining SCI people to stationary exercise. Mobile and dynamic rehabilitation like cycling requires powerful and portable devices of small size that allow people with SCI to move freely and without being disturbed by long wires.

The aim of this master thesis was to upgrade a recumbent therapy trike with an integrated and portable wireless controlled FES device that fulfills performance requirements for the activation of large human muscles needed for cycling.

# **Materials and Methods**

The recumbent therapy trike was developed by Prof. S. Tobler from Bern University of Applied Sciences (BFH-TI). The trike does not have an FES system, the therapy effect comes from passive movement of the legs that follow the movement of the arms in a mechanically synchronized manner. To make this therapy more complete, the recumbent trike has been upgraded with a wireless FES (WiFES) system. Such a system was developed by MSc Manuel Bracher at the Institute for Rehabilitation and Performance Technology (IRPT). Both the WiFES as well as the trike must be adapted for the proposed integration for creating a novel prototype trike.

The WiFES system consists of three major subunits. One is the coordination unit, which serves as graphical user interface (GUI) and manages the overall process. The GUI allows stimulation parameters to be changed for different muscles by means of current amplitude, pulse width, stimulation frequency and stimulation angle. It interacts wirelessly with the stimulation units, which form the second major sub-unit. Each stimulation unit is supplied by an 11.1V Li-Po battery and generates modulated electrical pulses on four channels simultaneously. The third major sub-unit is the sensor system that logs data needed for FES cycling and sends it wirelessly to the stimulation units. The whole sensor system is supplied by the trike's 42V Li-Ion battery and can be mounted



# Results

The whole system including the trike and WiFES system was optimized, integrated with the novel prototype trike and tested. Tests with able-bodied people have shown a very good performance regarding artificial muscle activation at corresponding pedal angles resulting in smooth cycling motion of the legs.

Sub-units of the WiFES can be placed in a way to keep the distance between them as short as possible. This reduces connection errors of the wireless communication and enables users to interact with the newly installed system. There are provided two interaction possibilities: An Android smart phone and the sensor data transmitter-box with its human-machine interface.



Fig. 2 Integrated wireless FES system

### Conclusion

In summary, this work presents a novel integration of wireless FES with a recumbent therapy trike. Therefore, the trike provides functionality for outdoor cycling applications and fulfills the performance requirements. This completes the therapy possibilities people with SCI.

For mobile outdoor FES cycling in SCI subjects, a clear conclusion is that arm cycling and/or motor assistance will be required in order to support locomotion by FES cycling. The development of power control strategies for mobile motor and arm assisted FES cycling must be an essential part of future work.





# **Real-time Tool Localization in Endovascular Treatment**

Stefan M. Funariu

 
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 Examiners:
 Prof. Dr.-Ing. Björn Jensen and Prof. Dr.-Ing. Stefan Weber

# Introduction

Minimally-invasive endovascular surgerv has become the standard treatment option for vascular diseases with an increasing number of interventions each year. Conventionally, interventions make use of bi-planar digital subtraction fluoroscopy and contrast agent to visualize the guide-wire inside the vascular structure. The guide-wire is navigated to the target area using the two fluoroscopic image planes. As the 3D structure of the vascular system is reduced onto 2D images, navigation can become complicated and time consuming, exposing the patient to ionizing radiation for a prolonged period. An image-guidance system relvina on preoperatively obtained 3D data of the targeted vascular structure and an electro-magnetically (EM) tracked guide-wire is the basis of this thesis. This method requires registration of the model to the image space by digitizing four landmarks using 2D fluoroscopy, again introducing the problem of 3D-2D space reduction. Problems can also arise due to local deformations of the patients vascular system and incorrectly registered reference systems.



Figure 1: Localization process: Particle distribution on a vascular branch. Measured EM tracker pose in green

### **Materials and Methods**

A Particle Filter algorithm (Sequential Monte Carlo Localization) was implemented to address the above mentioned problems. The pre-operatively obtained 3D model specifies the fixed frame and acts as a map, constraining the possible guide-wire locations to the lumen of the vessel. Besides one common point of reference in both the model space and the tracker space, the relative transformation of the tracker frame with respect to the fixed frame is uniformly distributed over the range of  $\pm 20^{\circ}$  and  $\pm 5$ mm. The system globally localizes the guide-wire by gradually converging the tracker frame towards the correct reference frame of the model and continues to track the guide-wire, making only use of the 5 DOF EM-tracking data and the segmented vascular structure. Measurements have been performed on two different 3D printed vascular structures, each with three different branch sequences for evaluation. To obtain a ground truth, radiographic images with the inserted and tracked guide-wire were manually labeled (Fig. 2).



Figure 2: C-Arm projection of 3D printed vascular structure with guide-wire inserted

# Results

The algorithm manages to globally localize the guide-wire from a depth of 45 mm inside the vascular structure. The converged tracker reference frame has an orientation accuracy of 6° with respect to the model frame. Additionally, it can compensate for small local deformations of the physical vascular structure with respect to the model due to the adaptive reference frame. The absolute position of the guide-wire is estimated with an accuracy of 3 mm w.r.t. ground truth and is localized in the correct vessel in 88.5% of all performed measurements. It has been observed, that more information about the guide-wire movement improves the overall localization process drastically.

# Discussion

The chosen algorithm has proven to be suitable for the problem of localizing a guide-wire in a vascular structure using EM-tracker data, needing only one reference point, therefore reducing the use of ionizing radiation. Results can further be enhanced by additional information, such as multiple EMsensors for curvature estimation, encoders for obtaining exact guide-wire displacement and inertial measurement units. Evaluation was performed on two different vascular systems, further and more extensive evaluation however might be advisable.

### Acknowledgements

I would like to thank Björn Jensen and Prof. Dr.-Ing. Stefan Weber for their support. A special thank goes to Marius Schwalbe





# **Exploring Virtual Reality in Medicine**

Stephan Gerber

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# Introduction

Patients in the intensive care unit (ICU) often have long-term functional deficits which results in a reduction of quality of life compared to the state before admitting the ICU. Up to 70 percent suffer from long-term cognitive impairment for the rest of their life<sup>1'</sup>. Typically, patients in the ICU fall into a lowstimulus condition due to overstimulation of noise, light, and bustle. The aim of the study is to measure attention and vital parameters in healthy subjects in the ICU while applying controlled visual and acoustic stimulation in a virtual reality (VR) setting that could be later used to develop early rehabilitative measures for cognitive impairments.



Figure 2. Pooled vital- and eye data of the control group (n=37, age =  $48 \pm 17$  years). The STD and SEM are calculated continuously whereas the STD of the moving average of the mean fixation duration (blue area) and number of fixations (green area) are calculated on each time point separately.

# **Materials and Methods**

The VR setup (Figure 1) consists of a headmounted display (Oculus Rift DK2, Facebook) that seals patients from overstimulation in combination with an eye tracker (SensoMotoric Instruments) to track the gaze behaviour (attention) and various sensors to monitor vital parameters. The stimulation consists of three 2D nature videos, each five minutes in length, with a break between videos. At the end participants were asked to fill out a questionnaire about usability, immersion (sense of being there) and cybersickness. The setting was tested on 37 healthy subjects (age=  $48 \pm 17$  years).



Figure 1. Participant lying on the bed in the ICU during stimulation, including the whole setup.

### Results

The mean arterial pressure (MAP), heart frequency

(HF), respiratory rate (RF), number of fixation, and mean fixation duration decreases during stimulation (MAP = -3.2 mm Hg, HF = -2.7 Beats/min and RF = -6.1 lmp/min, nr. of fix. = -0.6 nr./s and mean fix. dur. = -7.6 ms/s), as seen in Figure 2. The usability [4.5  $\pm$  0.6] of the whole system is close to the maximum of the questionnaire scale (max = 5) whereas sickness [1.2  $\pm$  0.5] is at a very low level and can therefore be neglected (min = 1).

### Discussion

Since the immersion and presence are at a high level, the participants are not aware of their surrounding and can therefore concentrate completely on watching the video. All vital parameters decrease (HF, RF, and MAP), except the peripheral capillary oxygen saturation (SpO<sub>2</sub>) in the course of the stimulation. This trend is strengthened by the decreasing moving average of number of fixations and mean fixation duration.

Overall, the stimulation has a strong relaxing and calming effect and does not evoke fear or stress in participants.

### Reference

<sup>1</sup> Wilcox, M. E., Brummel, N. E., Archer, K., Ely, E. W., Jackson, J. C., & Hopkins, R. O. (2013). Cognitive dysfunction in ICU patients: risk factors, predictors, and rehabilitation interventions. Critical care medicine, 41(9), S81-S98.





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# Adaptation and Optimization of an EIT System to Reduce Motion Artefacts in Applications for Animals and Children

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# Introduction

Electrical impedance tomography (EIT) is a noninvasive medical imaging technique that allows monitoring the lung function and to adjust mechanical ventilation of intensive care unit patients. The aim of a current veterinary project consists in monitoring the respiration of rhinoceroses during their translocation. This leads to several new requirements on EIT, as they had never been considered in the past. The main challenges are the adaptation of the EIT hardware and the compensation for motion artefacts. The latter may be beneficial in pediatrics, too. Although many studies showed the effect of artefacts due to thorax deformations, the artefacts have always been of synthetic origin [1].

# **Materials and Methods**

Based on previous works using EIT on horses, an EIT belt for rhinoceroses has been built and assessed on rhinoceroses during some preliminary measurements in South Africa.

One approach, considering the deformation of the thorax during respiration, has been implemented and evaluated. Based on simulations and on real EIT data, reconstruction models, originating from CT scans at the end-expiratory- and end-inspiratory phase (EEP, EIP), have been transformed into finite element models (FEM). They have been used to carry out forward and inverse simulations based on the GREIT algorithm implemented in EIDORS.



Fig. 1: Schematic representation of the proposed approach accounting for thorax deformations. Voltages at EEP are reconstructed using the EEP inverse model, and analogously for the EEP. The difference is used to determine the impedance change of one breath cycle.

# Results

EIT measurements on rhinoceroses have successfully been acquired and the lung ventilation of three rhinoceroses could be assessed based on

the reconstructed impedance images, using an FEM generated from a 3D scan of a live-sized rhinoceros model.



Fig. 2: Acquisition of EIT images on a sedated rhinoceros during some preliminary measurement sessions. The lungs are visible as two bright spots on the screen.

Evaluation of the reconstruction approach accounting for breathing-related thorax expansion could not show a substantial improvement in the accuracy of lung function parameters. Further, based on accelerometer data, a filtering algorithm adaptively reducing motion artefacts, was applied.

# Discussion

The simulations could show that the changes of the simulated voltages correlate to the changes in geometry, which occurred during respiration (thorax expansion). However, the differences in the reconstructed impedance images obtained by the proposed method and by a standard reconstruction are not significant. The accuracy for the determination of lung function parameters could not be improved. However, the behavior on the continuous image generation has not been assessed, allowing for future work.

Due to the lack of time, adaptive filtering based on accelerometer data, has only been assessed on the raw voltages with success, but not on the images, posing an additional future task.

# References

[1] Boyle, A., & Adler, A., "The impact of electrode area, contact impedance and boundary shape on EIT images", *Physiological measurement*, 2011

# Acknowledgements

I would like to address my gratitude to Andreas Waldmann (Swisstom) for the competent support. Also a warm thank to Prof. Dr. Volker M. Koch and Prof. Dr. Jörn Justiz for the guidance of this project.





# Development and Evaluation of an iPad-based Eye Gaze Tracker Application for Real Time Visual Exploration Data Extraction

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# Introduction

Globally, the older adult population is growing. Accordingly, it is expected that the proportion of people with age-related impaired cognitive functioning will increase as well. Tablet-based casual games are a promising solution to reduce or stabilize the age-related cognitive decline. The game has to be engaging to invoke any improvements. The currently available games engage the player by changing the game's difficulty through game characteristics. They do not take the personal and dynamic cognitive abilities levels into account. Therefore, it is desirable to develop methods to acquire the cognitive abilities levels real time. The cognitive ability, attention, is targeted by some of the casual training games and can be measured through visual exploration data acquired by an eye gaze tracker. The aim of this study was to develop and evaluate an iPad-based eye gaze tracker.

# **Materials and Methods**

The iPad-based eye gaze tracker was developed by using image frames extracted from the video stream of the front facing camera of the iPad. Image processing techniques were used, as thresholding and canny edge detection, to detect the participants' pupil positions (*figure 1*). These two locations were transferred to a point on the iPad screen, the gaze point. This was accomplished by using a transformation formula established through a 5point calibration. The iPad-based eye gaze tracker was compared in robustness, accuracy and precision to a commercially available eye gaze tracker, the SMI RED500. Sixteen participants had to perform six times the same task under varying lighting conditions and head positions.



Fig. 1 The main image processing steps of the iPad-based eye gaze tracker. The eye region is extracted (a.), filtered (b.), and binarized parallel through thresholding (c.) and a canny edge detection (d.).



# Results

Both pupil positions were estimated correctly in 58% of all the collected pupil detections. In around 10% of all the collected pupil detections, both pupil positions were detected incorrectly. In the end, the accuracy and precision values of the SMI RED500 eye gaze tracker were significantly lower than those of the iPad-based eye gaze tracker (p < 0.05) (*table 1*). No conclusive trends could be identified between the results of each one of the six different setups.

Table 1: Average accuracy and precision values of both the commercially available SMI RED500 and the developed iPad-based eye gaze tracker.

Device	Average accuracy (cm)	Average precision (cm)
SMI RED500	7.27	9.72
iPad-based	86.3	117

# Discussion

The accuracy and precision values of the iPadbased eye gaze tracker deviated negatively from research done on similar method-based eye gaze trackers. In 58% of all the pupil detections both pupils were correctly estimated. This score cannot lead to the significantly deviating accuracy and precision values of the iPad-based eye gaze tracker. It is expected that the transformation formula did not properly address the non-linearity of the gaze mapping. The gaze mapping should be critically evaluated to enhance the performance to more acceptable values. Also, a bigger data set of estimated gaze positions should be acquired to identify trends between the different evaluated conditions. Overall, the free head movement and the interpersonal variation remain challenging for all tablet-based eye gaze trackers.

# References

Ghani, M. U., Chaudhry, S., Sohail, M., & Geelani, M. N. (2013). *GazePointer: A real time mouse pointer control implementation based on eye gaze tracking.* Paper presented at the Multi Topic Conference (INMIC), 2013 16<sup>th</sup> International.

### Acknowledgements

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Bern University of Applied Sciences

# A Deep Learning-based Approach for Skull-Stripping

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# Introduction

Skull-stripping describes the process of separating brain tissue from non-brain tissue in volumetric data, where brain tissue includes gray and white matter as well as the cerebrospinal fluid of the lateral, 3rd and 4<sup>th</sup> ventricles. It represents a critical preprocessing step for a variety of neuroimaging tasks e.g. brain tumor segmentation or brain volumetric measurement. Due to large morphological differences among the population and notably distinct acquisition qualities, fully-automated skull-stripping remains a challenging task.

# **Materials and Methods**

A three-dimensional, fully convolutional neural network (FCNN) has been adopted. It consists of 17 layers and contains two max pooling/upsampling steps that allow capturing higher-level information. In order to increase the robustness, we rotate the MR volumes randomly during training and add random Gaussian noise. Additionally, a sample loss weighting is applied on behalf of a better training convergence and improved predictions. The weights are determined based on the geodesic distance from the brain boundary. The patch-based network was trained on 40 T1-weighted images of the publicly available datasets OASIS<sup>1</sup> and LPBA40<sup>2</sup>.



Fig. 1 Basic representation of the network. Volume sizes after each layer refer to the feature maps. Arrows illustrate connections between layers and the shortcut paths.

### Results

We compared our deep skull-stripping (DSS) approach to StripTS, the currently used skull-stripping technique in BraTumIA. The test data consisted of

<sup>&</sup>lt;sup>2</sup> www.loni.usc.edu



18 T1-weighted patient MR images from the public IBSR<sup>3</sup> dataset. A median Dice coefficient of 0.954 (IQR=0.0076) and an average surface distance of 1.779mm (IQR=0.3347) have been achieved.



Fig. 2 Descriptive results of the Dice coefficient, average surface distance (ASD) and relative volume.



Fig. 3 Visual comparison between StripTS and DSS results. One sagittal slice of the subjects 18, 3 and 1 is shown.

### Discussion

The proposed method is statistically significantly superior to StripTS with respect to Dice coefficient, average surface distance and relative volume. It further reaches at least state-of-the-art performance compared to other established skull-stripping approaches. A performed evaluation of depth and width changes on the neural network architecture revealed similar performance for shallow and deep models. Initial evidence suggests the usage of more shallow neural networks for performing skullstripping.

### References

O. Ronneberger, P. Fischer, and T. Brox. U-Net: Convolutional Networks for Biomedical Image Segmentation. Medical Image Computing and Computer-Assisted Intervention - MICCAI 2015, 2015

<sup>3</sup> www.nitrc.org/projects/ibsr



<sup>&</sup>lt;sup>1</sup> www.oasis-brains.org

# Tooth Scanning and Multilayer Modeling for 3D Printing of Aesthetic Dental Restorations

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# Introduction

Although CAD/CAM systems have existed for a long time in dentistry, dentists today still rely on dental technicians for the manufacturing of high quality esthetic dental restorations. Current CAD/CAM systems follow a subtractive approach and this doesn't allow them to copy the natural optical behavior of teeth. To overcome this limitation an additive approach must be followed, similar to the layering of porcelain performed by technicians. The only current technology with the potential to perform this function is 3D Printing. However, until today there hasn't been any application of this technology in the manufacturing of esthetic restorations. One of the limitations that we have to overcome is that 3D scanners can currently acquire only surface information of the teeth. The result is that 3D printing their scanned models wouldn't offer an advantage over subtractive manufacturing methods. Our goal in this thesis was to propose a solution to this limitation.

### **Materials and Methods**

The first step was to acquire a number of real tooth samples. We photographed those samples under special conditions and in such a way as to capture the maximum amount of the translucent enamel possible. We segmented the part of the tooth where only translucent enamel exists by using the active contours and the k-means algorithms. From this process a mask of the enamel was created (fig 1). We then overlaid this mask on the complete 3D model of the tooth which was scanned in a separate step.



Fig. 1 Tooth segmented from background (left), K-means clustering (center) and enamel mask (right)

Then we used advanced modeling techniques and our prior anatomical knowledge to separate the enamel completely from the dentin. We also measured the color of the real tooth sample and added it to our dentin model.

# Results

The result was the creation of two 3D models, one for the dentin, with color information, and one for the enamel without. The two models were 3D printed separately and fused together (fig. 2). In the end we had a copy of the initial tooth, created with a multilayer approach.



Fig. 2: Dentin model (left), dentin model with enamel model on top (center) and final 3D printed model (right).

Interesting observations were made and documented about the optical behavior of the final model. We came to the conclusion that our model behaves optically very similar to real teeth. Modern subtractive manufacturing methods can inherently not achieve a similar optical behavior.

# Discussion

We believe that this process can work in a real manufacturing application and be competitive, given the right material and 3D printing modality. It is only a matter of time before an approach like ours is state of the art in the manufacturing of esthetic dental restorations.

## References

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### Acknowledgements

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# **Combining SRT with OCT for Automated Dose-Control**

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# Introduction

Age related macula degeneration, diabetic retinopathy and similar diseases are challenging modern medicine more and more due to an increasing number of elderly people. Gold standard for treatment is laser-induced photocoagulation with the adverse effect of damaging photoreceptors in the retina<sup>1</sup>. Selective retina therapy (SRT) is less invasive because it only affects the retinal pigment epithelium (RPE) cells which are located below the photoreceptor layer. Lasers can be used to selectively treat these cells if pulses are shorter than the thermal diffusion constant of RPE-cells and the pulse energy does not exceed a certain threshold<sup>1</sup>. It has been found out that this threshold varies from eye to eye and even within one eye. Hence, to make SRT a safe and reliable treatment method, a real-time monitoring of the effects in the RPE is needed<sup>1</sup>. Optical coherence tomography (OCT) is a depth resolving image technique that allows a cross-sectional view of the retina with a fast acquisition speed. The aim of this thesis was to combine a SRT and an OCT system and to investigate whether OCT is an appropriate method to monitor SRT.

## Materials and Methods

After combining an OCT system with a central wavelength of 800 nm and the SRT system with a treatment laser of 527 nm and pulse duration of 1.7  $\mu$ s, experiments with different pulse energies on fresh ex-vivo porcine eyes have been performed. Eyes were available from a local slaughterhouse and were treated within 3 hours post-mortem.



Fig. 1 Cross-sectional view of the retina. The lower layer is represents the RPE, the upper lines correspond to the other cell-layers of the retina. The white arrow marks the time when the laser is shooting. As a result, the signal gets lost for a moment, and a black line appears.

The outcome of the OCT has been analyzed in time-resolved M-scans. Subsequently, the treated



eyes were fixated in Bouin, and cut in half in the frontal plane and then the vitreous body and upper layers of the retina were removed, so that microscopic as well as histological examinations could be performed. Changes observed in the Mscans were compared to visible lesions in the RPE under a microscope. Histological sections have also been made to verify the outcome on the OCT images.

# Results

Laser pulses were visible in M-scans as signal losses as it can be seen in Fig. 1. The presence of lesions in the RPE could be verified under the microscope (Fig. 2). Based on the M-scans, lesions on the RPE were predicted. Out of 163 lesions 152 were correctly predicted. Signal losses showed good correlation (accuracy > 93%) with the presence of lesions.



Fig. 2 Top-view on RPE under a microscope. Multiple lesions with different sizes are visible (white arrows).

# Discussion

With the top-view validation of the RPE we can introduce a novel method to see whether the laser energy was enough to make lesions in the RPE. To verify the potential of M-scans to regulate the laser energy during SRT, functional investigations using a slit-lamp during the treatment and biochemical markers for the evaluation must be executed in addition to the above mentioned top-view.

# Outlook

This thesis provides a rich base of knowledge and experience for future studies. Such clinical studies are planned in the context of the Swiss National Science Foundation project: "Automatic Dosimetry Control and Monitoring of Selective Retina Therapy using real-time Optical Coherence Tomography"

### References

<sup>1</sup>R.Brinkmann and R. Birngruber, Selektive Retina-Therapie (SRT), Zeitschrift für Medizinische Physik, vol. 17, no. 1, pp. 6\_22, 2007



# Development of Tools for Investigation of ULF to VLF HRV during Treadmill Exercise

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# Introduction

To maintain an adequate cardiorespiratory fitness (CRF), training with specific intensities dependent on either the maximum heart rate or the heart rate reserve (HRR) is recommended. For an accurate intensity control, the IRPT lab has developed analytical feedback design methods which use physiologically-accepted models of the heart rate response to changes in exercise work rate. But experience of the heart rate control at the IRPT lab has revealed a systematic oscillation phenomenon that can badly affect the performance of the heart rate control. This is known as heart rate variability (HRV). The very low frequency (VLF) component is of primary importance because this band usually incorporates the crossover region of the heart rate control feedback loop. Depending on the crossover region ultra low frequency (ULF) components can also affect the performance to some extent. But the influence of HRV seems to decrease considerably over time. The aim of this research was twofold: (1) Development of tools for the investigation of HRV and (2) statistical evaluation of ULF to VLF HRV during treadmill exercise.

# Materials and Methods

To investigate HRV during treadmill exercise a new HRV analysis tool was developed. The HRV analysis tool includes the four major categories for HRV analysis: time-domain analysis, frequency-domain analysis, nonlinear analysis, and time-frequency analysis. Statistical ULF and VLF HRV tests were performed here on a sample of 21 male subjects but three were excluded from analysis. Thus 18 subjects were used in a preliminary study to investigate ULF and VLF differences at different exercise intensities.



Fig. 1 Lomb-Scargle periodogram estimates for three different exercise phases. Frequency bands are labeled as ultra low frequency (ULF, 0-0.003 HZ), very low frequency (VLF, 0.003-0.04 Hz), low frequency (LF, 0.04-0.15 Hz), and high frequency (HF, 0.15-0.4 Hz)



15 of the 18 subjects were then used to investigate a potential decrease of ULF and VLF HRV over time at moderate intensity and all 18 subjects were used to investigate a potential decrease of ULF and VLF HRV over time at vigorous intensity. Moderate intensity corresponds to 40-60% of HRR and vigorous intensity corresponds to 60-90% HRR.

# Results

ULF and VLF power were significantly higher at moderate intensity exercise vs. vigorous intensity exercise (mean  $\pm$  SD): 0.79  $\pm$  0.36 ms<sup>2</sup> vs. 0.35  $\pm$  0.31 ms<sup>2</sup>, p < 0.001 for the ULF component and 1.49  $\pm$  0.27 ms<sup>2</sup> vs. 1.07  $\pm$  0.27 ms<sup>2</sup>, p < 0.001 for the VLF component. Moderate intensity showed a significant decrease over time in both ULF and VLF power: 0.85  $\pm$  0.48 ms<sup>2</sup> vs. 0.20  $\pm$  0.53 ms<sup>2</sup>, p=0.001 for the ULF component and 1.87  $\pm$  0.19 ms<sup>2</sup> vs. 1.74  $\pm$  0.27 ms<sup>2</sup>, p=0.007 for the VLF component. Vigorous intensity showed a significant decrease only in the VLF component: 1.57  $\pm$  0.32 ms<sup>2</sup> vs. 1.22  $\pm$  0.33 ms<sup>2</sup>, p < 0.001.



Fig. 2 LS VLF power outcomes for measurement setup v2: samples for all 15 subjects for start phase (w1) and end phase (w3); blue lines link the sample pairs from each subject. D is the difference between the paired samples. MD is the mean difference (red horizontal bar), with its 95% confidence interval (CI) in blue. The value 0 is outside the 95% CI, marking a significant difference between the means.

# Discussion

Statistical analyses have confirmed the experiences of the IRPT lab by revealing a significant decrease in ULF to VLF HRV over time during treadmill exercise. But the analysis also revealed high subject to subject differences in ULF to VLF HRV. Therefore a heart rate control based on a predefined HRV value is not suitable. The design approach should be to minimize the influence of the VLF component on the feedback loop.



# Intracardial Energy Harvesting by Aspring-Actuated Electromagnetic Conversion Mechanism

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# Introduction

There are about 3 million people in the world with an implanted pacemaker. cardiac Artificial pacemakers get implanted into patients whose heart's natural pacemaker is too slow or the electric conduction system of the heart is not working properly. Cardiac Pacemakers and defibrillators today are only a few centimeters long and wide. Since all of those devices run on an integrated battery, their lifetime is limited. After the battery is depleted it is necessary to replace the whole device in a surgery. The goal of this thesis was to develop a system which generates electrical energy out of the mechanical energy that the heart produces with every beat. The electrical energy can then be used to power a pacemaker. Such a pacemaker would reduce the necessary amount of surgical interventions.

# Methods

In order to convert the heart's mechanical energy into electrical energy an electromagnetic conversion mechanism was used. A beam is brought to vibration using the force of the blood flow in the right ventricle. A coil moving in between magnets then produces the electric energy. To characterize the behavior of the system a test rig (Fig. 1) as well as a numerical model were built. Needed dimensions of the parts were determined. A prototype (Fig.2) was built using the most promising approach in terms of energy output and manufacturability. The device was designed in a way that its size is small enough that it can be implanted minimally invasive. The prototype is a small tube of 6 mm inner diameter. The mechanism is only 27 mm long. The prototype was tested in a flow loop which represents the blood flows inside the heart. The device was measured at different hear rates.



Fig. 1 Cut view of the produced test rig





# Results

The simulation showed very similar energy outputs as the measurements in the test rig. The biggest deviation was 12.29  $\mu$ J (simulated: 38.2  $\mu$ J; measured: 25.91  $\mu$ J). It was possible to harvest up to 27.8  $\mu$ J with the help of a designed and build prototype placed in a flow similar to the blood flow in the right ventricle of the heart.





# Conclusion

The device actuated every heart beat at 140bpm this shows that it is possible, with further fine tuning of the system, to get a reliable actuation. Pacemaker electronics could be integrated in a similar device as the designed prototype and would allow to produce a pacemaker that needs no batteries. The energy output of the device is clearly higher than the power needs of a modern implantable pacemaker. It would also be possible to power other implantable devices such as long term ecg recorder.



# Optimization of Images for AMD Patients Using Digital Image Processing in a Portable Visual Aid

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# Introduction

People with age-related macular degeneration (AMD) suffer of central vision loss. Visual functions, such as visual acuity, visual field, and contrast sensitivity are severely limited due to an undersupply of photoreceptor cells in the retina. Especially reading, e.g., of a timetable, price tags or information panels are tasks that present difficulties for people with AMD. Many different treatments have been investigated, but none can completely restore vision that has been lost. Therefore, many investigations have focused on optical and nonoptical devices or instruments, which have been developed to compensate for the loss of visual function [1]. VoiSee is such a vision aid (voisee.ch). In cooperation with Reber Informatik + Engineering GmbH, a VoiSee prototype has been developed in parallel to this work. It is a portable near-to-eye device that provides a large field of view. This is needed to display as much information as possible, especially at large magnifications. The aim of this project was to find the best image enhancement filter (in terms of readability of text) in VoiSee for AMD patients and quantify the benefit of such a near-to-eye system. For this, vision acuity tests and seven different image enhancement filters were developed and tested in the form of a clinical study at the Insel hospital in Berne.

# **Materials and Methods**

10 different atrophic AMD affected eyes (ages 57 to 91 years, median age 80) underwent visual acuity tests by comparison of the corrected visual acuity to the visual acuity by using VoiSee. Subsequently, to find the optimal image enhancement filter, reading rates at the individual reading acuity threshold of the subjects could be determined using a modified version of the Rate of Reading Test<sup>®</sup> (German, nonsense font, upper case, Sloan letter, stationary text). The test image was filtered differently and displayed on the near-to-eye display. An unfiltered image was used as a control.



Fig. 1 A typical application example of the current VoiSee prototype



# Results

Even without additional magnification, the near-toeye system resulted in a mean enhancement of 5 the measured population. letters in This corresponds to a significant enhancement of one row in the visual acuity test. Using VoiSee with digital zoom, the mean enhancement of the measured population was 4 rows in the visual acuity test, which is highly significant. ANOVA and post hoc analyses indicated that there was no statistically significant difference in reading rates with the seven filter algorithms compared to the unfiltered image. A trend was seen for a contrast stretch and Peli's adaptive enhancement filter techniques [2].



Fig. 2 Comparison between the visual acuity achieved with VoiSee (without zooming) and the corrected visual acuity -If the measured point of a subject lies above the red diagonal line, it means that he or she performed better (could read more letters) in the visual acuity test by using VoiSee.

# Discussion

The promising results underlined the benefit of a near-to-eye vision aid such as VoiSee and should encourage further research into such aids. On the basis of the developed study design further clinical trials with more patients are needed to make the trends of the best filters statistically significant.

# References

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# Segmentation-Guided MRS Analysis of Brain Tumor Patients

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# Introduction

In recent years magnetic resonance spectroscopy (MRS) is used increasingly to gain additional information on a metabolic level to improve tumor diagnosis. The additional information comes at the cost of a considerable amount of experience needed by clinicians to translate spectral information into tissue information. Therefore, the aim of this work was to investigate a tissue segmentation method to help facilitate the use of MRS in neuro-oncologic glioblastoma assessment by automating the translation process.

# Materials and Methods

Metabolite-ratios extracted from 17 pre-operative MRS data sets, from patients with histologically confirmed glioblastoma multiforme, were clustered with the x-means algorithm [1] to find characteristic tissue spectra. The clustering revealed nine characteristic spectra (Necrosis 1, Necrosis 2, Necrosis + Active Tumor, Active Tumor, Active Tumor + Infiltration, Infiltration, Normal WM1, Normal WM2, and Normal GM). The nine spectra were then used to segment five test data sets which were excluded from the clustering.



Fig. 1 Nine characteristic spectra found by clustering of the training data. The spectra were ordered and labeled according to their malignancy.

The result of the segmentation was visualized as a map with colors ranging from red (malignant) to blue (healthy) for each type of tissue found. Additionally, a visual and spatial overlap comparison to a structural segmentation of the same data sets,



generated by the Brain Tumor Image Analysis (BraTumIA) software [2], was performed.

### Results

The resulting segmentation maps show a good visual resemblance of the structural segmentation. A quantitative analysis with the Dice similarity coefficient yielded a mean spatial overlap of  $0.62\pm0.29$  for the malignant regions and  $0.71\pm0.20$  for healthy regions, both areas excluding the Infiltration and Edema classes. Only a low correspondence of  $0.22\pm0.14$  was found between Infiltration and Edema.



Fig. 2 Comparison between BraTumIA segmentation (left) and MRSI segmentation (right) of the test data set with the highest spatial overlap of tumor tissue (shades of red).

# Discussion

We conclude that the proposed method has the potential to enhance the clinical use of MRS in neuro-oncologic glioblastoma assessment. It facilitates and largely automatizes the translation of spectral information into tissue information. In future research, the method could be applied to other types of brain tumors to gain a better understanding of the differences between those.

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### Acknowledgements

Master's Thesis in Biomedical Engineering

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# The Torpedo-Pacemaker – a Batteryless Cardiac Pacemaker Driven by Blood flow in the right Ventricular Outflow Tract

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# Introduction

Many patients with cardiac arrhythmias need to be treated with cardiac pacemakers (CPM). The power supply of these pacemakers is one of the big issues they bring along. Most CPM need to be replaced after at least 10 years to prevent that the battery is running out of power. These re-interventions may cause complications and high costs for the healthcare system and insurances. A self-powering CPM which harvests the needed energy by its own is an approach to solve this problem. The goal of this thesis is to realize a CPM which gains its energy from the blood flow in the right ventricular outflow tract (RVOT).

# Materials and Methods

A torpedo like housing, based on the concept of an axial turbine with magnetic propeller coupling, was designed and produced. To be able to implant the device during two animal trials, a self-expanding fixation system and a flexible propeller had to developed so that the device can be packed into a dedicated implantation catheter. The fixation was made out of Nitinol, the propellers were casted out of flexible polyurethane, the catheter is a modified ablation catheter.

Additionally the device was tested in a flow loop mimicking the flow conditions in the RVOT.

# Results

The design of the flexible propellers was a complex iterative process. In the end, we casted a 3D-printed propeller into silicone, which then was used as a mold for the casting of the polyurethane.

The device prototype (*Fig. 1*) was implanted in two pigs. We measured a mean power output of  $27.2\pm14.4\mu$ W (median of  $26.7\mu$ W (IQR  $14.6\mu$ W)) during an echocardiographically measured cardiac output of ~7I/min. The power is in the range of the required power of a contemporary cardiac pacemaker.

The dissections after the animal trials showed that the device did not harm the heart in a visible way, however the retraction thread was embedded in a small thrombus.

Bench tests after the trial showed that the propeller is not deforming visibly during cardiac systole even though it is flexible.



Fig. 1: The torpedo pacemaker (left) and the cap of the self-made implantation catheter (right). The self-expanding fixation is made out of Nitinol and the propeller (white) is casted out of polyurethane. The catheter is based on an ablation catheter. A retraction thread allows recapturing the device with the catheter.

# Discussion

The concept of scavenging energy out of the blood flow turned out to be promising; the measured energy output was sufficient to power a CPM. However, there are different parts requiring further improvement. The ideal propeller design and the magnetic coupling should be optimized to minimize shear stress and subsequent platelet activation. The chosen housing material was brass because of the manufacturability of the device and is not biocompatible. The retraction thread caused thrombosis which which likely impaired the device's performance also during the in vivo trial.

Even though these design issues will have to be considered in a future device, the current prototype has established a solid proof-of-concept.

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# Acknowledgements

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# Prediction analysis in paediatric obsessive-compulsive disorder (OCD) and attention-deficit hyperactivity disorder (ADHD) combining multimodal neuroimaging-genetic data

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# Introduction

Prediction of psychiatric disorders using machine learning approaches on neuroimaging data has been popular for more than a decade. Almost at the same time, closer investigations on genetic data for its association with psychiatric disorders started, and recently the combination of these two modalities came into focus. The current study is among the first to perform single subject prediction on combined neuroimaging and genetic data for the two neuropsychiatric disorders Attention Deficit Hyper-(ADHD) activity Disorder and Obsessive-Compulsive Disorder (OCD).

# Materials and Methods

57 adolescents between 12 and 18 years of age with either OCD or ADHD diagnosis and Healthy Controls (HCs) were classified with machine learning approaches. Available data modalities were 26 genetic polymorphisms, data from structural Magnetic Resonance Imaging (sMRI) and from resting state functional Magnetic Resonance Imaging (rsfMRI). Standard preprocessing pipelines were used to calculate various derivative measures on the imaging data. The measures were used to develop individual single- and one multimodal prediction model. Cross Validation (CV) measured the individual reported model performances and identified the best working classifier and feature selection strategy.



Fig. 1 T-Scores of alterations in brain activity (ReHo) between diagnostic groups illustrated on glass brains.

# Results

The best multimodal model classified the three diagnosis groups in a One-vs-Rest (OvR) multiclass



setup with an overall accuracy of 0.62. Best performing single modality models were based on Regional Homogeneity (ReHo) of rsfMRI and on subcortical regions from sMRI data, both with an accuracy of 0.58. A model based on genetic data showed lower discrimination power with an accuracy of 0.43.



Fig. 2 Confusion matrix for the multimodal model.

# Discussion

This study confirms the promising predictive power of structural and functional Magnetic Resonance Imaging (MRI) data for the two neuropsychiatric disorders OCD and ADHD. The combination of different modalities led to an increase of overall accuracy. The identified regions with disorder specific alterations were mostly consistent with previous studies. Genetic data increased the final accuracy but to a rather small extent. Further genetic studies with high sample sizes are needed to confirm the predictive power of the genetic data in practice.

# Acknowledgments

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# Fast Spinning Drill with Integrated Nerve Detection

Adrian Sallaz

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# Introduction

Drilling is an indispensable need during ear-nosethroat (ENT) surgeries. Depending on the anatomic location, there is a severe risk of irreparably damaging nerves, which could lead to serious physical and mental consequences for the patient's life [1]. Therefore, surgeons are using stimulation probes for nerve monitoring in order to minimize that risk.

However, this procedure needs a tool change (drill and probe) and nerve monitoring is therefore not continuous. The goal of this project was it to develop and optimize a system that combines a surgical drilling machine, as depicted in Figure 1, and an electrical stimulation probe in one product. This would allow the surgeon to monitor nerves while drilling with up to 80'000 rpm - without changing tools. Continuous nerve monitoring leads to improved safety for the patient, more confidence for the surgeon, and savings of time and costs.



Fig. 1: A commercially available surgical drilling machine, for example in ear-nose-throat (ENT) surgeries.

# Materials and Methods

A state of the art analysis comprising an assisted patent search at Swiss Federal Institute of Intellectual Property (IPI/IGE) in Bern and a literature review led to deeper understanding of the challenge and market.

Based on this analysis, promising principles were evaluated, focusing on industrial demand. The most promising one was pursued and a functional prototype was developed and built.



First in-house tests were made in an isotonic salt solution as depicted in Figure 2. In addition, a validation of the functional prototype was performed using phantom tests at the site of an industrial partner. These tests were based on one of their market-proven nerve monitoring systems.



Fig. 2: Setup for testing and measuring signal transmission of the drill system in an isotonic salt solution.

# Results

Based on a well-established surgical drill, a functional prototype with integrated nerve monitoring function has been developed. Tests confirm a good signal quality, even for usage up to 80'000 rpm.

### Discussion

The test results based on phantoms and a commercially available nerve monitoring system are promising and it is therefore reasonable to put further development effort into the proposed solution.

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### Acknowledgements

The project was supported by Bien-Air Surgery SA and the Bern University of Applied Sciences. The important contributions of the staff of the HuCE - BME Lab are gratefully acknowledged.





# Influence of the Sinus of Valsalva on the three-dimensional Flow Field behind a Prosthetic Valve

# **Dominic Sebastian Schmid**

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# Introduction

Several thousand prosthetic aortic valves are implanted in patients every year relieving them from aortic valve stenosis or insufficiency (Pilgrim 2010). These diseases put an additional load on the heart which tries to uphold the supply of oxygen and nutrients to the human body. Although prosthetic valves have been implanted for several decades, the impact on the hemodynamics in the aorta and in the sinus of Valsalva is still not completely understood. The latter are known to have an effect on the behaviour of the valve and the aortic flow field with many studies suggesting the occurrence of vortices in the sinus (Toninato 2016).

# Methods

With tomographic particle image velocimetry it is possible to analyse the three-dimensional flow field in-vitro posing a significant advantage over twodimensional techniques, where the desired area of interest has to be known in advance. The experimental setup consists of a mock flow loop of the left side of the heart with the respective resistance and compliance of the anatomical structures. The blood is represented by a blood mimicking fluid with similar viscosity and refractive phantoms matched to the silicone index representing the aortic root and ascending aorta. The index matching assured undistorted visual access to the flow field for the cameras, recording the movement of the laser-illuminated particles seeded in the fluid.

# Results

Our results show that the sinuses enable a back flow of fluid into the sinus during late systole but it remains unclear if this leads to enough wash out to prevent thrombosis around the valve. This flow characteristic is linked to the deviation of the outflow jet coming closer to the aortic wall on the side of the commissure leaving more space for a back flow to form on the sinus side. Furthermore, the crosssection of the outflow jet through the valve has a rounder and larger cross-sectional area compared to a more triangular shape, when no sinuses are present, indicating a difference in opening angle of the valve leaflets. Also, the sinuses seem to reduce the load on the leaflets at the beginning of systole, leading to an immediate opening of the valve, compared to the sinusless configuration, when the valve opens with a significant time delay.





End-systolic flow field behind the prosthetic valve, showing the back flow into the sinus: Streamwise velocity component V =  $\langle U_{y} \rangle$  in the yz-plane cutting through the sinus symmetrically

### Discussion

The Sinuses of Valsalva proved to impact the flow field in the aorta in terms of increasing the crosssection of the outflow jet, enabling the development of a back flow into the sinus region and leading to a smoother closure of the aortic valve. These effects have been associated with the forming of vortices in the sinuses, but could be caused by a different pressure distribution over the valve leaflets, which is not related to such vortices.

The fact that no vortices could be observed in the sinus is in our opinion due to a more physiological representation of the aortic root (as compared to earlier studies of sinus flow).

Hydraulic tests indicated that the pressure levels and flow rate differ somewhat from physiological conditions. Further steps have to be taken to improve the test setup.

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# Image-Based Localization Method for Automatic Cell Sheet Layering in Robotized Heart Regeneration Therapy System

# Sandro Michael Schultz

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# Introduction

Heart transplantations, defibrillators, pacemakers, radiation therapies and similar procedures contain high risk of rejections, inflammatory reactions and other negative effects during the operation. Cellbased therapies have been progressing rapidly in the past and have shown to be a suitable alternative with significantly reduced risks for the patient. Chiba University is currently working on a robotic system that is able to produce multi-layered cell sheets out of single-layered cell cultures. These multi-layered cell-sheets can then be applied on a beating human heart without stopping it in advance, which is a big advantage in respect of patient safety. The aim of this thesis was to create the program that is responsible for the segmentation, scooping and layering process of the cell-cultures.



Fig. 1 Robotic Scooping- and Layering-System.

# **Materials and Methods**

A C++ program was developed which is providing the necessary calibration, segmentation, scooping and layering functions. A semi-automatic approach based on the region-growing algorithm was chosen for the real-time segmentation of the cell-sheet. The robot-tip location had to be observed simultaneously in order to calculate the distance between robot-tip and cell-sheet. This data was then used to move the robot and to start the scooping / layering process.



Fig. 2 Program GUI, Segmentation of Real Cell-Sheet.

The system was then tested with real cell-sheets as well as with milk-sheets and under different

environmental light- and background conditions in order to make this process as stable as possible. For the evaluation, manual segmented examples were compared with the computer segmented results by using a dice-coefficient algorithm.

# Results

Assumed to work under good environmental settings, the dice coefficients for milk-sheets as well as for real cell-sheets showed to be reliable and over 0.9. The scooping process could be carried out successfully within a tolerance of around  $\pm 1$ mm and without damaging the cell-sheets. The layering process on the other hand only worked in around 10% of the cases. Relying on similar tests in the past, this is most likely due to mechanical problems, which should be examined in a continuative project. Nevertheless, successful tries showed to be accurate and within a tolerance of  $\pm 1$ mm.



Fig. 3 Double layered Milk-Sheet.

### Discussion

The results showed that the project is promising and that a reliable real-time segmentation, scooping and layering procedure is possible. Under well-defined environmental conditions, the scooping procedure could be carried out with nearly 100% chance of success, within the tolerances and without any damage of the cell-sheets. However, the layering process showed to be an issue and has to be examined in more detail in a continuative project.

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# Acknowledgements

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# **Evaluation and Improvement of Force-Based Tool Pose Estimation Confidence, Accuracy and Robustness**

Apollonius Schwarz

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# Introduction

Force based tool pose estimation is a method for the detection of the pose of a robot navigated surgical drill during machining of bone [1]. The technique relies on the heterogeneous nature of bone in the mastoid region, and the measurement of drilling process data (force). It provides an additional safety layer for surgical procedures in which the position of the drill cannot be directly visualized, such as minimally invasive cochlear implantation.

# **Materials and Methods**

The existing algorithm [2] was tested on data from previously performed experiments on 13 human temporal bone cadaver specimens, embalmed with formalin. The factors affecting the accuracy of the algorithm were subsequently investigated.

Firstly, as the algorithm relies on the heterogeneous nature of bone in the mastoid region, methods to evaluate the heterogeneity pre-operatively from computed tomography (CT) image data were studied. In addition, force, torque and position data acquisition and processing was investigated and improved.

Secondly, pre-operatively acquired CT image data is used to generate a search space in the region of interest (ROI). Relative force profiles are then predicted along candidate trajectories and intraoperatively compared to the force data acquired from the robot system. A method to predict relative drilling forces from CT image data was developed based on a supervised machine learning technique and evaluated.

In the third place, signal similarity metrics to compare measured force profiles and predicted force profiles were evaluated with receiver operating characteristic (ROC) graphs.

Finally, the search space was generated in a ROI of 3 mm by 3 mm along the drilled trajectory. This results in 441 discrete candidate drill positions on a two dimensional plane at target (Fig. 1). Those positions were then classified into predicted drill positions (predicted class positive) and save positions (predicted class negative). The method was evaluated using leave-one-out cross-validation.

# Results

A true positive rate (TPR) of 92.3% and a false positive rate (FPR) of 5.6% was noted (n=13, 13 true class positive and 5720 true class negative candidate drill positions at target).



Fig. 1 Candidate drill positions at target were classified and evaluated. True positive (TP), false negative (FN), false positive (FP), and true negative (TN), grid spacing 0.15 mm.

# Discussion

Methods to evaluate and improve key components of the algorithm were identified and implemented as evaluation framework. It is hypothesized that further reduction of artifacts introduced by the drilling process in the force data will result in a lower FPR and a higher TPR.

In conclusion, compared to the robot system accuracy (0.15 mm  $\pm$  0.08 mm [3]) the sensitivity and specificity of the algorithm needs to be improved.

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# Intracardial Piezoelectric Energy Harvesting

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## Introduction

Three million people are living with implanted cardiac pacemakers today. Many of these patients will have to undergo one or more pacemaker replacement procedures to exchange devices once the batteries have been spent. The goal of this work was to develop a energy harvesting system for intracardial implantation that could power a leadless pacemaker using the mechanical energy of the body and piezoelectric materials as the mechanical to electrical conversion mechanism.

### **Materials and Methods**

A prototype device was designed that harvests energy from the flow of blood in the right ventricular outflow tract (RVOT) of the heart. The device features a sail that is exposed to the flow of blood and is displaced during systole in order to actuate a free vibrating cantilever beam using a frequency-upconverted flicking mechanism. The device was designed to operate with two energy harvesting mechanisms: both a piezoelectric and an electromagnetic system were designed to be combined.

Commercially available PVDF foils were tested to assess the amount of strain in the beam and determine if more energy dense piezo materials could be used to harvest appreciable energy.



Fig. 1 The final prototype, ready for testing in the flow loop. One euro coin for scale.

The final prototype was tested in a flow loop mimicking the flow conditions in the RVOT. Energy of the electromagnetic system was measured at various heart rates and flow conditions. Actuation effectiveness was also measured.



# Results

Although the PVDF foils had negligible conversion efficiency and generated just 6 pico Jules per flick, the testing showed that strains of 0.041% could be achieved in the transverse direction of the films.

Flow loop testing of the prototype demonstrated consistent actuation and and as much as 28 micro Jules of energy per flick from the electromagnetic system. The prototype operated reliably across many heart rates and flow scenarios.



Fig. 2 The energy generated from the electromagnetic conversion principle and flow parameters plotted against heart rate in the flow loop.

### Discussion

As expected, the PVDF foils did not generate any appreciable power, however, the strain measured in the foils indicates that a more energy dense piezo material could provide useful amounts of energy to this prototype device. Lead zirconate titanate (PZT) films are the first films that will be examined in any future work.

The prototype shows promising results in the flow loop with actuation consistent over may heart rates and an excess of energy available to power a leadless pacemaker. The design has some areas of improvement that should examined in further work but the prototype built in this work has demonstrated that a sail based energy harvester utilizing the blood flow in the RVOT can reliably generate enough power to run leadless pacemaker.





# Human-in-the-loop Training Interface for a new active Balance Board

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# Introduction

Since 1960, the health-care costs in Switzerland are growing steadily. 50% of these costs are caused by people older than 60 years [1]. This proportion can be related to the normal human aging process, which may lead to a reduced postural control. Therefore, different trainings are proposed to improve gait stability, such as sensorimotor training, whole body vibration training (WBVT) and exergames (exercises and gaming), which may reduce the risk of falling. Three years ago, a project was started aiming at combining the mentioned training methods. A functional prototype of an active balance board (ABB) was the starting point for this thesis. The thesis aims at further improving control of the motion base and developing a human-in-theloop training in form of an exergame. Furthermore, the functionality of the final prototype should be characterized.



Fig. 1 Developed prototype (spinemime)

### Materials and Methods

To be able to develop an ABB with properties similar to a classical balance board (CBB), one needs to gain knowledge about the key values characterizing the dynamics of a CBB, such as the maximal acceleration and velocity. The dynamics of two different CBBs with three rotational degrees of freedom and different radii were assessed in a small study involving five volunteers performing balancing tasks. In order to perform the same tests with the ABB, some features of the platform had to be improved. The most important features include solving the inverse kinematics, improving the mechanical stability for safety reasons, further developing of the force controller and designing of a new electronic concept. Furthermore, a graphical user interface was developed for a more convenient user interaction with the platform. Additionally, two

exergames were implemented to bring the human into the loop. In a last step the ABB was characterized and compared with the CBBs. Therefore, the same participants repeated the balancing tasks on the ABB. Using the data obtained, the vibrational abilities and balancing behavior of the ABB were evaluated.

# Results

A maximum acceleration of 2196 °/s<sup>2</sup> and velocity of 129 °/s was measured on the CBB, whereas 1784 °/s<sup>2</sup> and 66 °/s were measured on the ABB. In addition, the acceleration frequency spectrum of the CBBs has the highest power from 2.5-5 Hz. The ABB showed a similar frequency spectrum for this range. Furthermore, changes in the support force of the ABB showed similar results in the acceleration power spectrum as the different CBB radii. The ABB could generate vibrations with an amplitude of 1° of a frequency of 4 Hz.

### Discussion

The ABB is able to simulate different levels of difficulties which can be compared to changing the CBBs radius. Furthermore, the ABB can be used for exergames. However, the dynamic parameters of the ABB are too low for a simulation of a CBB. In addition, a delay time of 50ms was discovered in the control loop of the ABB, which has a large influence on the balancing behavior. Furthermore, the performance during the vibration tests was insufficient, as the 20-50 Hz, proposed by [2], could not be reached.

The insufficient performance of the ABB can be related to the dynamic properties of the pneumatic artificial muscle.

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## Acknowledgements

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# Development of an Intracardiac Flow-based Energy Harvesting Mechanism for Cardiac Pacing

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# Introduction

Pacemakers (PMs) are a common method to treat various cardiac diseases. The electrodes of PMs deliver electrical impulses to stimulate the heart muscle. The major issues of conventional PMs are limited battery life and lead fracture. After approximately 10 years at the latest, the batteries have to be replaced in surgery. These reinterventions are costly and still risky, because the leads might break or dislocate and the skin has to be opened in order to retrieve the old PM bodies and insert the new ones. Leadless cardiac PMs with inexhaustible power supply would solve both main issues of the conventional pacemakers. The research area of intracardiac energy harvesting investigates possibilities to generate power within the heart.

# **Materials and Methods**

This thesis describes the development of an electromagnetic (EM) energy conversion mechanism. It is driven by a magnetically coupled lever arm that is transferring torque through a housing to the encapsulated energy conversion mechanism. The torque on the coupling is generated by a sail structure within the blood stream. The final prototype weighs 6.4 g and takes up a volume of 2 ml. It was tested in an experimental flow loop set-up that mimics the flow conditions within the right ventricular outflow tract, where the device shall be implanted. Moreover, the sail area of three different sail designs and their hemocompatibility was analyzed using blood flow simulations in COMSOL.



Fig. 1 CAD drawing of the final prototype (partial cut-view)



# Results

The developed prototype generated power outputs from 14.39  $\pm$  8.38  $\mu W$  at 60 bpm up to 82.64  $\pm$  17.14  $\mu W$  at 200 bpm in the in vitro experiments. A linear interpolation of the two given measurement points approximately describes the power output at the intermediate heart rates. The optimal sail in terms of minimal area, optimal hemocompatibility, manufacturability and broad applicability was identified as a circlular structure with a radius of 5.5 mm in the center of the RVOT.



Fig. 2 Velocity slice plot of the COMSOL blood flow simulation over the harvester body and the final sail structure to evaluate the resulting torque and hemocompatibility.

# Discussion

This thesis presents the proof of concept for blood flow harvesting with a sail lever magnetically coupled to an EM energy conversion system. It showed that the developed prototype can generate sufficient power to drive modern pacemakers in an experimental flow loop set-up and at an implantable size-scale. Moreover, the simulation results suggest that the hemocompatibility is guaranteed in terms of maximal occurring shear stresses.

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# An Evaluation of Image Motion Blur and its Effect on the Accuracy of Image Guided Surgery

# Jariyaporn Thongbudda

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# Introduction

minimally cochlear The invasive robotic implantation is a surgical procedure in which a small access hole for inserting cochlea implants is drilled behind the ear towards the middle ear cavity. This procedure demands a high precision and accuracy and is based on image guided navigation. navigation system requires Such а the segmentation and planning of the drilling trajectory from the patient specific anatomy usina preoperative acquired images. Any image artifact has the potential to reduce the accuracy of the navigation and the whole robotic system. Therefore, a method to evaluate the image quality before planning is required and evaluated in this thesis.

# Materials and Methods

This work is based on three different methods. First, an image blur evaluation-model has been developed by using the existing image quality asessments. To evaluate and validate these algorithms, the real CT images were used. Second, the effect of blur image to the image guided accuracy was investigated. For this, the fiducial detection algorithm has been used. This determined the fiducial localization error (FLE) in the image space. Finally, the correlation between these two outcomes was performed to find a threshold for image blur.

It was assumes that tiny motions of the patient affects the image quality (blur). Thus, the images were blurred using Guassian smooth filter.



# Fig. 1 The approach concepts which distributed in this thesis.



# Results

The model was able to distinguish the blur and each screw given a similar blur score. The image blur evaluation model could then assess the blurs of real CT images. The model was applied to eight bits input with a segmentation method as developed from the state-of-the-art metric.



Fig. 2 The blur screw images were used to validate the blur evaluation model and investigate the its effect to fiducial localization error.

The results from investigated image blur with screw detection showed a mean FLE of 0.082 mm with standard deviation of 0.039 mm. Finally, the correlation and linear regression was determined by using the mean FLE and mean image blur score and a final threshold was defined.

### Discussion

Although, the image blur evaluation model could be potentially implemented to assess the image blur, it assesses only two dimension. Due to volumetric DICOM images, the method needs to be further extend for 3D application. Additionally, the overall mean FLE indicated that this screw detection algorithm is robust against the blur image.

To render motion blur images, a simple smooth filter was used. This is however a simplification of image artifacts encountered in the clinics.

The correlation reveals a small dependency of image blur on FLE. In the future, more realistic image artifacts, induced by controlled motion of a phantom, needs to be analyzed.

### References

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### Acknowledgements

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# Introduction

With an upcoming prevalence of robotic support in medical routines, automatic or assisted navigation of needles and instruments is becoming more and more important. Thus several methods have been developed to detect and track instruments by different image modalities, such as laparoscopic image sequences or stereo vision. However, accurate optical detection and tracking of an object in a 3D space remains a challenging undertaking. Concurrently, Optical Coherence Tomography (OCT) is an image modality that leverages light to captor 3D images in a safe and non-invasive manner. In this work, we investigate a new method to detect an instrument tip within 3D OCT volumes, which can be utilized for detection based tracking in 4D OCT. This detector is presented in the application of automatic estimation of the distance between a needle tip and the retina.

# Materials and Methods

The instrument tip detector applies a 2D detector on the 3D OCT projection beforehand, in order to constrain the region where the 3D detector is deployed. To this end, a Viola & Jones detector is extended to 3D with proportion of edges at different locations and orientations as features and a new early stopping scheme. Furthermore we created a data set of 122 3D OCTs of a simplified retina model, comprising a needle and a surface, in which we estimate the distance between them by segmenting the surface and applying the proposed instrument tip detector.



Fig. 1 3D OCT in which the proposed method segments the surface (blue) and detects the needle tip (red) in order to estimate the distance between them.

# Results

The proposed instrument tip detector detects the needle tip within  $264 \pm 110$  ms with a true positive rate of 36.89%. Together with the surface



segmentation the distance can be estimated with an error of  $0.283 \pm 0.626$  mm.



Fig. 2 Receiver operating characteristic curve of the proposed instrument tip detector.



Fig. 3 Error of the distance estimated once between segmented surface and detected needle tip (left) and once between segmented surface and needle tip ground truth (right).

# Discussion

The distance error is mainly due to falsely detected needle tips. Although the proposed method is more than twice as fast as applying the 3D detector alone, it is not yet real time ready. Nevertheless it provides a basis for instrument detection in 3D OCT. Moreover the detector can be applied on offline data processing and can be adapted for other 3D image modalities, such as CT and MRI.

# References

Viola P. and Jones M. J., Robust real time face detector, International Journal of Computer Vision, 57(2): 137-154, May 2004.



# Estimation of Effective Yield Properties of Human Trabecular Bone Using Nonlinear Micro Finite Element Analysis

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# Introduction

Osteoporosis is a widely spread bone syndrome, where bone fragility increases with age. Bone strength depends on volume fraction (BV/TV) and fabric of trabecular bone, located in the core of most bone regions at fracture risk. Micro finite element (µFE) analyses are often used to determine the apparent elastic and yield properties of trabecular bone that are necessary for low-cost, homogenized FE (hFE) analyses of trabecular bone. However, due to the finite size of trabecular beams and plates, these apparent mechanical properties are highly dependent on the applied boundary conditions (BCs) [1]. Recently [2], "in situ" elastic properties were evaluated using an embedded configuration (Fig. 1). Those in situ properties approximate the effective elasticity of trabecular samples [2]. Our aim is to use a similar approach to assess the effective yield properties of trabecular bone samples.



Fig. 1 Left: In situ properties were evaluated for a ROI embedded in a larger cubic volume elements (CVE) loaded under PMUBCs. The loads are thus transmitted in directly to the ROI via a layer of bone. Right: This ROI was then extracted and subjected to PMUBCs and KUBCs.

### **Materials and Methods**

Twelve cubic, fabric oriented trabecular bone samples cored from human vertebrae and femorae were tested under kinematic uniform (KUBCs), periodicity-compatible mixed uniform (PMUBCs) and in in situ configuration via six load cases: uniaxial compression, tension, shear in two distinct planes and hydrostatic compression and tension. The sample group had a BV/TV ranging from 14% to 39%. The nonlinear FE analyses were performed using the parallel extension of the FE-code FEAP83 (parFEAP). A user macro was implemented into the FORTRAN environment of the FE-code to compute the in situ stresses and strains. Additionally, the FEcode was adapted to visualize the extent of damage in the samples. In the FE-model an isotropic elasticviscoplastic material model was used for trabecular



bone tissue [3]. Apparent yield was defined as a 0.2% reduction of the apparent elastic strain norm.

# Results

In log space, KUBCs- and PMUBCs-based yield stresses for all load cases are linearly related to the *in situ* yield stresses (Fig. 2). Yet, KUBCs yield stresses were 43% (±28%) higher than the *in situ* values and PMUBCs induced yield stresses 10% (±11%) lower than *in situ*.



Fig. 2 KUBCs- and PMUBCs-based yield stresses in relation to the in situ yield stresses in the log space. p-value < 0.001 in both relations.

# Discussion

Our findings indicate that yield stresses computed under KUBCs overestimate, while those under PMUBCs underestimate, but to a lower extent, those obtained under *in situ* configuration. This is consistent with results relative to the elastic properties [2]. Similar trends could also be observed for the damage distribution in the samples. PMUBCs and *in situ* indeed provide comparable damage levels, which were lower than those induced by KUBCs. Based on prior results relative to elasticity [2], PMUBCs could deliver good approximations of the effective yield properties.

# References

**[1]** Pahr 2009, Biomech Model Mechanobiol, 7(6):463-476; **[2]** Daszkiewicz 2016, Biomech Model Mechanobiol, in revision; **[3]** Schwiedrzik 2013, Biomech Model Mechanobiol, 12(2):201–213





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# Introduction

Recently accumulating evidence has put into question the role of large multinucleated giant cells (MNGCs) around bone biomaterials. While it is well known that cells derived from the monocyte/macrophage lineage are one of the first cell types in contact with implanted biomaterials, it was originally thought that specifically in bone tissues, all giant cells were bone-resorbing osteoclasts whereas MNGCs were typically associated with a connective tissue foreign body reaction resulting in fibrous encapsulation and/or material rejection. Despite the great majority of bone grafting materials routinely found with large osteoclasts characterized by their ability to resorb and replace bone grafting particles with newly formed native bone, a special subclass of bone biomaterials have recently been found surrounded by large MNGCs virtually incapable of resorbing bone grafts even years after their implantation.

# Materials and Methods

Tissue samples obtained within the dental clinic were harvested utilizing 2 bone grafting materials including deproteinized bovine bone matrix (DBBM) and a synthetic biphasic calcium phosphate (BCP). Samples from various patients were then processed histologically in paraffin, sections, and investigated for 17 specific markers including an array of CD-cell surface markers. Immunofluorescent and H&E staining were performed and outcomes were observed by fluorescence microscopy.

# Results

To directly compare the staining of various markers from human tissue samples, figure panels were created including markers for CD86, HLA-DR, TRAP, CTSK and CT-R. Figure 1 demonstrates DBBM and BCP samples were it was confirmed that giant cells found around DBBM particles express both markers for MNGCs and osteoclasts. It was found that the expression of CD86, HLA-DR and CTSK were highly expressed whereas typical osteoclast markers such as CT-R were found nonexpressed in giant cells. All giant cells expressed TRAP.

# Discussion

In this study, we show for the first time that the giant cells found around certain non-resorbable classes of bone grafts express non-osteoclast markers routinely found in soft-tissue MNGCs. Furthermore, it was observed that osteoclast markers including TRAP and CTSK were more highly expressed when compared to RANK and CT-R. We further demonstrate for the first time that these giant cells around bone particles were expressed for specific MNGC markers including CD86, CD98, HLA-DR and B7-H1. Interestingly, both bone grafting materials expressed very similar marker patterns and future research aims to discover which factors might be responsible for shifting the formation of osteoclasts versus MNGCs as presently little is known favoring their individual formation.

# References

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Fig. 1 Marker detection in human biopsies grafted with DBBM (BO). (A,B,D,E) Immunofluorescent staining of samples for CD86, HLA-DR, CTSK and CT-R antibodies (in green) and DAPI staining (in blue), (C) TRAP histochemistry, and (F,G,H,I) H&E staining of the same area. Observe the high expression of CD86, HLA-DR and CTSK and extremely low expression of CT-R in giant cells around DBBM.



Master's Thesis in Biomedical Engineering

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# A Lead- and Battery-less Cardiac Pacemaker Driven by a Massimbalance Oscillation Generator Andreas Walter Zumbrunnen

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### Introduction

Cardiac pacemakers of today rely on batteries as their power source. They need to be replaced after five to ten years, which involves surgery. A second weak point of today's pacemakers are the electrical leads. They connect the device with the point of stimulation inside the heart and are prone to complications such as cable fractures or cable dislocations. The latter was amended by the introduction of leadless pacemakers to the market. The concept of energy harvesting, combined with a leadless pacemaker, presents an interesting alterative power source. The aim of this study was to investigate the feasibility of the mass imbalance oscillation generator, as found in automatic watches, inside the dimensions of a leadless pacemaker.

### Materials and Methods

Different approaches of the energy harvesting mechanism were tested on a test rig. Further a mathematical simulation of a pendulum driven by the accelerations of a heart was set up, to investigate the behavior of the system. The gained insights were included into a prototype of an energy-harvesting device (Fig. 1).



Fig. 1 Housing of the energy-harvesting device.

The housing of the device was designed to fit into a steerable catheter for the implantation into the right ventricle of the heart. The device consists of a platinum oscillation weight, which is moved by the accelerations of the heart and drives a generator (Fig. 2). Four self-deploying nitinol hooks



on the front end of the device serve as fixation on the endocardium. The power output of the device was measured in vitro on a dedicated experimental setup. This setup was mimicking movements of a right ventricle.



Fig. 2 A cut through the energy harvesting device exposing the platinum oscillation weight and the generator.

### Results

On in vitro bench experiments a mean output power of  $22\mu W$  with a standard deviation of  $9\mu W$  was measured. The recorded peak output power was  $34\mu W$ .

### Discussion

The measured power outputs of the energyharvesting device are in the same range as the power consumption of today's leadless pacemakers. Thus the use of an mass imbalance oscillation generator as a power source for a leadless pacemaker is feasible. The developed mechanism represents the first technological solution to a lead- and battery-less endocardial pacemaker.

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