Bern University
of Applied Sciences

UNIVERSITÄT
BERN

Master Biomedical Engineering

Annual Report 2017

Contents

Introduction

Following its 10th birthday in 2016, I am very glad to report on the excellent health of our master's program in Biomedical Engineering. As shown on page 15, 43 regular new and 6 exchange students were admitted to the program and 35 master's degrees were delivered in 2017. A large fraction of our students stem from universities of applied sciences in Switzerland. Our program represents a remarkable opportunity for these students to achieve a master's degree at university level providing access to doctoral studies. Further hallmarks of our program remain the proximity to the local hospital network, the clinical application-oriented research, the internationality with all mandatory courses in English, the compatibility of the study calendar with a part-time job and the central location in the Bern area. Efforts to promote the program were continued by participating in the Master Messe in Zürich-Oerlikon.
The first preparation courses in electrical engineering, programming and mathematics were successfully deployed to help students with peripheral backgrounds to follow the courses of the basic modules in mathematics and biomedical engineering. The practical course in orthopedic surgery encountered a frank success and made the students aware of the complexity of the clinical tasks in this medical specialty. The trip to MEDICA, the world forum for medicine in Düsseldorf, was rescheduled in the 2017 academic calendar and proved to be highly appreciated by the participants despite a long road trip. An impressive number of master's theses with broad medical applications were deposited and defended orally. The one-page summaries can be found in the second part of this report.
The Biomedical Engineering Day 2017 attracted again numerous students, researchers, alumni and companies. Students from Swiss bachelor programs in relevant engineering areas were invited to attend the event and learn about biomedical engineering. We received again strong encouragements for our efforts to cultivate this relationship between students, research institutes and industrial partners. The University Clinic of Pediatric Surgery presented a live reconstruction of an adolescent anterior cruciate ligament brilliantly executed by Dr. Kai Ziebarth in the operating room of the Inselspital and kindly moderated by the head of the clinic, Prof. Steffen Berger, in the auditorium. The keynote lecture was given with humor and international expertise by Prof. Jess Snedeker, from the Institute for Biomechanics of the ETH in Zürich, about the challenges of translational research in soft tissue mechano-biology. I would like to thank all the participants for this ninth successful edition of the BME day!
I wish to conclude by expressing my deep appreciation to the internal but also the external teachers, who deliver year after year, the knowledge and skills that make the core value of our master's program. I would also like to reaffirm my thanks to the study coordination, Mrs Ulla Jakob, Alexandra Neuenschwander-Salazar and Julia Spyra for providing the best possible support to the students and lecturers of the program and for organizing events such as the BME day with professionalism and enthusiasm.

Philippe Zysset
Program Director

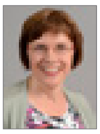
Organization

Management

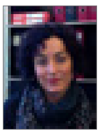
Ph. Zysset
Program Director

V. M. Koch
Deputy Program Director

Administration



U. Jakob-Burger
Study Coordinator



A. Neuenschwander Salazar
Study Coordinator

J. Spyra
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 module called "Complementary Skills" was introduced. In addition, the list of mandatory courses in both basic and major modules was revised.
More recently, in Fall Semester 2017, a module "Preparation Courses" was created. The courses in this module are intended to fill students' gaps regarding prerequisites for basic and advanced courses in the master's program Biomedical Engineering.

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.

Preparation Courses

Due to the interdisciplinary nature of the BME master's program, our students come from various fields of study. Especially students with a non-engineering background, for example in medicine, biology or related fields, do not fulfill all prerequisites for the courses of the master's program. Therefore, preperation courses in MATLAB, C++ Programming and Electrical Engineering as well as the tutorial-based course "Selected Chapters in Mathematics" were introduced and allow to create a tailor-made curriculum for these students. Students with a background in engineering, on the other hand, have the possibility to select these courses freely if they feel the need to refresh some of the knowledge provided.

Basic Modules

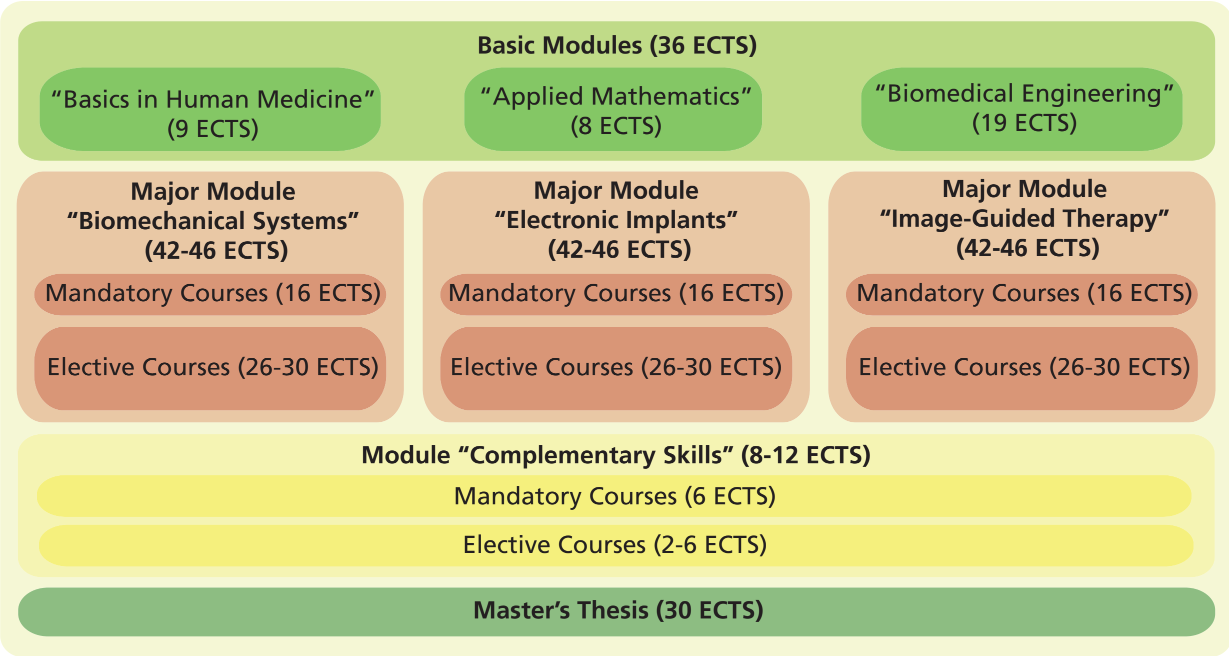
The basic modules provide the students with the necessary background to be able to fully understand the highly complex subject matter in the specialized courses. All students with an engineering background (for all other students, individual study plans are set up which may contain certain variations) 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 the 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

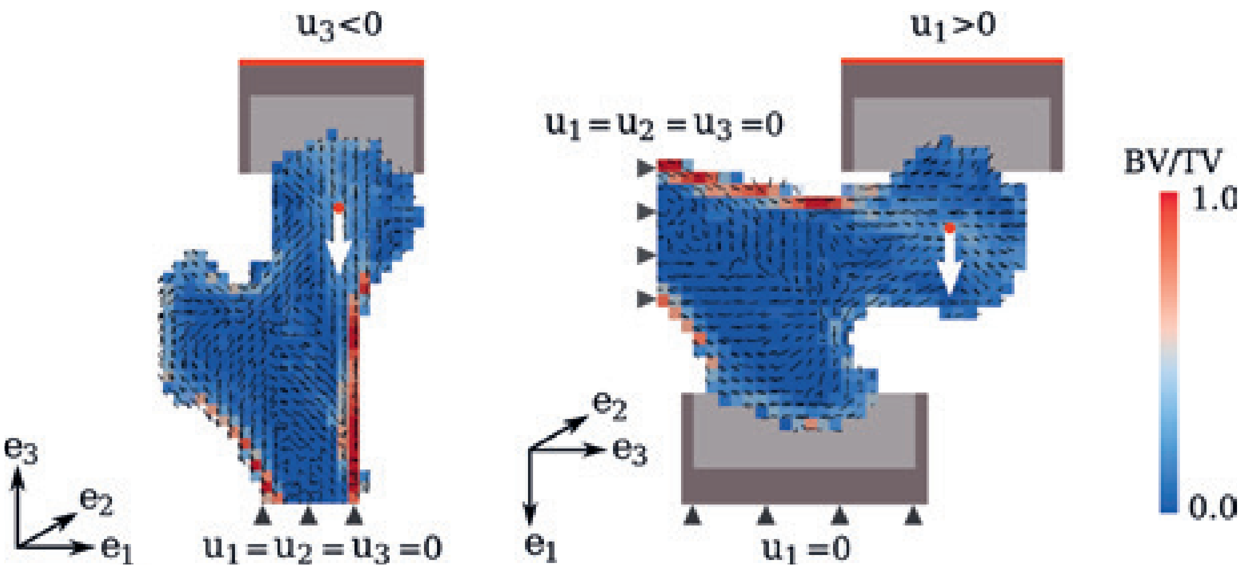
- Applied Biomaterials
- Basics of Applied Molecular Biology
- Basics in Physiology for Biomedical Engineering
- Biological Principles of Human Medicine
- Biomaterials
- Biomedical Sensors
- Biomedical Acoustics
- Biomedical Instrumentation
- Biomedical Laser Applications
- Biomedical Signal Processing 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
- Selected Chapters in Mathematics
- Short Introduction to MATLAB
- 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 respiratory, cardiovascular and musculoskeletal systems are the transport and structural bases for our physical activities and their health have a profound influence on our quality of life. Lung diseases, cardiovascular diseases, musculoskeletal injuries and pathologies are 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 gain a comprehensive understanding of the multi-scale organisation of the respiratory, cardiovascular and musculoskeletal systems, combining knowledge from the cell, tissue, organ to the body level. They learn how to apply engineering, biological and medical theory and methods to resolve complex problems in biomechanics and mechano-biology. Students learn to draw connections between tissue morphology and mechanical response, and vice versa. Students also gain the required expertise to apply their knowledge in relevant, practice-oriented problem solving in the fields of pneumology, 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 respiratory, 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 evaluation of aortic valve prostheses, monitoring of soft tissue stiffness in vitro, tissue engineering of the anterior cruciate ligament and tribology of the bone implant interface.
Career prospects are numerous. Many students proceed to further post-graduate education and research, pursuing doctoral research in the fields of biomechanics, tissue engineering, lab on chip or development of biomaterials. Most of the major companies in the fields of cardiovascular engineering, orthopedics, 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.



Stance and fall loading configuration of the human proximal femur: coarse voxel mesh with bone volume fraction (BV/TV) and principal direction of anisotropy mapped from an atlas.

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 Parkinson’s disease, obesity, depression, incontinence, hydrocephalus, pain, paraplegia, and joint diseases.

In this module, students will gain a comprehensive technical and application-oriented understanding that will allow them to select, use, design, and optimize electronic implants and similar biomedical systems. Since the work on such complex systems is usually done in interdisciplinary groups, another important goal is that graduates are able to work and communicate in teams consisting of, e.g., engineers, scientists, and medical doctors.

Specifically, students will learn about technology basics including intelligent implants and surgical instruments, biomedical signal processing and analysis, low-power microelectronics, wireless communications for medical devices, and microsystems engineering including MEMS technology. Application-oriented elective courses are also taught, e.g., cardiovascular technology, biomedical sensors, biomedical acoustics, biomedical laser applications, ophthalmic technologies, and diabetes management.

Students may already apply their knowledge as a part-time assistant in an institute 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“ implant’ manufacturers have recently become interested in electronic implants, e.g., measuring forces in knee implants.

Clean Room Medtech (ISO 14644 class 7) of the Institute for Human-Centered Engineering (HuCE). Currently, esophageal catheters for ECG recordings for a clinical study are being produced. This is possible due to an ISO 13485-2012 certification.

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.

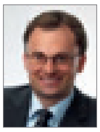
Students of the IGT module will study the clinical and technical fundamentals of image-guided therapy systems. They will develop an understanding of currently applied clinical standards as well as an overview of latest advancements in research. Successful students will be enabled to develop novel clinic-technological 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.

Robotic cochlear implantation, Inselspital Bern (© ARTORG Center, 2017).

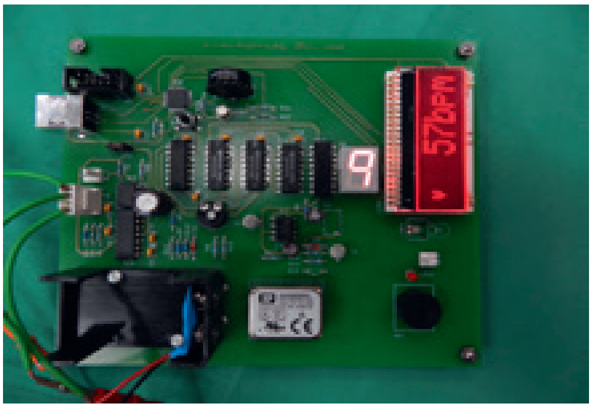
New Courses

Introduction to Electrical Engineering



Prof. Dr. Volker M. Koch

This course is aimed at providing a reasonable grounding in the foundations of electrical engineering. The topics covered are an important prerequisite for other courses of the Master of Science in Biomedical Engineering program, e.g., Biomedical Instrumentation. At the end, students are expected to be able to understand basic principles associated with the following topics: electric quantities (e.g., charge, current, voltage), circuit components (e.g., resistors, diodes, transistors, operational amplifiers), circuit analysis techniques, digital logic, digital circuits, and alternating voltages and currents. To learn about these basics, at the center stands a biomedical application: the amplification, filtering and analysis of heart signals. Students use the ciruit simulation software TINA and, to a smaller degree, the computing environment MATLAB to exercise the theory taught. This course aims primarily at students who have never taken an electrical engineering class. Some basics in physics and math are, however, required. The course is compulsory for students without a basic knowledge in electrical engineering.



This depicted circuit board was specifically developed for this course. It contains a driven-right-leg circuit to record ECG signals. The signals are then filtered and analyzed using analog and digital electronics.

Selected Chapter in Mathematics

Prof. Dr. Andreas Stahel

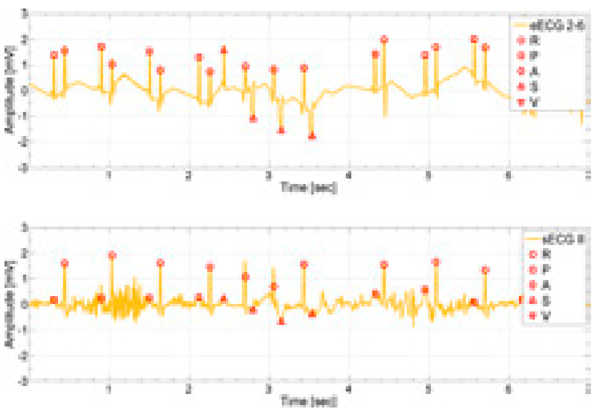
The students in the master's program Biomedical Engineering come from many different schools and countries. Thus their mathematical background is very far from uniform. This causes a few headaches for the students (and professors) in advanced classes. With this new class the program is helping the students to freshen up their mathematical knowledge and skills.
The students obtain an extensive set of exercises to be worked on before class. Then they have the opportunity to obtain answers in class to their open questions and thus fill some of the gaps in their knowledge. The selection of topics is based on the mathematics used during the program, and it cannot replace a solid foundation obtained during the preceding bachelor programs. For most students this might be a short recap of what they already master, at least for most of the topics.

The topics to be covered are:
- Basic linear algebra: matrices, linear mappings, small systems of linear equations, eigen values and eigen vectors.
- Calculus: Taylor approximation for functions with one and two variables, line integrals and double integrals, vectors fields, Green's theorem, conservation laws.
- Differential equations: elementary equations of order 1, visualization, linear second order equations, qualitative behavior of solution of partial differential equations.
- Fourier: Fourier series, spectrum, DFT/FFT, Fourier transform.
- Probability and statistics: basic concepts of probability, events, Bayes' theorem, conditional probability, some distributions, multivariate distributions.

Short Introduction to MATLAB

Dr. Thomas Niederhauser

MATLAB (The MathWorks Inc., USA) is a high-level language and interactive environment for numerical computation, visualization, and programming. It includes built-in mathematical functions as well as powerful toolboxes for solving engineering and scientific problems. As the name suggests, MATLAB is especially designed for matrix computations: solving systems of linear equations, computing eigenvalues and eigenvectors, factoring matrices, and so on. The problems are solved numerically, that is, in finite-precision arithmetic and the results can be visualized immediately using simple graphics commands. Furthermore, MATLAB is a modern programming language environment: it has sophisticated data structures, contains built-in editing and debugging tools, and supports object-oriented programming.
In this course, the basic principles and functions of MATLAB are introduced in a problem-based approach. The student learns how to efficiently use the build-in documentation for and to apply toolboxes mainly on specific questions arising in the field of biomedical engineering. The handling of big data, creating nice figures and to providing computational efficient solutions are key learning outcomes of this course.



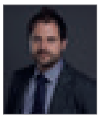
Segment of a long-term ECG signal processed with MATLAB.

Practical Course in Orthopaedic Surgery

Dr. Philipp Henle

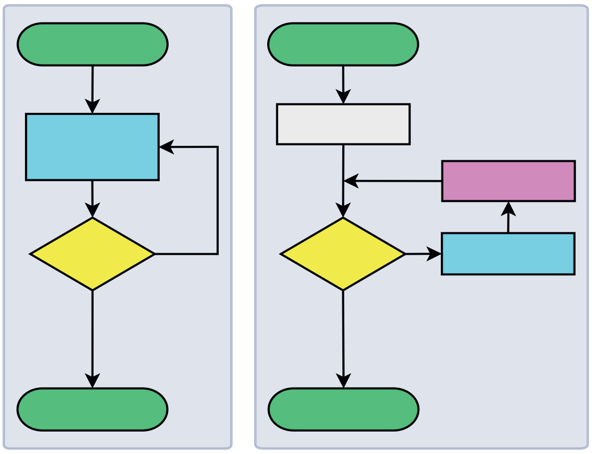
Medical and surgical treatment of musculoskeletal problems has developed enormously over the past decades. In the beginning, the correction of deformities especially in children was the main center of interest. Most of these treatments consisted of different forms of braces, casts or the use of orthotic devices.
Modern orthopedic surgery comprises the entire spectrum of conservative (non-operative), medical and an increasing variety of surgical interventions. The use of mechanical replacements of biological structures such as joints has revolutionized the treatment of degenerative pathologies on the musculoskeletal system.
With an increasing number of treatment options, thorough analysis and decision making are the prerequisite for successful interventions and patient satisfaction.
The "Practical Course in Orthopaedic Surgery" offers the students a behind-the-scenes view on a modern orthopedic surgery center. Students accompany surgeons and their residents during the clinical routine of morning rounds, outpatient clinic and the operating theater.
During the staff meeting in the morning, patients that were admitted to the hospital the day before as well as other interesting cases are presented with their radiographs and the respective treatment is discussed.
In the outpatient clinic students are able to see new patients with acute or chronic musculoskeletal problems. The value of different diagnostic measures such as the clinical examination, radiographs or magnetic resonance imaging can be discussed. The students can experience how treatment decisions are made. In addition, patients with follow-up after surgical interventions are seen in the outpatient clinic.
In the operating theater, students are given the opportunity to attend a great variety of different surgical interventions. Orthopedic subspecialties covered are upper extremity (shoulder and elbow), hip and pelvis, knee surgery and surgery of the foot and ankle.
During the one-week course, students are asked to complete a short summary about one of the patients they observed during the course in the operating room or the outpatient clinic. For that the students can use the electronic history as well as images taken before or during the intervention.
Once per day, a presentation will be given by one of the senior surgeons with current topics of their respective subspecialty. There will also be time to discuss questions brought up by the students or which might have risen up during the course.

Introduction to Programming



Prof. Andreas Habegger

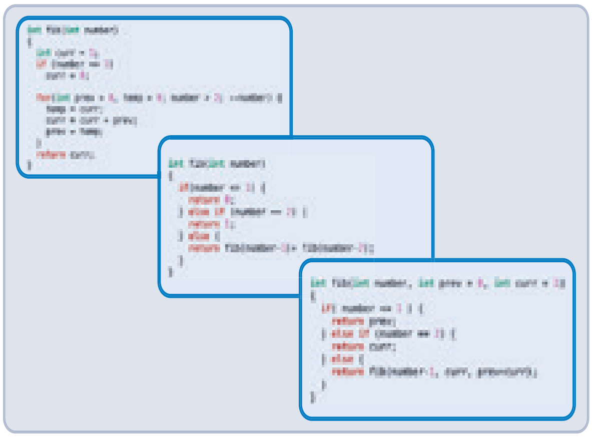
Nowadays, problems in science, health care, engineering and many other areas can be solved or strongly simplified by computers. This makes computer science and thus writing software a key competence for all graduated students. As always, there is a point where we are starting with a new subject. Learning something new takes time and demands a lot of effort to get a certain level of experience.



One way to look at procedural programming – A flow-chart snippet.

In this module, students gain a fundamental understanding of procedural software development based on concepts and examples inspired by the computer engineering domain. To develop a sense of what we must consider while writing, compiling and testing code, we look at the fundamentals of how a computer works. Due to the binary number system used by computers we will look at number systems in general and how to convert between number systems. Representation of numbers is key in the domain, which raises the discussion of encodings and its representation by data types in many computer languages.

Introduction to Programming is not just writing code to solve problems. It is more about writing self-documenting code, which is easy to maintain. Coding, however, a skill which is still important asks for implementation concepts. It's the method we use to solve a problem that makes the difference. That's why we compare different methods to solve the same problem and discuss its advantages and disadvantages. Having this in mind students gain the freedom to choose the more adequate concept for a certain problem.

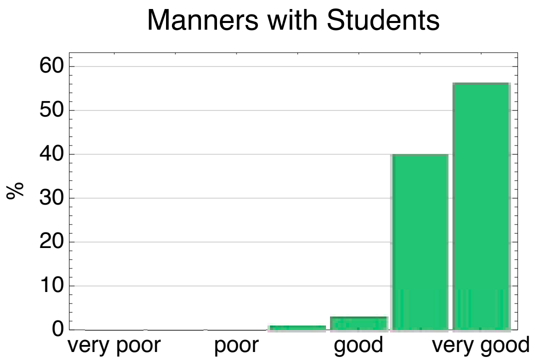


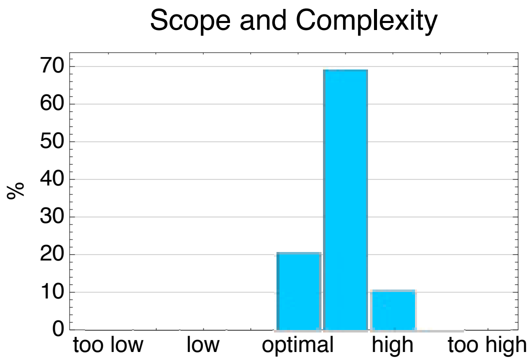
The difference which matters – Three implementations of Fibonacci Series.

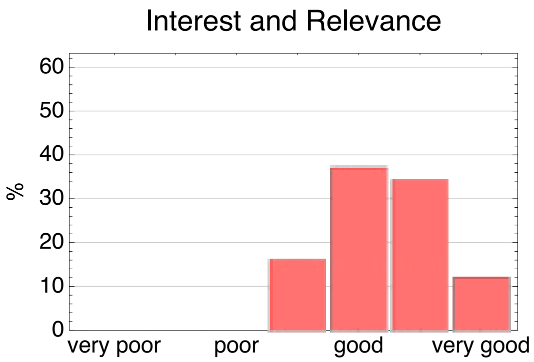
Knowledge gained during the course enables computer science novices to further improve their programming skills in follow-up courses such as C++ Programming I and II.

Evaluation of Courses in the Academic Year 2016/2017

Like in the previous years, the master's program was evaluated in fall semester 2016 and spring semester 2017 according to the guidelines of the University of Bern. Both semesters were considered leading to 50 course evaluations involving almost 900 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.







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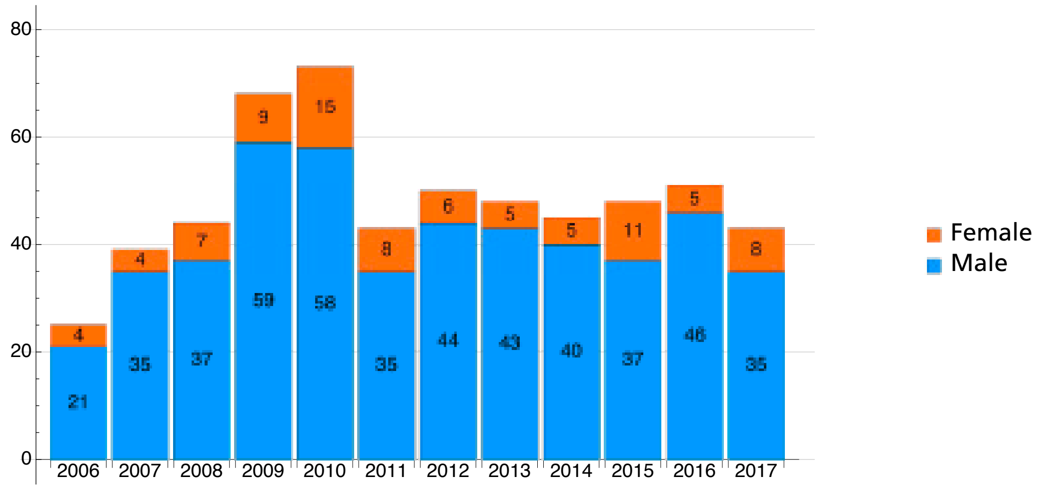
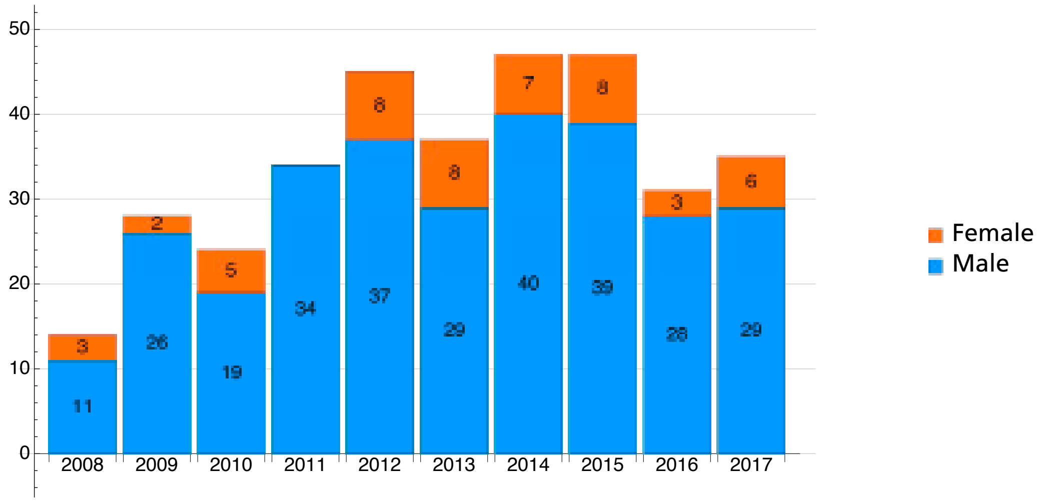
Reto Lerf, Dr.
Lukas Lichtensteiger, Dr.
Reto Luginbühl, Dr.
Simon Milligan, Dr.
Walter Moser, Dr.
Richard Nyffeler, PD Dr.
Yves Pauchard, Dr.
Matthias Peterhans, Dr.
Jorge Sague, Dr.
Birgit Schäfer, PD Dr.
Matthias Schwenkglenks, PD Dr.
Jivko Stoyanov, PD Dr.
Tim Vanbellingen, Dr.
Jürgen Vogt, Dr.
André Weber, Dr.

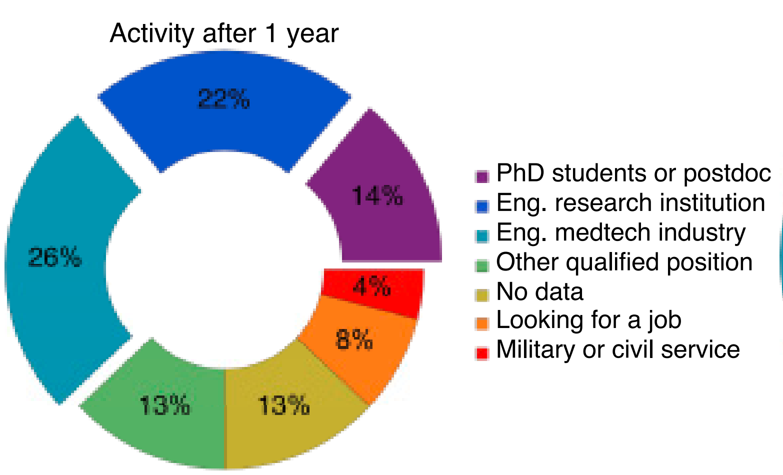
Statistics

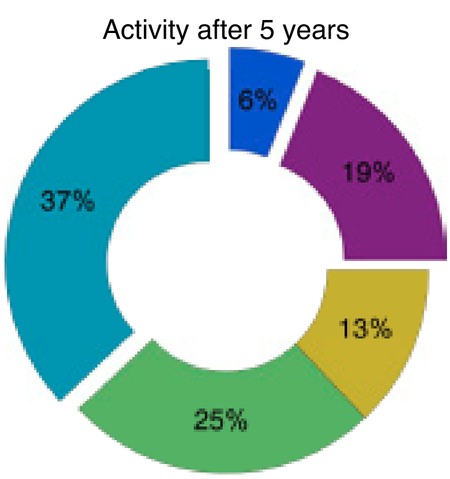
Number of New Students and Graduates per Year





Profession after Graduation





Graduation Ceremony

In September 2014, after my successfully completed BSc studies in Life Science Technologies, I started my master's studies in Biomedical Engineering at the University of Bern. We were approximately 40 national and international students with backgrounds in mechanical, electrical, and industrial engineering, computer sciences, micro technology, life sciences, and many more. The first semester contained mainly general courses. In the second and third semester, each student could choose one out of three major modules and supplement the mandatory courses with a huge variety of elective courses. Beside my master's studies, I worked at the ARTORG Center for Biomedical Engineering Research in the CVE group, where I spent a very interesting and educational time. After completing my master's thesis in the CVE group in February 2017, I finished my MSc Studies in Biomedical Engineering.
Today, 11 March 2017, after very interesting, demanding, and time consuming two years of study, I finally sit on one of these outstanding chairs in a gorgeous hall. The graduation ceremony is organized by the Faculty of Medicine of the University of Bern and takes place in the glamorous "Grosser Saal" at the Kultur Casino in Bern. After a short introduction given by the Dean of the Faculty of Medicine, the story of the third and fourth chapter of Gulliver's Travels, and a wonderful classical concert, the diploma delivery part starts. All newly graduated doctors in medicine and dentistry, as well as all newly graduated PhD students in biomedical Sciences and biomedical Engineering receive their diploma. Finally my pulse accelerates and my row of seats starts to walk towards the stage. All biomedical engineers who completed their master's studies at the University of Bern, are proud to finally receive their diploma.
We as biomedical engineers are all people who work in a very interdisciplinary, fast developing, and demanding field. We are professionals who enthusiastically work to improve the lives of patients be that as researchers in basic or applied sciences, in the industry, in hospitals, or in any other institution. Our work aims at improving medical technology, ranging from bone implants to brain computer interfaces, diagnosis technologies, surgical assisting systems, energy harvesting pacemakers, and much more. Working in the field of biomedical engineering is my passion and looking back I would say that every minute I invested in my studies to reach this goal was worth it.

Andrea Nienhaus, BME alumni

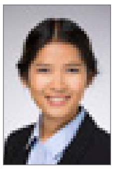
Our alumni 2017
Top (from left to right): Tess Groeneveld, Dominik Brügger, Stephan Gerber, Dominic Schmid, Maximillien Tholl, Apollonius Schwarz
Bottom (from left to right): Yannick Rösch, Benjamin Meier, Andrea Nienhaus, Hamoon Zohdi, Jariyaporn Thongbudda

RMS Award

The RMS Award is an award of excellence. Each year, the Robert Mathys Stiftung (RMS), an independent service laboratory and research institute, gives it to the best BME student for his/her outstanding achievements.
The award of 1000 CHF honors the student who receives the best grade point average over the course of the two year BME master's program.
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 2017
Alain Jungo receives the RMS Award 2017 from Philippe Zysset.

Graduation Profile



Jariyaporn Thongbudda, BME Alumnus (2017)

Q: What was your academic and professional background prior to your BME studies?
A: I got my bachelor degree in Electrical Engineering from Bangkok in Thailand. Afterwards, I worked for three years as test engineer at NXP semiconductor in Bangkok.

Q: Why did you choose to pursue your master's studies at the University of Bern / Bern University of Applied Sciences?
A: One reason is that my mother lives in Switzerland and was willing to support me during the studies.
Another main reason is that I had some biomedical engineering topics in my bachelor classes which I found very interesting.
Also, the program is taught in English and the description sounded very promising and fitted well with my studies.

Q: You continued to work during your studies. How was this experience?
A: I worked as research assistant at ARTORG center parallel to my master's thesis. I really like the work because I learned a lot and had the chance to use the theoretical knowledge in a more practical way.

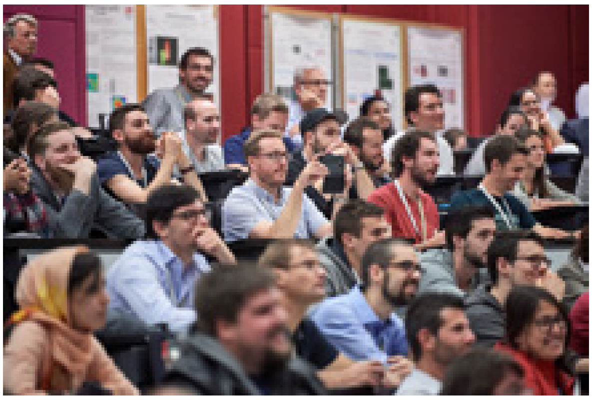
Q: What was your career plan after the completion of your degree?
A: I wanted to find a job in Switzerland. It would especially be great to find a job which related to electrical biomedical engineering.

Q: What is the benefit of the master studies with regard to your current professional activity?
A: I found a job as production engineer in a company which also produces medical devices. The job is not directly linked to biomedical engineering, but I can use a large part of my knowledge that I gained during the master's program.

Biomedical Engineering Day 2017

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

On May 19, 2017, 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 ninth time.

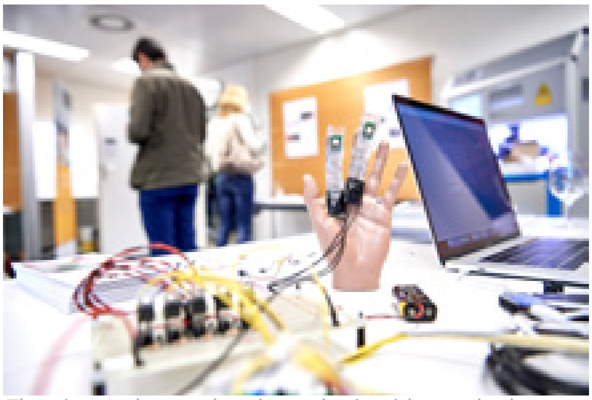


Participants in the auditorium.
Photo: Adrian Moser

The event is an efficient platform in Switzerland for networking of MS 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.

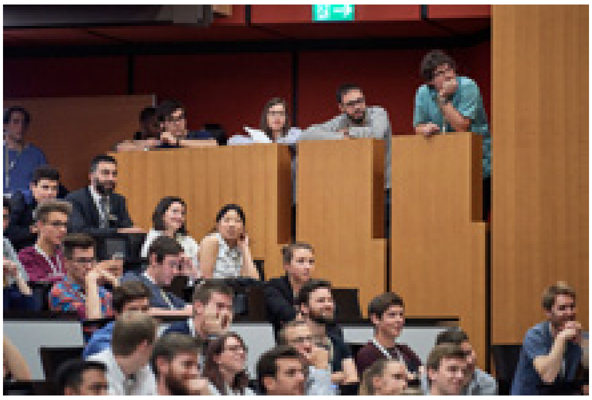
A post-doc, a PhD student and a BME alumna talk to a company representative.
Photo: Adrian Moser

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's program, used the possibility of presenting current research projects to more than 300 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.



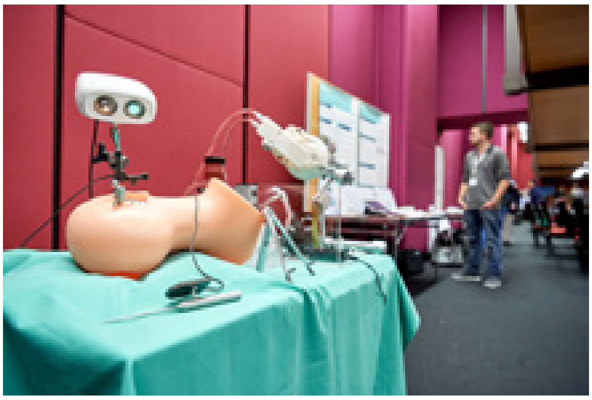
The picture shows a hand prosthesis with attached sensors allowing an amputee to get touch feedback and for improved body ownership (NanoTera WiseSkin project).
Photo: Adrian Moser

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



The audience enjoys watching the live surgery.
Photo: Adrian Moser

One highlight of the day was the successful live knee surgery by Kai Ziebarth, Department of Pediatric Surgery, Inselspital Bern. Illustrative explanations in the auditorium were given by Steffen Berger from the same department.



The IGT group's booth in the auditorium.
Photo: Adrian Moser

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: **Andrea Nienhaus** (Bacterial Cellulose-Based Patches for Heart Surgery -Investigation of Culturing Conditions and Material Characterization)
2. SICAS Award for the best PhD thesis: **Janick Stucki** (Development of a Breathing Lung-on-a-Chip)
3. BME Club Award for the best poster: **Sandro De Zanet** (Retinal Slit Lamp Stitching)
4. BME Club Award for the best master's thesis abstract: **Michael Indermaur** (Visualization of Trabecular Bone Damage using MicroCT)

SICAS Award winners: Janick Stucki and Andrea Nienhaus
Photo: Adrian Moser

BME Club Award winner: Sandro de Zanet
Photo: Prabitha Urwyler

BME Club Award winner: Michael Indermaur
Photo: Adrian Moser

We thank our sponsors and exhibitors

Anton Paar

Biomedical Engineering Club

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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. A dedicated executive committee follows the principles of our constitution.

We are an enthusiastic and versatile group with diverse activities:

- 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's program
- organization of an annual alumni gathering
- sponsorship of the poster and abstract awards at the annual BME day
- sponsorship of conference travel grants
- provide access to the Medical Cluster events
- automatic joint membership with Alumni UniBE
- 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 welcoming you!

The BME Club Board in 2017

Prabitha Urwyler
President
M.Sc. class 2006

Tom de Bruyne
Vice President+PR
M.Sc. class 2009

Andrea Nienhaus
Secretary + Treasurer
M.Sc. class 2014

Tobias Imfeld
Webmaster
M.Sc. class 2009

Jonas Maturo
PhD Students
M.Sc. class 2015

Stephan Gerber
Master Students
M.Sc. class 2014

Fatih Toy
M. Sc. Alumni
M.Sc. class 2009

Trip to Medica 2017

Like every year at the beginning of the winter, the BME club organized a trip to Medica, the world's leading trade fair for the medical industry. We were 20 engineers taking part in the trip to Düsseldorf from Tuesday evening to Friday morning. Most classes were suspended during this time.

A tiny part of MEDICA.
Photo: Pierre Cuony

On Friday, we met in a bar in Bern at 9 pm to wait for the overnight bus. This was a good occasion to get to know each other and meet students from other fields. At 10 pm, we got on the comfortable bus, direction North Rhine-Westphalia.

BME students test an innovative message table
Photo: Pierre Cuony

When we arrived in Düsseldorf, the first good surprise was that the temperature was about 10°C warmer than in Bern. The second was that it was only 8 am and we had two full days to explore the 20 halls and visit the 5000 exhibitors present at the trade.

The exposed products were ranged in different categories: laboratory equipment, electro-medical equipment / medical technology, diagnostic device, physiotherapy / orthopaedic technology, information technology, surgery instrumentation.

The group at one of the traditional breweries in the historic town of Düsseldorf.
Photo: Pierre Cuony

This year, the trends seemed to be the imaging/video assistance and the portable devices.

After a long day walking through the stands, it was time to go back to the hostel where a barbecue was prepared for us. After eating, the more motivated among us went out for a drink. The whole city center was full of people coming from all over the world for the event.

The next day, we finished the visit of the exhibition. These two days permitted us to get a very good overview over what's moving in the medical technology field. It will help lot to make choices in the Master's program and to reach the job of our dream. And one day work for one of the exhibitors at Medica.

In the evening, we had dinner at a traditional brewery before we boarded the bus that brought us back to Bern.

BME Club Annual Barbecue

The annual BME Club barbecue has become somewhat legendary. The 2017 edition lacked the great weather experienced in former years.

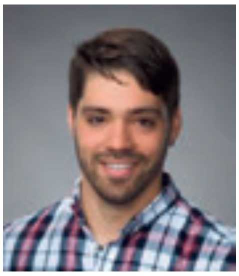
The BME Club's excellent „chefs" Tom de Bruyne and Prabitha Urwyler test their recently sponsored barbecue on the ARTORG terrace.

Master's Theses 2017

Design and Development of a Skin Patch with Integrated Dry Electrodes

Tobias Bertos

Supervisors: Dr. Thomas Niederhauser, Prof. Dr. Marcel Jacomet
Institutions: Bern University of Applied Sciences, Institute for Human Centered Engineering
Examiners: Dr. Thomas Niederhauser, Prof. Dr. Josef Götte



Introduction

Atrial fibrillation (AF) is the most common heart rhythm disorder, but is rarely life-threatening. Nevertheless, it is a risk factor for secondary complications such as strokes and may cause permanent disability. Due to its unpredictable nature, occurring in rare and short episodes, AF may only be detected by long-term electrocardiography (ECG) [1]. Standard electrodes face the problem of irritating the skin after several days when applied to the body. Dry electrodes do not irritate the skin, but are prone to motion artefacts.

The aim of this thesis is to develop a new mechanical design for dry electrodes to reduce motion artefacts and enhance signal quality in long-term ECG recordings.

Materials and Methods

FEM simulations were done with the final design to examine the mechanical behaviour when exposed to movements and loads in different directions (Abaqus). Previously calculated maximum loads were compared to the simulation. Finally, a test setup was created to mimic skin movement and to measure the impedance of the electrode when applied to the moving electrically conductive silicone.

Fig. 1 FEM simulations demonstrated maximum appearing stresses at transition points between the outer ring and the spiral. A load of 5 N was applied for all simulations.

Results

The simulated mechanical behaviour was very close to the previously calculated values and does not show an unusual behaviour. The calculated applicable forces for the electrode are in a reasonable range of 0 N to 4.2 N before plastic deformation occurs and 4.2 N to 6.8 N before the electrode ruptures. Depending on the position of the applied load of 5 N, FEM simulations showed maximal occurring stresses of 493.3 MPa, capable of deforming but not rupturing the electrode. The highest stresses occur at the insertion points of the spiral to the outer ring (see figure 1).

A test setup was constructed to conduct impedance measurements with simulated skin movements. Air is pumped into a cylinder, which is covered by an electrically conductive silicone skin to mimic skin movement. The impedance was measured from the silicone to the electrode. First impedance measurements showed promising behaviour of the new design. Impedance values from 543 Ω to 549 Ω were measured while the silicone skin was inflated and from 8 kΩ to 19 kΩ after deflation. A consistent skin contact was ensured between the electrode and the silicone skin during movement.

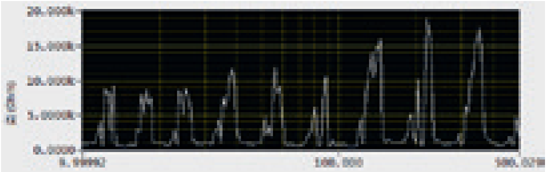


Fig. 2 Impedance measurement of the new electrode design from 10 Hz to 500 Hz while the pump was activated for moving the silicone skin. Clearly visible change of the impedance while inflating and deflating the silicone skin.

Discussion

The dry electrode design developed in this thesis takes an entirely novel approach to prevent motion artefacts. A simple spiral element allows consistent skin contact, even when the pressure on the electrode decreases. This simple design is able to compensate movements not only in two, but in three dimensions.

References

[1] K. Rainer and S. Stefan. Physiologie, volume 7. Thieme, 2014.

Acknowledgements

The project was supported by the BFH Institute for Applied Laser, Photonics and Surface Technologies. Special thanks to the important contribution of Stefan Remund for manufacturing the designed electrodes.

Fluid Dynamic Classification of a Transcatheter Aortic Valve Prosthesis

Désirée Biedermann

Supervisors: PhD David Hasler, PhD Silje Ekroll Jahren
Institutions: ARTORG Center, Biomedical Engineering Research, Universität Bern
Examiners: Prof. Dr. Dominik Obrist, Prof. Dr. Thomas Pilgrim

Introduction

Transcatheter aortic valve implantation has become the standard procedure for high-risk patients with severe, symptomatic aortic valve stenosis since its first implantation in 2002. However, adverse events including paravalvular leakage, pacemaker requirements, durability, stroke and subclinical leaflet thrombosis remain an issue. Especially ischemic events and leaflet thrombosis have been related to unphysiological hemodynamics due to transcatheter aortic valve prostheses. The aim of the thesis was to identify the main flow characteristics of a transcatheter aortic valve prosthesis in different rotational positions and their influence on the hemodynamic performance of the prosthesis.

Materials and Methods

Three experiments were conducted in an in-vitro simulator reproducing the main characteristics of the left heart circulation. The instantaneous velocity vector fields past the aortic valve prosthesis, placed according to a native valve and after a 60° rotation around the axial axis of the valve, were measured in three different idealized aortic root phantoms using tomographic particle image velocimetry.

Fig. 1 Reference (left) and rotated (right) position of the transcatheter aortic valve prostheses within the idealized aortic root.

Results

The results revealed four distinct fluid dynamic characteristics, namely, the fluid expulsion during the valve opening, a high-speed central jet, the formation of a start-up vortex and three backflow regions. Furthermore, a strong influence of the axial valve position was observed on the size and the location of the start-up vortex and the sinus washout.

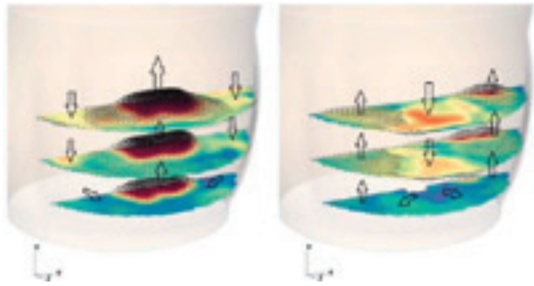


Fig. 2 The mean velocity field at peak flow within the cardiac cycle of the reference (left) and the rotated (right) position.

Discussion

The rotational positioning of the transcatheter aortic valve has a serious impact on the fluid dynamic situation within the sinus. In detail, the 60° rotation of the valve let to a completely opposite backflow pattern compared to the backflow pattern produced by the native valve position. Furthermore, sinus washout in the lower half of the sinus and over the complete cardiac cycle is assumed to be slightly more efficient in the rotated position. However, further investigation including the measurement of the particle residence time is required. In contrast, the higher axial position of the prosthesis led to a larger stagnation zone in the base of the sinus, which could increase the risk of blood clotting and thrombus formation.

References

Hamm CW. et al., The future of transcatheter aortic valve implantation, European Heart Journal: 37(10): 803-810, 2016.

Acknowledgements

The project was enabled by Prof. Dr. Obrist and David Hasler who provided great support throughout this research project.

ECG-Vest for Long-Term Non-Invasive Cardiac Rhythm Monitoring

William Bovy

Supervisors: Dr. med. Romy Sweda, Dr. med. Dr. phil. Andreas Häberlin
Institutions: ARTORG Center for Biomedical Engineering Research, Universität Bern
Dept. of Cardiology, Inselspital, Bern University Hospital
Examiners: Dr. med. Dr. phil. Andreas Häberlin, Dr. med. Romy Sweda

Introduction

Cardiac diseases are one of the leading causes of death in developed countries. A cornerstone in the diagnosis of heart rhythm disorders, the prevention and long-term treatment of arrhythmias is long-term cardiac monitoring using electrocardiography(ECG). Conventional surface electrodes are taped on the skin of the patient and use gel as interface to register the time-dependant electrical field of the heart on the body surface. The electrode gel begins to irritate the skin of the patient after a few hours. Therefore, new electrodes without gel are developed to be integrated in a garment that could be comfortably worn. The major drawback of dry electrodes is the sensitivity to motion. Motion artefacts appear when the electrode slips on the skin, creating friction and inducing noise that makes the signal unreadable.

Materials and Methods

This thesis presents a method to characterize the properties of dry textile electrodes with the development of a dedicated bench test and a prototype of ECG-monitor-harness. The bench test is designed to isolate the interface's impedance between the electrode and a skin phantom out of agar. The harness serves to test textile electrodes in real-life conditions and to improve their design.

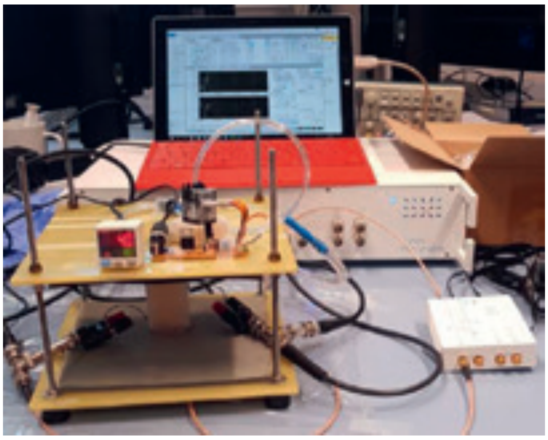


Figure 1 : Picture of the bench test and instrumentations.

Results and discussion

During measurements with the bench test, problems of polarization of the agar phantom were observed which prevent to isolate the interface's impedance. However, the bench test has given sufficient information to find that the cover factor of the electrode impacts its sensitivity. Results of skin-electrode impedance confirm alongside with biocompatibility that silver-containing dry electrodes are the best candidate amongst materials tested.

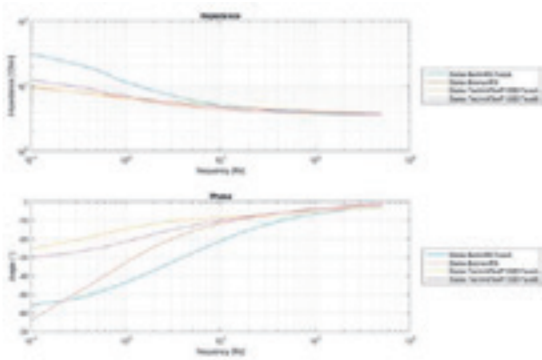


Figure 2 : Best textile electrodes on the bench test.

The ECGs acquired with the harness were qualitatively of good quality and confirm previous research about the important effect of cover factor of textile. Motion artefacts still stay the major difficulties to overcome as no ECG were readable during movements of the chest.

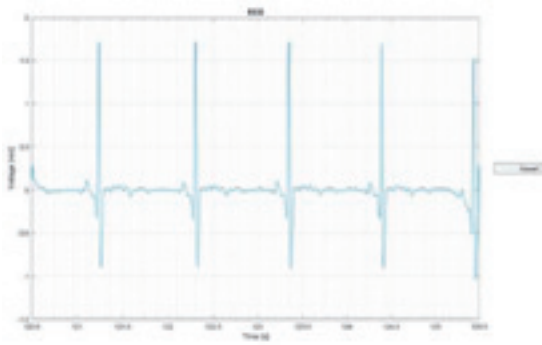


Figure 3 : ECG acquired with one textile electrode.

Conclusion and outlook

The thesis proposes methods to identify the most suitable electrode materials for a long-term ECG harness. Further improvements of the test bench and measurement methodology are required to generalize the results and help to test new designed dry electrodes under realistic and repeatable conditions.

Towards a Hemodynamic Characterization of Microcirculation-Involving Peripheral Arterio-Venous Malformations

Tarcisi Cantieni

Supervisors: MSc Sabrina Frey, Dr. med. Axel Haine
Institutions: University of Bern, ARTORG Center for Biomedical Engineering Research
University Hospital Bern (Inselspital), Department of Angiology
Examiners: Prof. Dr. Dominik Obrist, Dr. med. Axel Haine

Introduction

Arteriovenous Malformations (AVM) are a rather complex medical condition and require a lot of experience to be diagnosed correctly and not infrequently they pose a challenge even to seasoned professionals. To research opportunities towards automatic AVM diagnosis and classification, various models have been established, none of which comprised any microcirculation-involving subtypes, although these constitute one of the bigger challenges to diagnosing. Recently an additional of which has been proposed: capillary-venous AVM (cvAVM).

Materials and Methods

To find out which parameters represent which tissue structure, a baseline testing network (TN) was set up according to studies documenting the microcirculation, and its indicator-dilution curve was computed. Then the developed operator was applied on the concentration curve sampled at the TN inlet and its four parameters were tweaked to optimally fit the operator's output to the TN's outlet curve and subsequently translated to descriptive parameters t and RD. This procedure was repeated for various possible (and impossible) tissue architectures and properties and the resulting parameters were compared among each other and to findings from digital subtraction angiography (DSA) images made of hands of different health statuses (healthy, AVM types II, IV and CV).

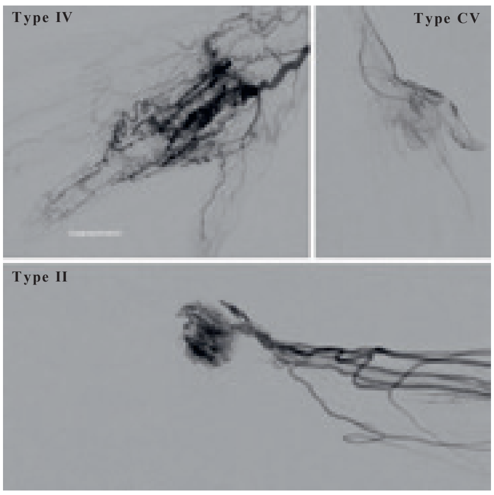


Figure 1: Exemplary angiograms of types IV, CV and II

These angiograms were treated similarly: Levels of opacity were translated to CA concentrations, inlet and outlet concentrations were sampled and the operator to connect the two curves was sought.

Results

In figure 2 the comparison of the main parameters mean transit time (t), relative dispersion (RD) and absolute dispersion (AD) are depicted.

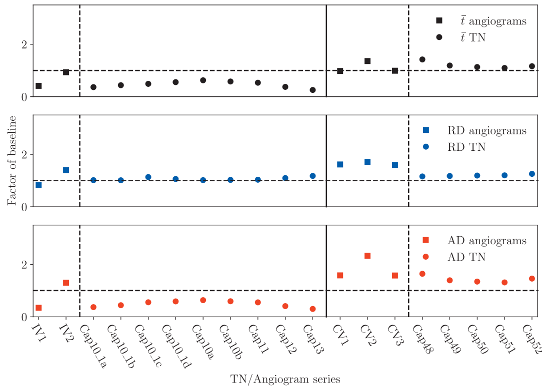


Figure 2: Comparison of TN results to angiograms

Discussion

The findings from the TN and from the angiograms match well, and consequently, one must conclude that the approach chosen to model the microcirculation mirrors the physical behavior of which sufficiently well. Therefore, the hypothesis for the morphology of the cvAVM type, is not only not refuted, but can cautiously be confirmed by this work. Furthermore, it was pointed out, that the implemented transfer function can be used to reproduce nearly any kind of indicator transport, making it a valuable tool for further use. For instance, one could set up studies for the investigation of Yakes type IV and cvAVM, similarly as did Frey et al. in [1] for types I and III.

References

[1] S. Frey, A. Haine, R. Kammer, H. von Tengg-Kobligk, D. Obrist and I. Baumgartner, “Hemodynamic Charakterization of Peripheral Arterio-venous Malformations”, Ann Biomed Eng., Vol. 45, No. 6, pp. 1449-1461, June, 2017.

Continuous Neuromonitoring for Minimally Invasive Cochlear Surgery using Drill Integrated Multi-Channel Electrode: a Feasibility Study

Aarati Rachel Chacko

Supervisors: Dr. Kerstin Thorwarth, Dr Juan Ansó
Institutions: Empa, Swiss Federal Laboratories for Material Sciences, Dübendorf
University of Bern, ARTORG Center for Biomedical Engineering Research
Examiners: Prof. Dr. Stefan Weber, Prof. Dr. Hans Josef Hug

Introduction

Neuromonitoring (NM) during surgical procedures is an area of active research interest, as damage to nervous tissue could result in impaired muscle function. In image-guided, mini-invasive, robotic cochlear implantation surgery (RCI), a direct access tunnel to the cochlea is drilled that passes at submillimeter distances to the facial nerve. NM for this application has been investigated and the nerve could be reliably detected at these distances using a multi-electrode probe [1], however the need to interrupt drilling to allow for NM adds minutes and complexity to the surgical procedure. There is therefore a need to drill and monitor nerve proximity in tandem. The aim of this project was to investigated a coatings-based approach to drill integrated NM.

Materials and Methods

A drill-coating setup was implemented in a magnetron sputtering system (fig.1) that allowed for two levels of substrate rotation, as required to coat the complex 3-d geometry of drill bits. Coating recipes for insulator and conductor materials were determined using hysteresis experiments (fig.2, top), and a set of coated drill bits were produced (fig.2, bottom). Functional properties were evaluated using an in-bone wear test, electrochemical impedance spectroscopy (EIS), and optical and electron imaging.

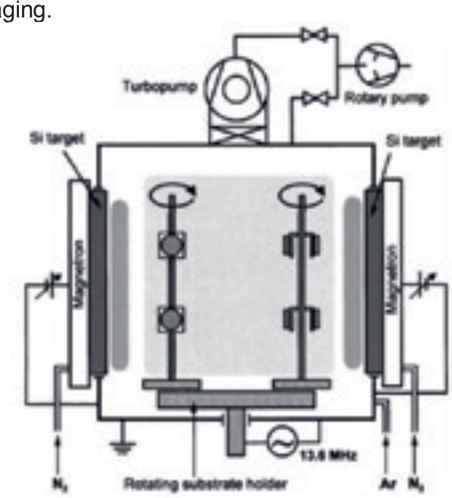


Fig. 1 Magnetron sputtering setup used to coat the drill bits (schematic modified from [2])

Results

Coating recipes were successfully determined and imaging showed that we could produce distinct conducting and insulating surfaces (also seen in fig.2, bottom). Visual evidence of extensive arc-induced damage was confirmed by the inability of coating layers to prevent electrical cross-talk between conductive layers, so the EIS results were largely inconclusive in determining coating damage due to in-bone drilling.

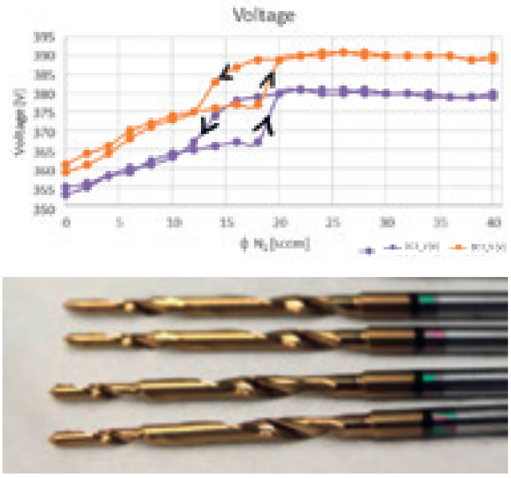


Fig. 2, top, hysteresis curve showing the change in voltage with increasing and decreasing the flow of nitrogen to the chamber; bottom, coated drill bits produced after the successful determination of the coating recipe.

Discussion

Although functional properties could not be tested from the coated drills, the coating setup we implemented in this thesis was successful in producing distinct conductor and insulator surfaces, and in so doing, has shown concept feasibility.

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[2] Diserens M, et al. Improving the properties of titanium nitride by incorporation of silicon. Surface and Coatings Technology 1998; 108-109: 241–246.

Acknowledgements

I thank both Empa and ARTORG for giving me the opportunity to work on this project.

Providing Tactile Feedback for Hand Amputees

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Examiners: Prof. Dr. Volker M. Koch and Dr. John Farserotu

Introduction

The loss of a limb due to an amputation is a traumatic event and has a deep impact on the daily life of the amputee.

To ease the acceptance of the loss of a limb, a prosthetic one can be provided. Since commercially available prostheses do not provide tactile feedback, the amputee has to rely solely on visual and auditory feedback to control it. Such focus can be mentally demanding, as it does not feel natural. This is a reason why myoelectric prostheses, the state of the art in prostheses, are abandoned. Instead, simpler models, such as body-powered ones, are preferred. Indeed, they offer a semblance of feedback through the tension felt in the cables used to control them.

Amputees have often reminiscing sensations in the stump, i.e., by touching certain regions, it feels as if no longer existing fingers were touched. These regions form a phantom map. However, not every amputee has one. This project investigates the restoration of tactile sensations by substituting the pressure felt on the fingers with vibrotactile cues on the sole of the foot.

Materials and Methods

A demonstrator composed of a tactile feedback device embedded in the sole of a shoe and a sensory device compatible with a commercially available prosthesis was developed. The feedback device could be monitored with a PC but all the processing of the pressure data was performed in the microcontroller unit of the system.

Fig. 1 Test hardware: 1. shoe with embedded tactile feedback device, 2. emergency module, 3. sensor module with sensor on the hand, 4. PC with an XBee radio running the testing program

The effectiveness of the system was demonstrated by designing and conducting an experiment with an amputee. The ability to localize the finger stimulated and to discriminate the intensity level was tested. In addition, the ability to discern the hardness of a material was also evaluated.

Results

The results for the first experiment showed that in 70% of the cases, the participant could correctly discern which finger was stimulated and its corresponding intensity. In the second experiment, the coding pattern with the overall intensity represented by different actuators located at different positions enabled the subject to intuitively distinguish different level of hardness for various materials.

Given Feedback		Given Stimulus: Thumb L	Thumb M	Thumb H	Index L	Index M	Index H	Middle L	Middle M	Middle H
Thumb	L	10								
	M		7	1						
	H		3	9						
Index	L				4	4				
	M				3	4	4			
	H					1	4			
Middle	L				3		1	9		
	M					1	1	1	7	1
	H								3	9

Tab. 2 Confusion matrix of the passive tactile test. L, M and H stand for low, medium and high frequency stimulation, respectively. The results showed a good discrimination for the big and third toes and more confused results for the second toe, for both localization and level discrimination.

Discussion

These results show that the foot is a good site for touch feedback stimulation. However, the locations of the actuators and the coding pattern need to be further investigated to confirm the validity of these results since the system has been demonstrated only with one amputee subject.

References

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Acknowledgements

The project was funded by Nano-Tera (SNF) and the State Secretariat for Education, Research, and Innovation (SERI). Botta Orthopaedie, Biel is gratefully acknowledged for the research of test participant.

Master's Thesis in Biomedical Engineering

Wash-out Effect and Flow Visualization in the Aortic Sinuses

Christian Robert Fröhlicher

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Examiners: Prof. Dr. Dominik Obrist, PD Dr. Stefan Stortecky

Introduction

It has been shown that bioprosthetic heart valve thrombosis is more common than first assumed. Thrombus formation on a heart valve not only impairs the function of the valve, but poses a risk for embolisms as well. The motivation for this study is to investigate potential relationships between the prosthetic valve design and blood flow. Such results might help to enhance the clinical outcome of heart valve replacement with improved products and more accurately adapted implantation.

Materials and Methods

To investigate factors inducing blood coagulation, the flow phenomena in the aortic sinuses of Valsalva were reproduced in an in vitro model. A bovine pericardial bioprosthesis was set into an idealized silicone phantom of the aortic root. Two out of three aortic sinuses included a coronary ostium where the coronary arteries evolve. Thereby, the novelty of this wash-out study was the use of a sophisticated model mimicking the characteristic flow of both the left and right coronary flow simultaneously. A controlled piston pump actuated the flow loop, allowing adjustable physiological conditions. The flow field in the aortic root was visualized and recorded with a high speed camera.

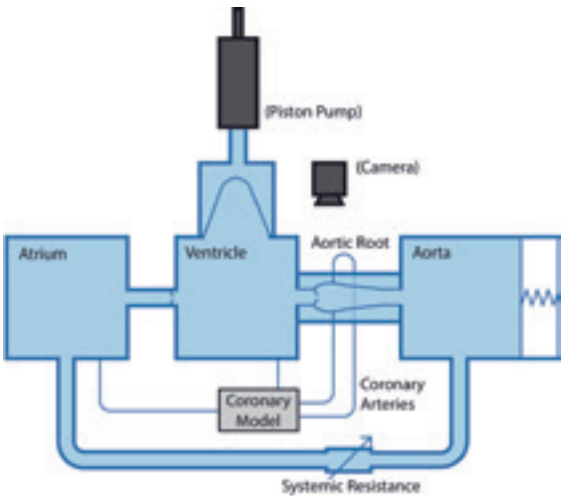

Fig. 1 Scheme of the experimental flow loop setup to mimic the left heart

Each of the three aortic sinuses was investigated with and without coronary flow. Thereby, two methods were used. First, water was colored with food dye as a contrast agent. Second, a water, glycerol and salt mixture matching the viscosity of blood was mixed with particles of the same density as the fluid. The motion of the particles was then tracked using particle image velocimetry (PIV).

Results

The observed wash-out in the aortic sinuses was found to be enhanced for the sinuses containing coronaries (left sinus 36% and right sinus 25% longer average resident times with closed compared to open coronaries). The asymmetric coronary flow seems to enhance the flow in circumferential direction around the valve, slightly inhibiting the wash-out in the non-coronary sinus (non-coronary sinus 9% shorter average resident time with closed compared to open coronaries).

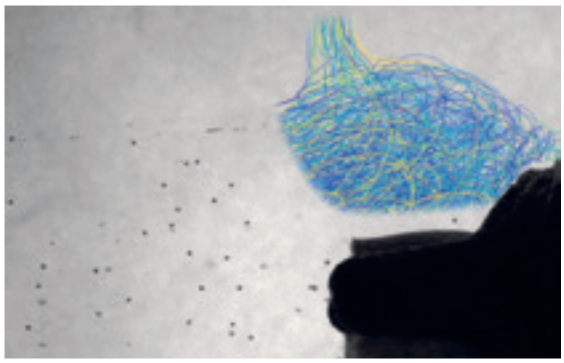

Fig. 2 Particle track visualization for the right aortic sinus with open coronaries

Discussion

The sinus vortex, induced by the aortic backflow, seems to play an important role for the wash-out of the sinus portions. The impact of the coronary flow impairs this vortex and is mainly visible during diastole. The coronary flow only slightly affects the wash-out deep in the aortic sinuses. However, the minor impact of the coronary flow should still be considered when describing flow phenomena in the aortic root.

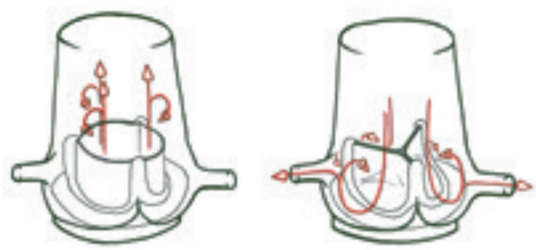

Fig. 3 Flow directions during systole (l.) and diastole (r.)

Towards a Percutaneously Implantable Ventricular Assist Device

Maxime Genilloud

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Examiners: Andreas Häberlin, MD, PhD, Prof. Dominik Obrist, PhD

Introduction

Heart failure (HF) is a growing concern, with an increasing volume of cases driven by an ageing population and improvements in myocardial infarction and HF treatment. Percutaneously implantable ventricular assist devices (PVADs) do not require surgery, can be implanted within a few minutes and may unload the left ventricle effectively, however, they are intended for short term use only due to constant need of purge, risk of thrombosis, and entry site infection. The aim of this thesis was to investigate the key challenges for a novel PVAD located in the ascending aorta and suitable for long-term use.

Materials and Methods

Considering dimension as a key point to make the prototype percutaneously implantable, the first step of the development was to design a suitable housing and impellers with a diameter lower than 7mm. To overcome the continuous need to purge the current PVADs due to imperfect sealing, the second most important design consideration was to develop a method to perfectly seal the motor against fluids (i.e. blood), whilst keeping the device's ability to transfer rotational motion to impellers outside of the sealing. The sealing and proper motion transfer was realized by a magnetic coupling mechanism between two 4-poles magnets at 0.7mm from each other.

Fig. 1 Final prototype. On the right, a 3D printed impeller is fixed on a cone actuated by magnetic coupling from a magnet rotating within the motor shaft. The motor is encapsulated within a hermetic housing. A simple fixation mechanism is attached in addition

Shear stress on erythrocytes which may cause relevant hemolysis was computed and compared to the Tillman diagram, which demonstrates the threshold of shear stress as a function of the time over which hemolysis occurs. Preliminary experiments with a first device prototype were conducted on a flow loop mimicking the left-heart to assess the functionality of the device.

Results

A device prototype (Ø6x37mm, 5.4g) containing a high-performance micro-motor and a magnetic coupling mechanism was successfully developed (Fig. 1). The device was immersed into water during several days and stayed perfectly dry, indicating a suitable sealing design with the magnetic coupling. The maximum torque generated by the coupling was computed at 1.05mNm, while the torque needed to rotate the impellers within blood at a rotation speed of 40000 RPM was computed at 0.39mNm. The shear stress induced by the impellers on erythrocytes exceeds the Tillman threshold of hemolysis, with shear stresses of 437N/mm^2, 838N/mm^2, and 1376N/mm^2 for the three impellers, which are comparable to clinical studies conducted on current PVADs[1].

Cardiac output measured on the test bench only increased minimally by 0.1l/min.

Discussion

Our results suggest that a magnetic coupling mechanism may allow building (1) a miniaturized and (2) a properly sealed PVAD overcoming key limitations of contemporary systems. The generated flow rate of the present first prototype is low due to the impellers' design and the impellers' rotation speed. Further impeller design improvements and computational fluid dynamic simulations may be required to improve the performance of such devices.

References

[1] Selgrade B. et al., Computational Fluid Dynamics Analysis to Determine Shear Stresses and Rates in a Centrifugal Left Ventricular Assist (2012).

Effects on OCT Signal properties due to Laser Tissue Interaction in SRT

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Institutions: Bern University of Applied Sciences, Institute for Human Centered Engineering
Examiners: Prof. Christoph Meier, Dr. Michael Jaeger

Introduction

Selective Retina Treatment (SRT) is a novel form of laser therapy with possible applications for the treatment of variety of retinal diseases. In contrast to conventional photocoagulation, SRT selectively destroys the retinal pigment epithelium (RPE) without harming the photoreceptors. For many conditions, the destruction and subsequent regeneration of the RPE alone is responsible for the desired therapeutic effects. Since the generation of SRT lesions is not visually assessable, other means of dose control are needed. Previous work at the *BFH* has shown that losses (washouts) in the signal of optical coherence tomography (OCT) measurements during SRT are an accurate indication for lesion generation. The aim of this thesis was to deepen the understanding of the OCT signal washouts observed during SRT and to investigate the underlying effects due to laser-tissue interactions.

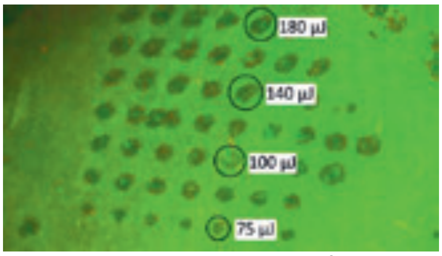

Fig. 1 Fluorescence microscopy image of a retina sample with lesions induces by varying laser pulse energy.

Materials and Methods

A frequency doubled Nd:YAG laser with a wavelength of 532nm and pulse duration of 4ns has been integrated into an existing OCT system. Freshly enucleated porcine eyes were used as samples. Two experimental protocols were applied. Lesions were induced with varying laser pulse energy and the OCT M-scan signals (time resolved axial profiles) were recorded at the point of laser impact. Other measurements were conducted with the OCT laser displaced relative to the SRT laser. Treated retina samples were assessed by means of fluorescence microscopy with a live/death staining.

Results

Energy threshold for lesion generation was 156mJ/cm^2. OCT signal washouts showed a strong dependency on applied laser energy. A different behavior of the signal washout was observed in the RPE and the upper retina. Displaced measurements showed that the signal washout is detectable up to distances of 300µm from laser impact.

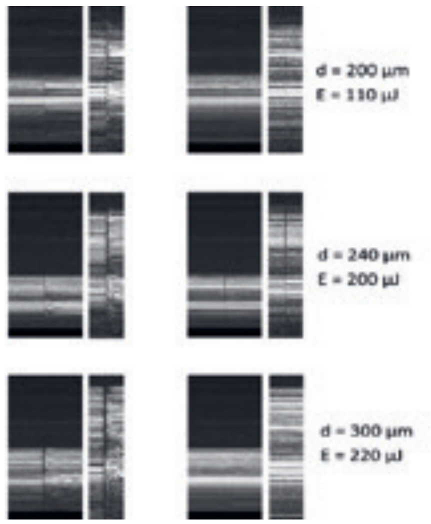

Fig. 2 M-scans with OCT and SRT laser aligned (left) and with OCT laser displaced relative to the SRT laser (right).

Discussion

The cause for damage in RPE cells during SRT is believed to be the formation of microbubbles due to vaporization around strongly light absorbing melanosomes. After consideration of several possible effects, it was concluded that the generation of microbubbles is also the most probable origin of the signal washout observed in OCT M-scans during lesion generation. Further investigation with a swept source OCT integrated into the system could be conducted to verify this assumption.

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Christoph Meier and Jörn Justiz were of great help during this project, as were the other members of the optoLab and BME group at the BFH in Biel.

CNN Based Representation Learning with Gaze Supervision for Diversified Medical Image Data

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Institutions: ARTORG Center for Biomedical Engineering Research
Examiners: Prof. Dr. Raphael Sznitman, PD Dr. Stavroula Mougiakakou

Introduction

The performance of machine learning algorithms is highly dependent on the amount of example data. Many recent applications in medical imaging use a supervised learning method and are thus reliant on labeled data. Generating such annotations on many images using a mouse is in general tedious and time-consuming. Furthermore, when dealing with medical images, the task often requires expert knowledge, which is rare. The present work is a contribution to an ongoing project where an eye-gaze tracker is used in replacement of the traditional mouse-based approach. The typical protocol thus consists in asking the expert to stare at a given object of interest and recording the location of his/her gaze on the images. A final segmentation is then generated by leveraging the time and space consistency of the video or volumetric sequence. The existing method relies on the training of a foreground model in a Positive-Unlabeled setup. In this frame, the generation of highly discriminative features is valuable.

Materials and Methods

This work suggests several feature extraction methods, some of which being based on Convolution Neural Networks (CNN). Particularly, we first considered the CNN-based U-Net architecture which we trained in an autoencoder (unsupervised) fashion. We then elaborated on the latter model by adding the gaze-point as an object prior.
Three baseline methods were considered: A transfer learning approach using a pre-trained VGG-16 network, a Bag of Visual Words approach (*BoVW*), and a Sparse-coded Spatial Pyramid approach (*ScSP*). The two latter methods being based on encoding SIFT descriptors.

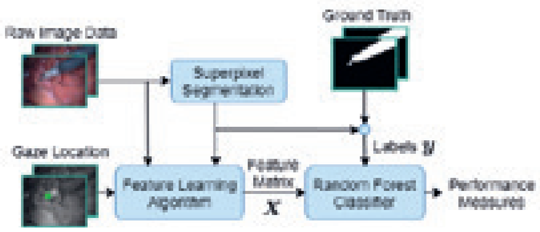

*Fig. 1: Overall framework. Feature learning algorithm construct feature matrix **X**, describing each superpixel. A Random Forest classifies foreground and background superpixels, providing a measure of feature performance.*

The performance of our models was assessed by classifying foreground and background using a Random Forest classifier. The main comparison measures were *Precision-Recall curve* and *max F1-Score*. The overall framework is shown in Fig. 1.
Our models were evaluated on four image modalities: A colonoscopy surgical video showing a tweezer, an MRI sequence of a brain showing a tumor, a CT scan of the inner ear, and slit-lamp video recording showing a retina.

Results

Let us compare our best U-Net based model (*U-Net Reconstruct*, trained in autoencoder fashion) with the best baseline, which is *ScSP*. In terms of *max F1-Score*, our best model outperforms *ScSP* by 9.24% (surgical video), 11.97% (brain MRI) and 12.9% (inner ear CT). For the slit-lamp sequences, the two methods are neck-and-neck, with a 0.08% advantage to *ScSP*.
Introducing the gaze-point as object prior does not allow a clear-cut decision on the benefit of that prior in terms of *max F1-Score*. However, it showed an improvement in reproducibility by increasing the standard deviation over 10 experiments by 10.8%.
In Fig. 2 we show a Precision-Recall curve of two U-Net based methods compared to the baselines.

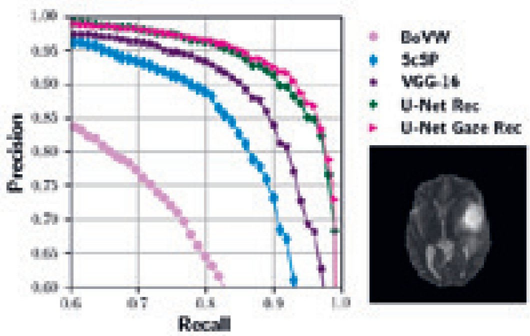

Fig. 2: Precision-Recall curve of the Random Forest classifier. It shows four different feature extracting methods applied on a brain MRI dataset, showing a tumor.

Discussion

Our experiments revealed that U-Net based models considerably outperform the baseline methods. Overall, we could show a notable improvement against the current implemented *ScSP* method.
The gaze-point object prior gave a noticeable improvement in reproducibility.

Population Based Phantom Design for Robotic Inner Ear Access

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Examiners: Dr. Wilhelm Wimmer, MSc Daniel Schneider

Introduction
Robotic cochlear implantation requires a minimally invasive opening of the scala tympani in the cochlea while maintaining sensitive anatomical structures at the target. The aim of this study was to analyze the different density profiles expected to access the inner ear and represent them in phantoms to aid in understanding of the access difficulty due to the variable anatomy.

Materials and Methods
An algorithm for density profile extraction with weighting of pixels with custom-built kernel representing surgical milling burr was implemented and validated. Bone densities along trajectories tangential to the targets at the basal turn of the cochlea were extracted for 22 data sets from Computed Tomography (CT) images, starting from the center of the round window (RW) along the cochlea.

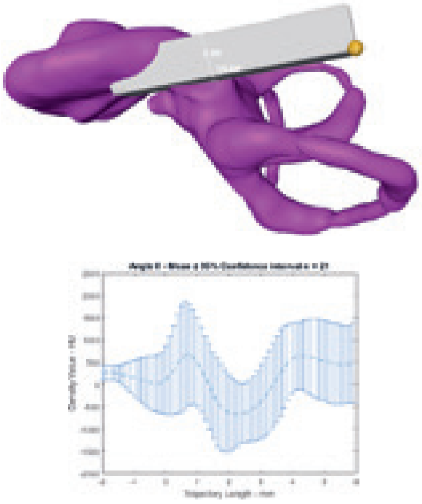

Fig. 1 The 3D surface model of the cochlea (purple) and the trajectory volume (gray) for one target are shown. The mean ± 95% confidence interval density for RW at 0º.

The obtained weighted density profiles were classified based on access types and angular positions using quantitative and qualitative assessment. Phantoms were designed and manufactured to represent majority of the anatomical variability based on statistical analysis. Breakthrough detection from the literature was validated by milling these phantoms. Linear correlation coefficients between drilling force and density for all the phantoms were computed.

Results
Our classification approach indicated that targets beyond 14º can be considered pure cochleostomy (CO) access. The majority (mean ± standard deviation) of the variability in bone width for the access types were represented in phantoms, however, the variability in intensity values could not be reciprocated. The state of the art breakthrough detection gave inconsistent results based on force data from the milled phantoms, although the force-density showed strong linear correlation.

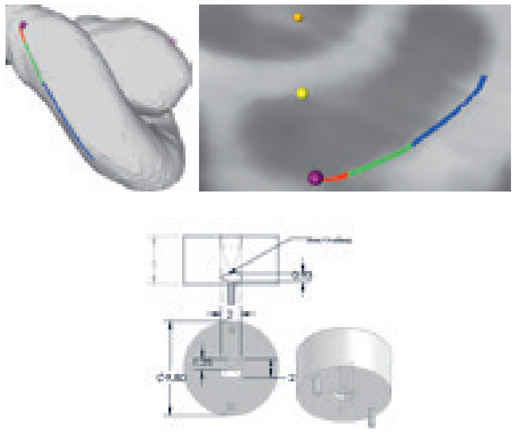

Fig. 2 Results from classification of density profile with access type. Red, green and blue curves show RW, extended RW and CO access types. Design for RW at 0º phantom for mean bone width.

Discussion
The results confirm the high variability in bone for RW niche anatomy. An image-based planning assessment can help to understand the difficulty and aid in developing robust breakthrough detection algorithm for atraumatic access.

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Leadless Cardiac Multi-Site Pacemaker System

Mirco Gysin

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Examiners: Dr. med. et phil. Andreas Häberlin, Prof. Dr. Martin Kucera

Introduction

Conventional cardiac pacemakers have leads that deliver the electrical impulses to the heart to stimulate it. These leads are prone to failure e.g. due to mechanical wear. To overcome this problem, leadless pacemakers have been introduced. However, these devices are not able to perform multi-chamber pacing. Multi-chamber pacing could be enabled by implanting several leadless pacemakers that communicate wirelessly to synchronize. The goal of this thesis was to develop prototypes of pacemaker modules that can perform cardiac pacing and bidirectional wireless communication.

Materials and Methods

As communication method, galvanic coupled intra body communication (IBC) was used. The hardware is based on a microcontroller development board (ST Microelectronics nucleo) in conjunction with the developed analog electronics. The data is pulse position modulated and directly applied to the heart tissue by needle electrodes. The software was written using Keil's Real Time Operating System CMSIS. Communication reliability between two modules was tested on porcine heart tissue.

Results

Prototype modules which allow pacing and bidirectional communication using IBC were developed (Figure 1). The data is pulse position modulated with adjustable frequency in the range between 100 kHz and 5 MHz. To allow the analog to digital converter to detect the high frequency pulses, an envelope detector was introduced in the input stage (Figure 2). The modules feature different use cases which can be accessed over a built-in user interface. Preliminary tests on cardiac tissue allowed to verify the functionality of the prototype. Two devices were able to communicate over the tissue with needle electrodes with a channel attenuation of 60 dB. Reliability tests were performed at several frequencies sending 5 Byte of data in continuous mode (4000 data packets). At a communication frequency of 200kHz, 74.3% of the sent packets could be demodulated correctly by the receiver module.

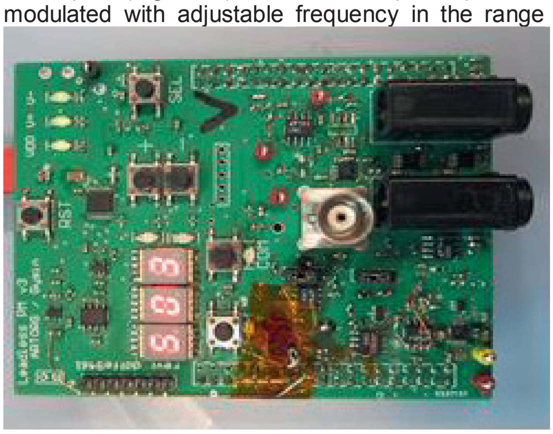

Figure 1 Developed prototype modules

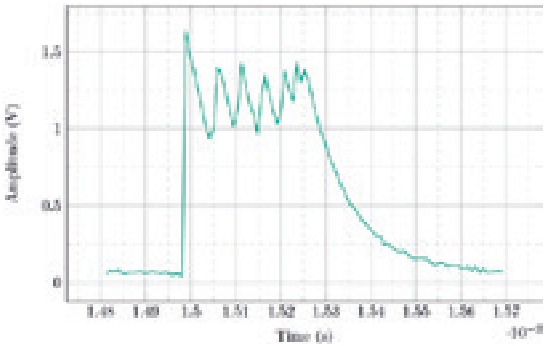

Figure 2 Received data pulses, measured at the output of the envelope detector

Discussion

Two functional leadless pacemaker modules using IBC were developed. The modules can be used for testing in-vitro and in-vivo. However, some parts of the analog hardware need to be modified to achieve a higher communication reliability.

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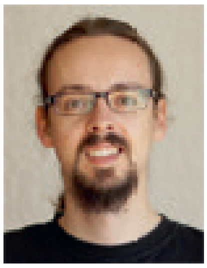
Acknowledgements

ARTORG Center for Biomedical Engineering, University of Bern, Institute for Human Centered Engineering, Bern University of Applied Science, Department of Cardiology, Bern University Hospital

Development of a Cost Optimized Optical 3D Motion Capture System

Thomas S. Heutschi



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Institutions: Physiotherapy Lab, Bern University of Applied Sciences
Examiners: Prof. Dr. Heiner Baur and Patric Eichelberger

Introduction

Optical motion capture systems are used in biomechanics, engineering, entertainment and medical fields to measure and track three dimensional motions of objects. With at least two cameras and active or passive markers on the tracking object allow to reconstruct 3D coordinates. With multiple markers even pose and orientation can be measured.
Unfortunately, this technology is mostly found at physiotherapeutic laboratories and specialized institutions only. At practices of orthopedic technicians or physiotherapists they are usually missing. Installations are prevented by high cost and system complexity.
In this thesis, a specialized motion capture system for routine assessments is developed to further spread 3D capture technology.

Materials and Methods

Two industrial cameras are used to capture passive retro-reflective markers which are illuminated with 850 nm infrared light emitting diodes mounted on top of each camera. The cameras are calibrated with thin prism model.
Based on epipolar geometry, which is established through the 8-point algorithm, pairs of 2D marker coordinates are searched and matched in both views and reconstructed by optimal triangulation.
Temporal correspondence and labeling is performed through linear extrapolation of the current velocity between the last two frames and brute force matching by smallest L^2 norm.

Fig. 1 Camera with quad IR LED array on heatsink mounted on tripod.

Performance measures include static precision and accuracy at multiple locations and orientations and dynamic displacements along a strait pole for a marker pair.

Results

Frames are captured at 30 Hz and synchronized by software trigger. Achieved static accuracy is (1.487±1.103) mm with (0.0235±.0131) mm precision in a 600 mm x 1000 mm x 600 mm volume. Dynamic accuracy for inter marker tracking is 0.41 mm with precision of 0.34 mm.

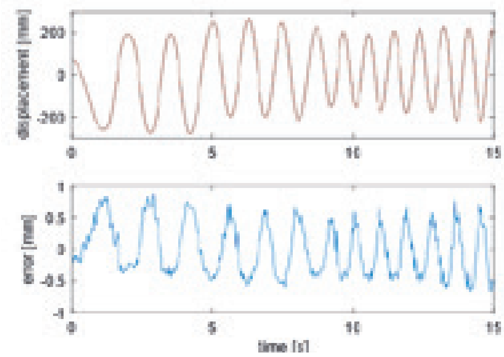

Fig. 2 Marker path in upper plot and measured error in lower plot for a marker pair moved along a single direction.

Discussion

Static measurements show a location dependent accuracy. Precision is high and comparable to commercial motion capture systems.
The dynamic test did not reveal significant problems with camera synchronization even with software based triggering. But both tests show marker tracking is suffering from partial occlusion. With these results, it can be stated that a competitive low cost motion capture system is possible with industrial cameras of the shelf on any recent workstation.

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Acknowledgements

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Visualization of Trabecular Bone Damage using MicroCT

Michael Indermaur

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Examiners: Prof. Dr. Philippe K. Zysset and Benjamin Voumard

Introduction

Trabecular bone plays an important role in osteoporosis-related fractures and its stiffness as well as yield strength can be estimated by non-linear micro-finite element analysis (µFEA) where the tissue material properties are assumed to be homogeneous [1]. Bone yields by accumulation of micro-damage but micro-cracks are also produced in fatigue *in vivo* and their density increases exponentially with age. However, their influence on bone strength remains unclear. Beyond fluorescent markers and time-consuming serial milling, visualization of micro-damage seems possible using x-ray contrast agents with micro-computed tomography (µCT). The aim of this research was to validate a non-linear micro-finite element (µFE) method for identification of micro-damage location in trabecular bone.

Materials and Methods

Eight bovine trabecular bone samples in fully wet condition were compressed to ultimate load in an uniaxial test setup, in order to induce substantial micro-damage in the central region with reduced cross-sectional area (Fig. 1). Displacement and applied force were measured using an extensometer and a load cell respectively. After loading, the damaged samples were stained with barium sulphate ($BaSO_4$) [2].

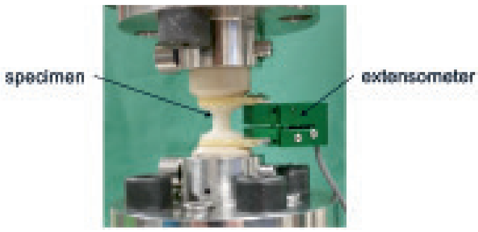

Fig. 1 Test setup for mechanical compression, containing the specimen, extensometer and the fixtures.

µCT scans of the whole samples were performed before mechanical testing and after staining. Scans realized prior to mechanical testing were used to generate a voxel mesh for non-linear µFEA. In this simulation, the measured displacement was applied as a boundary condition on the top surface of the samples. The µFEA delivered force displacement curves and the damage produced in every voxel. First, reaction forces and displacements of the µFEA were compared to the mechanical test data. Then, the damage distributions of the µFEA were visually compared to the stained µCT scan.

Results

The µFE results, stiffness and yield stress, correlated well with the mechanical tests (R^2=0.96 and R^2= 0.84 respectively). Also, damage values from the µFE analysis and the stained µCT regions showed good visual correspondence. Damage was indeed located at spots where the trabeculae were exposed to high strains. (Fig. 2)

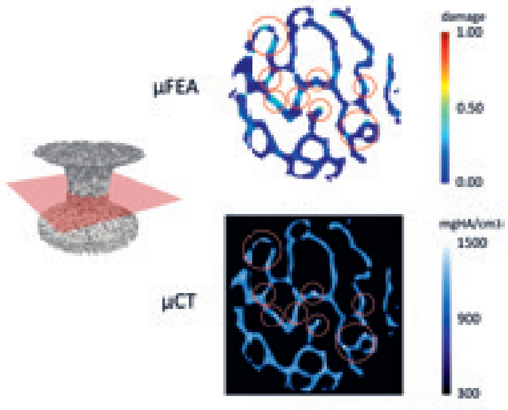

Fig. 2 Visual comparison between damage value of µFEA and stained greyscale image of sample 4. Matching damage regions are highlighted with red circles.

Discussion

The results confirm that forces, displacements and yield strength can be predicted rather precisely by µFEA [1]. Furthermore, it seems that µFEA is able to reproduce the staining patterns found experimentally. However, the study relies on visual comparison and no statistical relationship could yet be established between damage and staining intensity. In a next step, the use of alternative contrast agents will be explored to better differentiate between bone and stained areas.

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Acknowledgements

I would like to thank Benjamin Voumard, Prof. Dr. Philippe Zysset, Marc Stadelmann, Dr. Ghislain Maquer and acknowledge the great support of Urs Rohrer and his team for manufacturing the test setup.

Master's Thesis in Biomedical Engineering

Automatic Segmentation of the Lumbar Vertebra using Deep Learning

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Introduction

Back injuries caused by physical trauma or by bone diseases such as osteoporosis or tumors may permanently change the affected person's body functions. Injuries in the lumbar region can lead to a total loss of sensation in the lower body parts. Segmentations provide computer-assisted techniques with additional information. However, manual segmentation is time-consuming, not reproducible and extremely expensive. The difficulty in segmenting the spine into distinguishable vertebrae lies in the curvature and the different poses of the spine, in the similar shape and size of neighbouring vertebrae and in the requirement of segmenting deformed or fractured vertebrae. Fast accurate automatic segmentation of the individual vertebrae assists early diagnosis, surgical planning as well as detection and localization of pathologies, such as degenerative disorders, deformations, trauma, tumors and fractures.

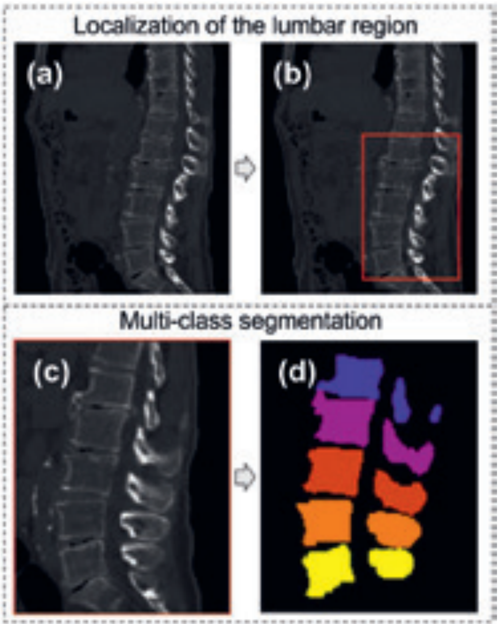

Fig. 1 A schematic illustration of the proposed two-stage approach. The first stage is the localization of the lumbar region and the second stage is the multi-class segmentation of the lumbar spine. (a) The CT input volume. (b) Detected boundary box around the lumbar region. (c) Sub-volume of the localized lumbar region. (d) Multi-class segmentation of the lumbar spine.

Materials and Methods

Based on this motivation, a fully automatic two-stage approach for segmenting volumetric CT data of lumbar vertebrae was developed during this thesis. The first stage is the localization of the lumbar region to restrict the segmentation problem to a smaller area. The localization of the lumbar region is done via boundary box detection using a convolutional neural network with regression. The final lumbar region is then obtained by kernel density estimation of the regressed results. The second stage is the multi-class segmentation of the individual vertebra by another convolutional neural network, based on a 3D U-net like architecture. The fully convolutional neural network performs a pixel-wise multi-class segmentation and allocates all five lumbar vertebrae to a corresponding class. To increase the number of training images, data augmentation was applied on-the-fly during training. A 5-fold cross validation was performed on two publicly available datasets with manual ground truth segmentation labels containing healthy, fractured and scoliotic spines.

Results

The proposed method achieves an average Dice coefficient and average symmetric surface distance of 95.77 ± 0.81 % and 0.37 ± 0.06 mm, respectively when evaluated on the 15 training images of the dataset of the MICCAI 2016 xVertSeg segmentation challenge and 94.47 ± 5.58 % and 0.55 ± 0.85 mm respectively on the mixed protocol when the evaluation is conducted using the xVertSeg dataset together with the additional images of the 2014 MICCAI Computational Spine Imaging (CSI) Workshop.

Discussion and Conclusion

During this thesis, a deep-learning based two-stage approach for fully automatically segmenting lumber vertebrae was developed. Evaluated on two public datasets, i.e., the dataset from the MICCAI 2016 xVertSeg segmentation challenge and the dataset from the MICCAI 2014 CSI Workshop, our method achieved a performance that is equivalent to or better than the state-of-the-art methods.

In conclusion, despite the fact that the training set consists of a limited number of CT images, it was possible to create a fully automatic multi-class segmentation approach that yields a reasonably good performance and segments both healthy and diseased vertebrae.

A Novel Leadless Cardiac Dual-Chamber Pacemaker

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Cardiovascular Engineering Group, University of Bern
Examiners: Dr. med. et phil. Andreas Häberlin, Prof. Dr. Dominik Obrist

Introduction

Conventional pacemakers (PM) usually consist of two parts. A pulse generator, containing electronics and a battery, and one or several transvenous leads, leading into the cavities of the heart. Those leads are prone to conductor fracture, dislocation, and isolation defects. Recently introduced intracardiac leadless PM overcome this drawback, but the functionality is reduced due to single-site pacing. To enable more physiological leadless multisite (e.g. dual-chamber) pacing, a wireless data communication between two leadless devices is necessary. As the power dissipation of common radio frequency technologies is too high and would deplete a PM battery within few days, we propose to make use of the electrical conductivity of tissue and use the myocardium as the communication channel.

Materials and Methods

A wireless communication between the atrium and the ventricle is proposed. An end to end simulation, allowing performance estimation and tuning of the

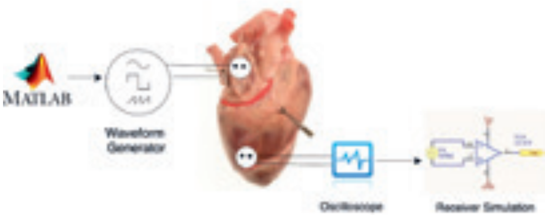

Fig 2 Simulation toolchain for protocol performance estimation

proposed wireless communication is implemented (Fig 2). To validate the simulation, a first electronic prototype is produced. A wideband, monophasic, pulse position modulated signal is generated by a microcontroller, galvanically coupled to the myocardium, using two stainless steel electrodes, and transmitted baseband at 1 MHz. At this frequency, the lowest signal attenuation of -18.4 ±4.4 dB is achieved. The 100 μA transmitting signal, which is well below the pacing threshold of myocardial tissue, induces a voltage of more than 10 mV at the receiver (Fig 1). The measured signal in the ventricle can be processed further. After initial amplification and filtering, the obtained analog signal gets digitalized, sampled by the microcontroller, and data gets reconstructed. By this means, small packages of data can be transmitted and allow the synchronization of the two devices. Two generations of communication module prototypes are produced (Fig 3) and validated in vitro, including a Langendorff setup.

Results

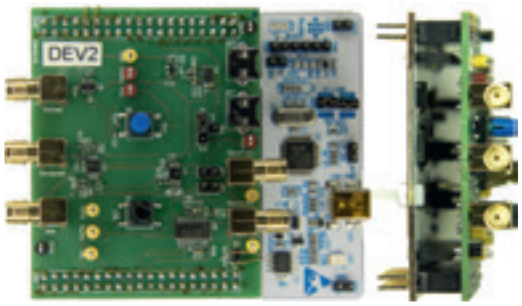

Fig 3 Communication module prototype hooked onto a nucleo 64 microcontroller board.

With the proposed wireless communication, the power dissipated to the tissue is calculated to be 0.44 nW for the synchronization between the atrium

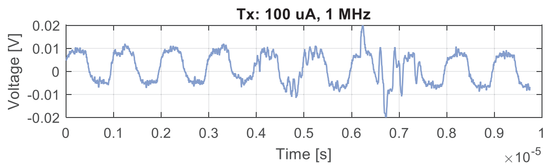

Fig 1 Signal measured at the ventricular electrodes, after transmitting a 100µA, current controlled signal from the atrium through the myocardium. The measurement is performed on a perfused porcine heart.

and the ventricle, at 60 bpm. Despite aiming for low power electronics, the signal generation and the reconstruction of the data require additional power in the mW-range.

Discussion

The promising results suggest, that a very low power multi-site pacing system is possible. A higher degree of electronics integration would reduce the power consumption drastically. The charge imbalance, evoked by the monophasic transmission signal, may damage the electrodes or harm the tissue, and should be avoided.

References

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Evaluation of Novel Fixable Cell Viability Methods for Tissue Engineering in Anterior Cruciate Ligament and Intervertebral Disc Tissues

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Introduction

Anterior cruciate ligament ruptures are one of the most common knee injuries, and intervertebral disc degeneration is one of the most important problems in industrialized societies. Both issues require the need of research for more effective treatment options, which has to go through the use of organ culture coupled with cell viability (CV) monitoring.

The assessment of cell viability is of particular importance in the field of tissue engineering. It is a key point to study tissue development, to calculate the long-term survival of cells. A wide variety of CV assays is commercially available and each has its own specificity and limitations influencing the interpretation of experimental results.

Fixable dead cell stains referring to amine-reactive dyes (ARDs) are a new class of viability dye using the principle of dead cell exclusion. It is currently unknown whether the ARD is able to evaluate CV as accurately as other live and dead staining methods. Thus, the aim is to compare ARD against well-established CV assays on cell suspensions and tissue samples.

Materials and Methods

Primary human anterior cruciate ligament cells were obtained from patients undergoing total knee replacement. Cells were cultured in monolayer and then various CV mixtures (0, 25, 50, 75, and 100%) were prepared by obtaining non-viable cells by HCl treatment. The CV was then assessed by three different methods: i) trypan blue (TB) assay and hand counting method of the ARD ii) flow cytometry and iii) confocal laser scanning microscopy imaging. Furthermore, the fixable dead cell dye was tested on fresh bovine nucleus pulposus (NP) pieces and the method was compared to the standard Calcein-AM/Ethidium homodimer-1 (CaAM/EthH-1) live and dead staining.

Results

In the cases of cell suspension with fixable dead cell staining, hand counting method after ARD staining and FACS had less than 1% error compared to TB in the estimation of CV. For all methods, the 100% CV mix was underestimated. Confocal image analysis of cells embedded into agarose carriers underestimated live/dead ratio.

Tissue staining with ARD did not allow the evaluation of CV whereas CaAM/EthH-1 was successful. The fixation of the CaAM/EthH-1 staining did not alter the fluorescence emission of the dyes after 7 days.

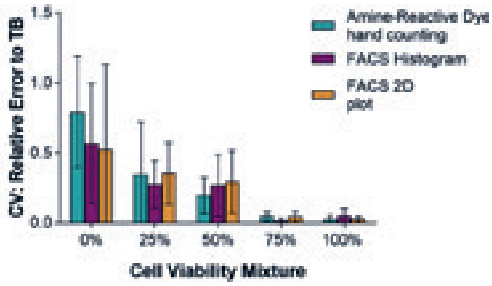
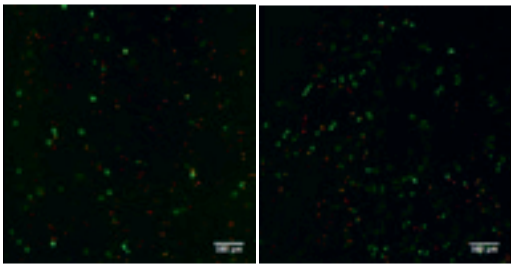


Fig.1: Relative error to TB assay for CV determined by hand counting, FACS histogram and 2D plot.



Day 1 Day 7

Fig.2: bNP tissue samples stained with CaAM/EthH-1 followed by fixation and imaged at day 1 and day 7.

Discussion

The tested fixable ARD provides a good CV estimation, but only while using cells in suspension. Its application for tissue engineering remains rather limited with only 3D scaffolds knowing that the image analysis has to be improved to obtain proper results. The CaAM/EthH-1 staining remains the method of choice to investigate the CV of tissue samples. As the fixation of the staining do not alter the expression of the dyes, it allows more flexibility in the handling of the staining.

To conclude, this new ARD dye might be more suitable for toxicology screening than application for tissue engineering with mostly 3D scaffolds.

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Indentation Properties of Metastatic Vertebral Bone

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Examiners: Prof. Dr. Philippe Zysset, MSc Benjamin Voumard

Introduction

Metastatic bone disease can change the structural properties of trabecular bone. So-called osteolytic lesions can form, which lead to resorption of bone. Osteoblastic regions, on the other hand, lead to increased bone formation and thickening of the trabecular structure. A mix of both effects is also common. Vertebral bodies affected by metastases can be weakened and in certain cases fracture [1]. Little is known about the mechanical properties of the bone affected by metastatic cancer compared to normal bone. The objective of this project is to investigate the differences in mechanical properties of bone affected by metastatic cancer. This information can be implemented in Finite Element Analysis (FEA) to predict vertebral body fractures.

Materials and Methods

Fourteen human vertebral bodies with metastases were examined. Parallel sections of 3 mm thickness were prepared and infiltrated with PMMA. Regions in the trabecular structure were classified by two experienced medical readers as normal, osteoblastic or osteolytic.

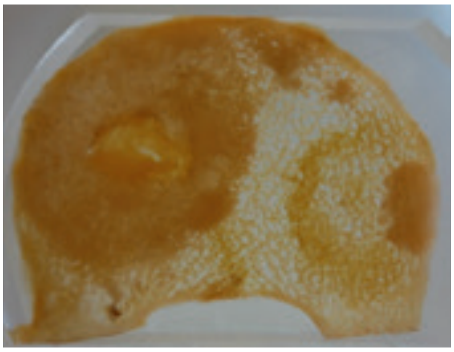

Fig. 1 Prepared sample of a vertebral body section with metastatic bone disease.

Thirty-two indentations in each of these regions were performed using a Berkovich indenter tip and an indentation depth of 1 µm. A 30 sec hold time was introduced at the maximal displacement to minimize the effect of creep. From the resulting force-displacement curve, indentation modulus, indentation hardness, plastic and elastic deformation energies were calculated. The measured properties were then statistically analyzed with a linear mixed effect model including a patient-specific random-effect.

Results

The osteoblastic regions show significantly lower indentation moduli (5.08%, $p<0.001$) and significantly higher elastic deformation energy (15.43%, $p<0.001$) compared to normal trabecular structures. No significant differences in hardness and plastic deformation energy could be shown between normal and osteoblastic trabecular structures. No significant differences in any material properties between normal and osteolytic regions were found. The type of primary cancer doesn't appear to have any significant effect on the material properties. Further analysis of normal regions also shows that trabeculae show a higher indentation modulus in axial compared to transverse orientation and that the indentations in the center of a trabecula show a higher indentation modulus than at the periphery.

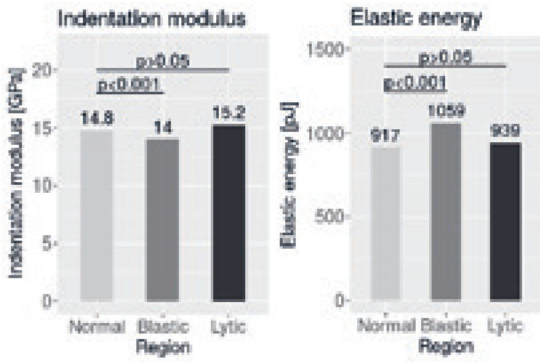

Fig. 2 Comparison of indentation modulus and elastic energy between the different regions

Discussion

The results reveal a significant reduction in mechanical properties of osteoblastic bone metastases, thus supporting the hypothesis that the osteoblastic regions have an unorganized structure, with no clear directionality of the collagen fibers. Whether this information about osteoblastic structures can improve FEA of vertebral bodies with osteoblastic metastases needs further investigation. The lack of difference between normal and osteolytic regions suggests that the same material properties for both regions can be used in FEA.

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Low-Power AC/DC Conversion and Energy Management for a Novel Lead and Batteryless Cardiac Pacemaker

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Introduction
Pacemakers are one of the most important medical implants today. They help prolong the life of a patient by providing antibradycardia pacing. Even though the current pacemakers are small enough to be implanted in the heart, they have one major drawback; their battery life. Since these pacemakers can only last 10 years [1], a patient may need to go to surgery to implant another pacemaker. Therefore, there is a need to overcome this drawback. This can be done using energy harvesters that harvest energy from blood flow or movement of the heart itself. This thesis aims to design an energy harvesting system that can convert the AC signal produced by certain harvesters and use that power to pace the heart.

Materials and Methods
Certain criteria were defined to help with designing the energy management system. These criteria were defined using one of the energy harvesters that was designed in an earlier thesis. These criteria were power, voltage and size. Low power consumption, the range below 10µW was desired. A minimum start up voltage of 100mV (200mV peak-peak) was deemed appropriate. The size needed to be as small as possible, but the above two criteria were given more importance. To achieve this goal, the design needed four stages. The first stage converts the AC signal produced from the harvester into a DC signal. The second stage steps up this DC voltage into a higher DC voltage. This DC voltage is then temporarily stored in a storage element before it is supplied to a pacing circuit that stimulates the heart.

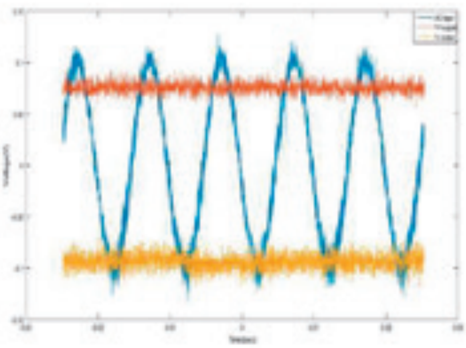

Figure 1: The output of the AC-DC rectification stage at an input voltage of 100mV (200mV peak-peak)

Results
After simulations were done, a PCB with the AC-DC rectification stage and the DC-DC step up stage was built. This prototype was able to produce an output of 4.2V, with a housekeeping power lower than 10µW, and the minimum AC voltage needed for pacing is 200mV (400mV peak-peak). At a pulse rate of 120bpm and a pulse width of 488µs, the total power consumption lies around 17µW (Figure 1).

Figure 2: The prototype that was built which consist of the AC-DC rectification stage and the DC-DC step up stage

Discussion
The prototype (Figure 2) that was built was able to produce enough voltage to pace the heart, but it could not achieve this within the criteria that was defined. The design needs to be tested with the harvester to get more accurate efficiency readings. Using more efficient components or integrating the design in a chip in the future can make the design more efficient and smaller.

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Acknowledgements
I would like to thank the ARTORG Cardiovascular group, the BFH Biel microLab and the Department of Cadiology, Bern University for giving me the opportunity to work in this project.

Towards Monitoring Tissue Stiffness in-Vitro

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Examiners: Prof. Dr. Olivier Guenat, Dr. Janick Stucki

Introduction

Fibrosis is an excessive accumulation of extracellular matrix (ECM). It is caused by repeated tissue injury or dysregulated wound healing process. Myofibroblast is the main cell type involved in fibrosis. It produces ECM when activated by proinflammatory factors. The excessive ECM results in tissue hardening which further promotes myoflbroblast activation. As fibrosis becomes progressive, it can lead to organ dysfunction and even death. As the stiffness plays an important role in fibrotic disease, the aim of this study is to implement a stiffness measurement setup to experimentally measure stiffness of the cells cultured on chip and to develop a finite element (FE) simulation to give insight for future design improvement of the chip.

Materials and Methods

This project contains an experimental part for the deflection measurement of the setup and a FE simulation part to give insight for future design modification of the chip. Chips that were modified from lung–on-chip platform was used. The stiffness can be measured by the deflection of the membrane using a microscope with reflected light.

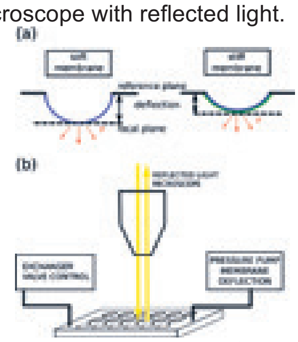

Fig. 1 Schematic representation of the measurement setup.

Measurement technique was applied on three different models. We started with inorganic model, pure PDMS membrane integrated in the chip, to characterize the measurement setup. Followed with collagen on chip model which is easier to handle and has a higher relevance. Finally, the hepatic stellate cells (HSC) were cultured on chip and the deflection measured. On the simulation part, a single membrane model and a simplified two membranes model was implemented. The simulation was done with different dimensions and membrane thicknesses to an idea for future optimization of the chip.

Results

The deflection of naked PDMS membrane was measured to calculate the Young's modulus. By fitting with an analytical Neo-Hookean hyperelastic model, the resulted E_{pdms} is 4.01MPa. The stiffness of 1mg/ml and 2mg/ml collagen concentration gel was characterized, it increased the stiffness of the chip membrane to 233% and 249%, respectively. The HSC cultured on chip had increase of collagen deposition when treated with AA2P inducer. Unfortunately, the stiffness of HSC could not be assed due to cell culture issues. The FE simulation results suggest that a reduction of membrane thickness only little improves the sensitivity, but an increase in membrane radius would significantly improve the sensitivity.

Discussion

The measurement setup was successfully applied to characterize the Young's modulus of PDMS and collagen gel on chip. HSC cell s were successfully cultured on chip and collagen deposition was quantified. Unfortunately, the cell layer was detached after the membrane deflection. Thus, the tissue stiffness could not be measured. The correlation between collagen deposition and stiffness could therefore not be acquired.
Suggested by the FE simulation results, the stiffness change of thin biological tissue with E~10KPa level is too small to be measured with the current chip design. Further modifications of the chip are needed to reduce the stiffness of the base membrane and increase the sensitivity of the system. Although the stiffness change of the cell layer and the collagen deposition could not be measured with the current setup, we made important progress towards a liver-fibrosis-on-chip model and give future perspectives for important design changes.

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Acknowledgements

We thank the Visceral and Transplantation Surgery group of Department of Biomedical research, University of Bern for providing the cells and cell culture protocol.

Eye Movement Tracking with OCT Imaging

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Examiners: Prof. Dr. Raphael Sznitman, PD Dr. Stavroula Mougiakakou

Introduction

Optical Coherence Tomography (OCT) is a widely used non-invasive medical imaging modality, to acquire high-resolution volumetric data from the retina. Recently, its use has rapidly increased in the field of ophthalmic applications. By using the principle of optical interferometry, it provides cross-sectional data for the analysis of retinal pathologies and treatment planning of ocular disorders. The quality of volumetric OCT data is correlated to the scanning speed of the instrument (A-scans) and the processed B- and C-scans. Considerable motion occurs during OCT data acquisition through involuntary eye movements, respiratory movements, heartbeat or head posture changes during the procedure. Therefore, we propose methods to track eye movement and to co-align the fundus images after image acquisition.

Today, two broad categories of motion artifact correction are known: hardware-based solutions and software-based solutions. Deep Learning methods based on Convolutional Neural Networks (CNN) are well known for their success in image segmentation, and matching tasks.

Due to their flexibility in handling legacy data and their adaptability to system requirements we proposed two software-based methods (with CNN approach). We explored suitable CNN architectures to correct motion artifacts by co-aligning images and evaluate their reconstruction performance on non-synthetical medical imaging data.

Materials and Methods

The first software-based method is estimating the overlapping area between image pairs. It is trained on learning feature representations and feature matching from randomly transformed natural images with synthetical created ground truth labels. We tested and verified a fully supervised CNN architecture (U-Net) on image tracking of synthetical imaging data. The second software-based method is estimating the pixelwise motion (optical flow) between image pairs. The optical flow information is used to reconstruct the misaligned image pairs by creating image mosaics. There we used a supervised CNN architecture, called FlowNet as a baseline and fine-tuned the architecture to estimate motion fields with various sizes. The generalization on unseen data was established by strong data augmentation. For this method, we used synthetical and non-synthetical data sets, namely: Pascal VOC2012 natural images, Retinal OCT Fluid B-scans, Kaggle Retinopathy fundus images and FIRE fundus images.

Results

134 Fundus image pairs from the FIRE data set, categorized in three groups (A, P, S), were evaluated. For each category, the mean endpoint error (EPE) was measured and analyzed. For category A, we obtained an average EPE of 5.08, for category P 24.01 and for category S 4.11.

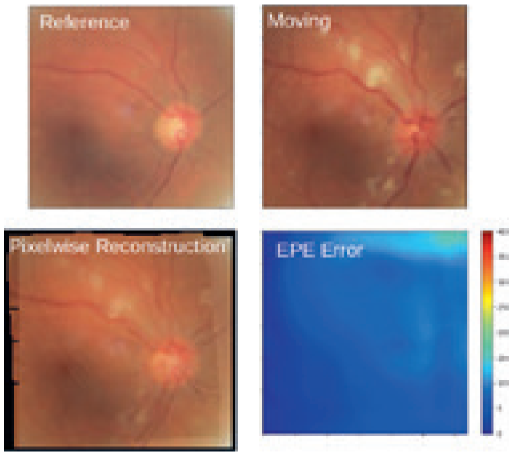

Fig. 1 Automated pixelwise reconstruction of two FIRE fundus images and the corresponding EPE map.

Discussion

The results showed promising performance on image reconstruction of medical data based on CNN architectures.

This thesis provides further important research results for the deep learning methods and also the pixelwise reconstruction. We developed a weighted custom loss function, which helped the network to learn small and large motions simultaneously.

Additionally, the results showed, that traditional matching methods based on hand-crafted feature descriptors can be more and more replaced by deep learning encoder-decoder methods.

Acknowledgements

I would like to thank all members from the OTL group for their valuable support, especially to my supervisor Prof. Dr. Raphael Sznitman.

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Bacterial Cellulose-Based Patches for Heart Surgery - Investigation of Culturing Conditions and Material Characterization

Andrea Nienhaus

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Examiners: Prof. Dr. Dominik Obrist and Dr. med. Paul Philipp Heinisch

Introduction

Atrial (ASD) and ventricular septal defects (VSD) are the most common congenital heart defects, which might need surgical treatment. A bovine pericardium patch is used to surgically restore physiological flow, and anatomical continuity. The main problem with pericardium patches is the tendency to calcify over time, which can lead to re-operation. The aim of this master thesis, was to investigate whether bacterial cellulose (BC) might be an alternative biomaterial for application in heart surgery, to treat e.g. ASD and VSD. To the best knowledge of the author, till date there are no publications available with this topic.

Materials and Methods

The BC producing bacteria Acetobacter Xylinum (AX) were cultured in two different environments (in ambient conditions and in a bioreactor), to investigate the optimal culturing conditions. The bioreactor ensured a constant temperature, oxygen and nutrients supply, and the waste gas removal, whereas in ambient conditions none of these parameters were controlled. Additionally, the influence of the culturing medium exchange upon the produced BC patches (Fig. 1a), was investigated. For the mechanical characterization, the method of inflation for bi-axial testing was used. Therefore, an inflation testing setup (Fig. 1b), similar to the one presented by W. Buerzle et al. in 2012 [1], was developed. A static pressure was applied until the BC patch ruptured. The applied pressure, deflection height, and the thickness of each BC patch were measured. Furthermore, a displacement and strain distribution analysis was performed for four representative BC patches, as well as for a bovine pericardium patch.

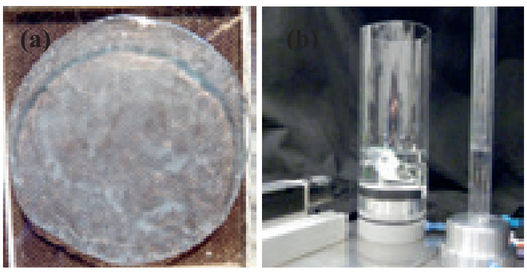

Fig. 1 (a) shows a BC patch after 12 days of incubation and sterilization. (b) Shows the mechanical testing set up with the high speed camera, water column and the cylinder with the fixed BC patch sample.

Results

The resulting BC patches were homogenous and stable, when culturing AX at 29°C, 60% O_2, and a culturing medium exchange every third day for a total incubation time of 12 days. BC can be characterized as a durable and flexible material, with observed strains ranging from 0.6% to 4% for an applied pressure of 80 mmHg (Fig. 2). All three parameters, pressure resistance, maximal deflection height, and thickness, showed large variations up to 66%, 86%, and 43%, respectively.

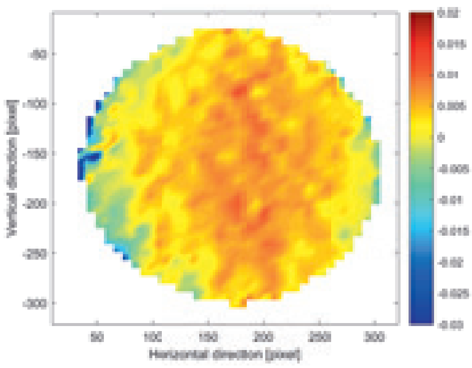

Fig. 2 shows a typical strain distribution map of one of the representative BC patch samples.

Discussion and Conclusion

This feasibility study showed that BC is a promising biomaterial for the application as surgical patch in heart surgery. However, the culturing conditions of AX have to be further optimized, to improve reproducibility of the BC patch quality. The developed mechanical testing setup was suitable for our application, and the handling in general was feasible.

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Acknowledgements

I thank the CVE group, especially Prof. Dr. Dominik Obrist and Silje Jahren as well as Dr. med. Paul Philipp Heinisch and Dr. med. Amiq Gazdhar for all the support.

Prediction of Micro-Damage Localization in Bovine Trabecular Bone Using Non-Linear Micro-FEA

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Introduction

Since trabecular bone plays a crucial role in osteoporotic fractures, a better understanding of the micromechanical yield/damage properties is needed. Even though non-linear µFEA estimates properly stiffness and yield properties of trabecular bone samples, not much is known about the degree of realism of the simulated damage distribution. In previous work [1], µFEA damage localization was related qualitatively to experimental cracks stained with barium-sulfate. Yet, a quantitative relationship could not be established. Accordingly, the objective of this master thesis was the quantitative validation of damage localization computed by µFEA.

Materials and Methods

Ten waisted bovine trabecular bone samples were compressed to ultimate load in fully wet conditions. Displacement was measured with an optical extensometer and reaction force by a load cell. After testing, the samples were stained for 48h with barium-sulfate under cyclic compression at 0.014 Hz. The stained samples were then scanned by µCT. The resulting reconstructions were converted into µFE models with homogenous, non-linear but isotropic tissue properties and subjected to the experimental boundary conditions. Overall displacement, reaction force and damage for every element were recorded.

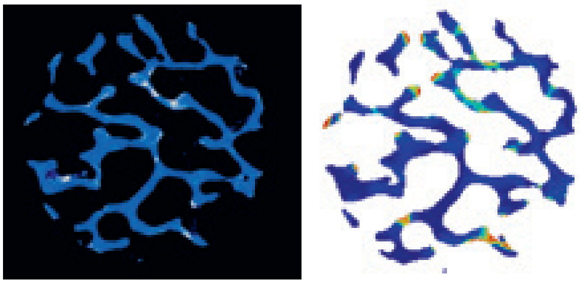

Fig. 1: Cross-section of a stained sample (left) and the corresponding µFEA damage occurrence (right).

The quantitative agreement between simulated (D_{FE}) and experimental (D_{exp}) damage localizations was evaluated by three distinct methods: (i) Linear Dipole Algorithm [2] D_{FE} and D_{exp} damage sites are superimposed. D_{FE} within a sphere (r=45µm) among 1.000 random D_{exp} locations are collected. Their mean volume is divided by the mean volume of D_{FE} within a sphere positioned at 1.000 arbitrary regions to obtain a probability of coincidence (ii) histogram-based element-to-voxel comparison; (iii) confusion matrix - D_{FE} and D_{exp} are binarized. Specificity, sensitivity, and accuracy are calculated.

Results

Although BV/TV was slightly higher (6.77% ± 3.6%) for the µFEA compared to the experiment due to the coarsening of the µCT measurement, the simulated stiffness correlated very well with experimental values (R^2=0.98; RSME=3000N/mm). The probability of damage coincidence to predict damage location lead to results up to 1.3. The highest sensitivity of the experiment was estimated to 0.93 leading to an accuracy of 0.70 for the location prediction of damaged and not damaged voxels in the specific sample. Voxel-to-element comparison (Fig. 2) of the same sample shows high accordance of D_{FE} to D_{exp}. In general, the higher the damage in the experiment, the higher the probability of coincidence.

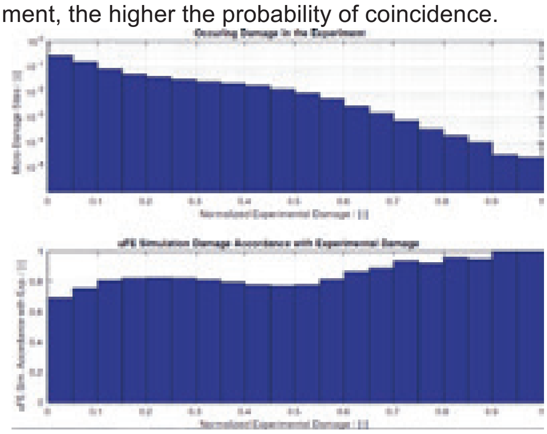

Fig. 2: Voxel-to-element analysis: The upper histogram shows the absolute amount of D_{exp} according their level of the normalized damage. The second histogram below presents the accordance of binarized D_{FE} proportion of the µFEA to the voxels collected in the upper histogram.

Discussion

The results from all 3 quantitative comparisons support that some relation exists between experimental and µFEA damage sites. The compression of heterogeneous samples may produce spurious moments and/or lateral forces that are not accounted in the µFEA. On the other hand, experimental characterization of damage may be improved by the use of higher X-ray energy for the µCT scan (higher contrast) or an alternative contrast agent such as gold nano-particles.

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Acknowledgements

I would like to thank Philippe Zysset, Benjamin Voumard, and Michael Indermaur for their support.

Intraoperative Ablation Validation using Compound 3D Ultrasound

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Introduction

Local thermal ablation is a treatment method for liver tumors which is preferred in cases where surgical resection is not feasible. Tumor cells are locally destroyed by heat induced necrosis, which is applied by microwaves or radiofrequencies. The volume in which the cells will be destroyed depends on the ablation device and its settings and is located around a fixed point on the ablation probe. Therefore, it is crucial to place the probe precisely and with respect to a tumor target and such that the ablation volume completely covers the tumor and destruction of healthy parenchyma is minimized. In current clinical practice the completeness of ablation is verified using postoperative follow-up CT scans. Incomplete ablation potentially leads to local recurrence. Ideally, inaccurate probe placement and incomplete ablations are detected already during the surgery, allowing for immediate correction.
The aim of this project was to investigate compound 3D ultrasound for intraoperative verification of probe placement and completeness of ablation.

Materials and Methods

Firstly, a 3D US compounding algorithm was developed and integrated into an existing navigation platform (Fig. 1). A method for validation of the geometric accuracy was developed and implemented. The method was used to investigate accuracy of geometric reconstruction using different US systems and tracking devices.

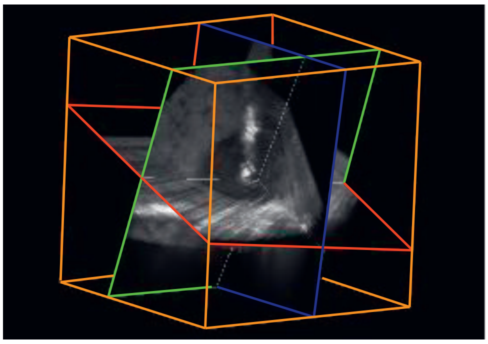

Fig. 1 A compounded 3D ultrasound image with oblique slices along and perpendicular to the probe trajectory. This allows to identify the tip precisely and measure the TPE intra-operatively.

This 3D US method was then used to evaluate the accuracy of a previously developed navigation approach and compared to the conventional LUS-guided approach in a phantom study. Additionally, technical feasibility of ablation volume validation was demonstrated in a phantom study.

Results

Validation of the geometric accuracy of the 3D US reconstruction showed a median error of 0.4 mm (IQR 0.2-0.8 mm). Target positioning errors of image- vs LUS guided approaches were median 4.2 mm ($CI_{95\%}$ 3.6-4.9 mm) and 6mm ($CI_{95\%}$ 5.3-6.9 mm) respectively (Fig. 2).

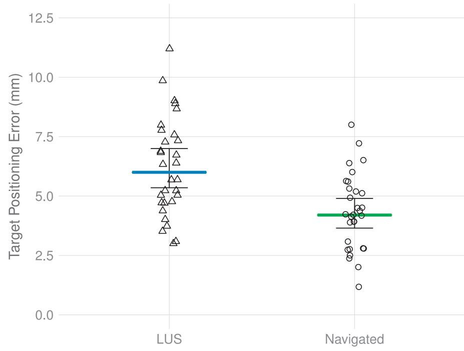

Fig. 2 Median and 95% CI of the accuracy measurements comparing navigated and conventional LUS-guided laparoscopic ablation probe placement with respect to TPE measured using intra-operative compounded 3D US.

Discussion

The developed 3D US validation method allowed the quantitative comparison of a navigation approach against the conventional approach for laparoscopic ablation probe placement and showed statistically significant better accuracy for the navigated approach ($p<0.01$). Additionally, technical feasibility of ablation volume validation using 3D contrast enhanced ultrasound could be shown. However, its clinical feasibility has to be proven in a clinical study. In upcoming clinical investigations of new navigation approaches this validation method will also be used to quantify the in-vivo accuracy and therefore provide a quantitative comparison.

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Evaluation of Deformable Registration Algorithms for Deep Brain Stimulation

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Examiners: Prof. Dr. Mauricio Reyes, Dr. Andreas Nowacki

Introduction

Deep Brain Stimulation is a neurosurgical procedure for the treatment of movement and neuropsychiatric disorders and provides therapeutic benefits for otherwise treatment resistant disorders such as Parkinson's disease. The location for electrode implantation is computed by mapping the anterior and posterior commissure lines from a ventriculographic or MRI scan obtained under stereotactic conditions to an existent 2D brain atlas.

Figure 1: Postoperative X-Ray scan of bilateral Deep Brain Stimulation electrodes and connecting wires.

To facilitate target selection and to improve the localization of the electrodes in preoperative planning a 3D brain atlas could be registered to the patients MRI scan. For this purpose, a selection of seven deformable registration algorithms (Symmetric Forces Demons, Diffeomorphic Demons, Fast Symmetric Forces Demons, Level Set Motion, Cubic B-splines Free Form Deformation, Symmetric Normalization and Landmark Pointwise Mutual Information) is evaluated in this work.

Materials and Methods

The algorithms were evaluated on a publicly available database. The Internet Brain Segmentation Repository consists of raw and skull-stripped, T1-weighted MRI scans of 18 healthy subjects, which are manually delineated by experts resulting in 31 labeled anatomical regions. Five of these deformable registration algorithms, were implemented in a processing pipeline to efficiently evaluate their registration accuracy on anatomical regions of interest for Deep Brain Stimulation. The semi-automatic Landmark Pointwise Mutual Information algorithm is evaluated using the in-house software tool Medical Viewer. Additionally, the Symmetric Normalization algorithm is evaluated as a reference method, which showed best performance in various registration algorithm evaluations, such as in [1]. The effect of linear preregistration, the use of skull-stripped images compared to raw images are evaluated using the Dice Sorensen Coefficient (DSC).

Results

The best performing algorithms on the anatomical regions of interest for Deep Brain Stimulation such as the thalamus and basal ganglia structures are the Symmetric Normalization with an averaged DSC of 0.815±0.061, the Diffeomorphic Demons (0.797±0.069) as well as the Fast Symmetric Forces Demons (0.789±0.087) algorithm. Both, the Level Set Motion and the Symmetric Forces Demons algorithm introduce artefacts during the registration process and generally show poor registration accuracy with averaged DSC of less than 0.723±0.118 and 0.722±0.144, respectively. The low dimensional parametrized Cubic B-splines Free Form Deformation algorithm achieved an averaged DSC of 0.711±0.106. The overall lowest registration accuracy is obtained by the Landmark Pointwise Mutual Information algorithm with an overall DSC of 0.699±0.065.

References

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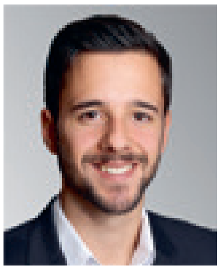
Acknowledgements

All members of the Medical Image Analysis research group from the Institute for Surgical Technologies and Biomechanics in Bern (ISTB), especially Dr. Waldo Valenzuela and Prof. Dr. Mauricio Reyes are gratefully acknowledged. Thanks also goes to Dr. Andreas Nowacki from the Department of Neurosurgery from the University Hospital (Inselspital) in Bern.

HR-pQCT and hFE Protocols for the Reproducible Assessment of Wrist Strength

Denis Elia Schenk



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Introduction

Osteoporosis is a major burden on both individuals and health care systems. Its most severe consequences are fractures, including at the radius. Bone strength, a critical factor for fractures, depends on bone density and 3D architecture. Clinicians are thus hoping to improve fracture risk estimation via high-resolution peripheral QCT (HR-pQCT: 60.7 µm), a modality able to capture both information *in vivo* and provide the basis for finite element (FE)-based prediction of bone strength. An automatic pipeline was developed to provide patient-specific 3D bone structure for FE analysis, keeping in mind that processing time and reproducibility are of essential importance for clinical application.

Materials and Methods

Previously, 24 human forearms were scanned by HR-pQCT (Scanco Medical AG) at the usual fracture site [1]. First, each radius was separated from the soft tissue and ulna. Two masks were then defined for the cortical and trabecular regions that were finally segmented based on two thresholds (450 mgHA/cm^3 and 320 mgHA/cm^3, respectively).

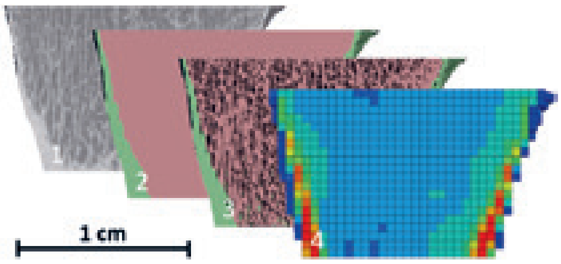

Fig 1: Overview pipeline for patient specific bone strength estimation. (1) Masked greyscale image; (2) cortical mask (green) and trabecular mask (red); (3) segmentations; (4) FE model showing BV/TV of the homogenized elements.

Based on their distinct multiscale architecture, cortical and trabecular bones have different mechanical properties. The two-phase bone segmentation enables the FE model to account for heterogeneity of bone tissue. A new material mapping was thus proposed and evaluated against the experimental data obtained from the compressive tests from Hosseini et al. [1]. The material properties were finally scaled to fit the *in vitro* stiffness (S), ultimate load (F_{ult}), and displacement at ultimate load (d_{ult}). Additionally, a phantom composed of real embedded human radii was designed to ensure multicenter cross-calibration.

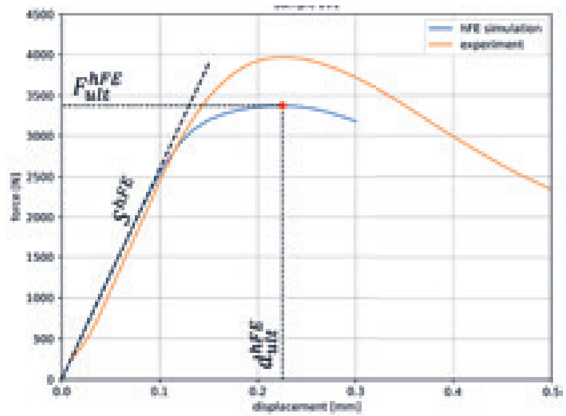

Fig. 2: Ultimate load hFE compared to experimental results.

Results

The image-processing pipeline automatically masks and segments the HR-pQCT images in around 12 min. It takes roughly 30 min for an experienced user to do the same with the semi-automatic pipeline provided by the manufacturer. The generation and analysis of the FE model needs another 12 min.
After fitting, the FE stiffness and ultimate load correlated linearly with *in vitro* values:

$$S^{FE}=0.978*S^{EXP}+4708 \qquad R^2=0.846$$
$$F_{ult}^{FE}=1.001*F_{ult}^{EXP}-451 \qquad R^2=0.975$$

d_{ult} was predicted within a root mean square error of 0.0545mm.

Discussion

The duration of the image-processing allows clinical use, but can still be decreased by up to 95% if the user manually defines a region of interest around the radius at the beginning of the pipeline.
The fitting results confirm that the proposed material mapping could improve the FE predictions. Yet, an intercept remains in the regressions and this has to be solved for the FE to provide quantitative results.
This pipeline could be used in multicenter clinical studies once the phantom is completed and calibrated.

References

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I would like to thank Prof. Dr. P. Zysset, Dr. G. Maquer and MSc M. Stadelmann and MSc Benjamin Voumard for their support.

A Novel Pacemaker System for Transcatheter Aortic Valve Implantation

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Examiners: Dr. med. et phil. Andreas Häberlin and Prof. Dr. phil. Dominik Obrist

Introduction

Aortic valve stenosis and regurgitation are two of the most frequent occurring aortic valve diseases, and often require valve replacement with a prosthetic valve. Recently, transcatheter aortic valve implantation (TAVI) has become a valuable and minimally invasive treatment option for high risk patients, avoiding open heart surgery. However, TAVI can cause electrical disturbances, and in the worst case a complete AV block, which requires a subsequent permanent pacemaker implantation (PPM). The risk of PPM after TAVI can be assessed from several indications like gender, right bundle branch block, AV block, or left anterior hemiblock before TAVI. The aim of this project was to combine the implantation of a prosthetic valve with the implantation of a permanent pacemaker, resulting in a prototype of a TAVI valve, which can perform leadless ventricular pacing in case of a complete AV block. Such a device could be used for patients with a high risk of PPM after TAVI.

Materials and Methods

In this master thesis, a prototype of a battery powered pacemaker that can be attached to an Edwards Sapien TAVI valve (TAVI-PM) was developed. The TAVI-PM was tested in a flow loop setup to determine the change in hemodynamics of the valve. The leaflet motion, valve orifice, pressure gradient and the regurgitant volume were measured for the TAVI and the TAVI-PM separately for different heart rates and mean cardiac outputs.

Fig. 1 Prototype of the pacemaker which can be attached to the Edwards Sapien TAVI valve

Results

The developed pacemaker weighs 6.6 g and has a volume of approximately 1.5 cm^3. The pacemaker is sewed on the TAVI valve with surgical suture. The TAVI-PM can be implanted in the heart using a transapical approach. It enables asynchronous pacing at the interventricular septum in the left ventricle with a pacing rate of 120 bpm, a pulse width of 1 ms, and a pacing amplitude of 2.3 V. The leaflet motion and the valve orifice were not affected by the attached pacemaker. The measured regurgitant volumes of the TAVI and the TAVI-PM would only correspond to mild valvular regurgitation according to the recommendations of the European Association of Echocardiography (<30 ml). The attached pacemaker had a significant influence on the pressure gradient, which was approximately 50% higher for the TAVI-PM compared to the TAVI valve. The increased pressure gradients of the TAVI-PM indicate a moderate aortic stenosis according to the guidelines of the European Society of Cardiology. However, the pressure gradient is only one of several indicators used for the grading of aortic stenosis.

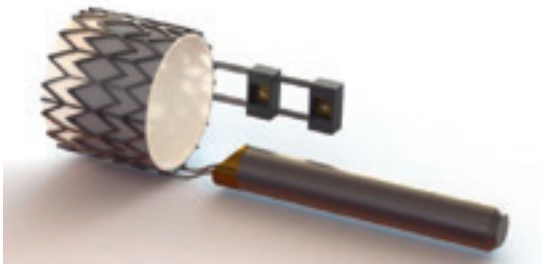

Fig. 2 CAD drawing of the assembled TAVI-PM

Discussion

This master thesis shows that from the measured parameters only the pressure gradient is significantly affected by the attached pacemaker. The design of the pacemaker has to be further optimized, to minimize the increase in pressure gradient. The subsequent implantation of a pacemaker would no longer be necessary. However, the effectiveness of a TAVI-PM has to be tested in further trials regarding the feasibility of a TAVI-PM implantation, and the reliability of the pacemaker.

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Weakly Supervised Methods for fast OCT Pathology Segmentation

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Introduction

Optical Coherence Tomography (OCT) has gained a significant importance for diagnosis and monitoring of Age-related Macular Degeneration (AMD). In developed countries, AMD is among the most common causes of blindness. To correctly identify AMD, an ophthalmologist must tediously look through 50-128 cross-sectional B-scans in one OCT volume of a patient. The same is true if an expert has to manually segment said B-scans to generate ground-truth data.
Given this, the ophthalmic medical imaging community is looking to reduce time clinicians require to properly detect and segment AMD pathologies in OCT data. One such way is to replace the strong pixel-level annotations with weak annotations, such as bounding boxes. To this end, two novel semi-supervised methods to fully automatic segment retinal cysts in OCT B-scans are proposed in this thesis.

Materials and Methods

The proposed semi-supervised methods use Convolutional Neural Networks (CNNs) which are trained with a mix of weak and strong labels. Both methods use a two-stage architecture to combine the annotations. In the first stage, regions of interest (ROIs) are extracted with a CNN that uses weak labels to train on. In the second stage, the found ROIs are then improved in a refinement CNN, which uses the B-scan with its corresponding ROI mask as inputs and trains with strong pixel-level annotations.
To improve the retinal cysts detection rate of the CNN that was used in all approaches, an initial CNN, based on the U-Net architecture, was finetuned to the given sparse and diverse dataset.
To increase the sample size of a small training dataset, we propose 6 different OCT B-scans image transformations for data augmentation, which result in biologically plausible B-scans. The data augmentation was used aggressively to increase the number of positive samples in the training set.
Baselines were generated by using the CNN architecture in a fully supervised manner and by implementing a state of the art semi-supervised method.

Results

All the implemented methods were evaluated using a test set comprised of 234 B-scans. The fully supervised CNN achieves an area under the curve (AUC) performance of 0.96 and a mean dice coefficient of 0.92. The network shows good generalization in the diverse dataset. Our semi-supervised methods segmented the test images with comparable results. Both obtained a mean dice coefficient of 0.88 and AUC score of 0.95, or 0.92 respectively. Both outperform a state of the art semi-supervised deep learning approach.

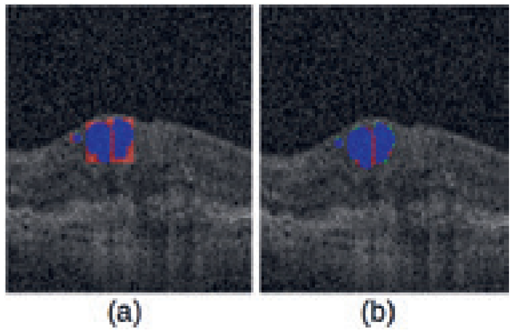

Fig. 1 Automated segmentation result of an OCT B-scan with AMD. (a) Extracted ROIs. (b) Refined segmentation of the retinal cyst. Red pixel mean false positives, green pixel are false negatives and the blue pixel are true positives.

Discussion

These results show great performance for binary retinal cysts segmentation of OCT B-scans. The results for the semi-supervised methods show state of the art performance and are a solid foundation for further research.

Acknowledgements

I would like to thank everyone from the OTL group for their support. Special thanks go to my supervisors Prof. Dr. Raphael Sznitman and Dr. Carlos Ciller.

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Investigation of Urinary Bladder and Ureter Contractions by Means of Electrophysiological Recording

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Introduction

Overactive bladder (OAB) syndrome is a common and complex dysfunction of the lower urinary tract. It is characterized by urinary urgency often combined with frequent urination and at times, incontinence. There is a hypothesis, that the disease may be caused by an abnormal electrophysiological behavior of the bladder and/or ureters. However, because of their complexity, the electrical behavior of the urinary bladder and ureters is still not well known. The aim of this project was therefore to develop a dedicated setup for electrophysiological examinations of pig urinary bladders and ureters in order to investigate electrical tissue characteristics.

Materials and Methods

First, a life sustaining environment for ex vivo measurements was developed. It consists of an organ bath filled with HEPES buffered Tyrode's solution, which is bubbled with 100% oxygen and maintained at a constant temperature of 36°C. Subsequently, conventional needle electrodes were used together with a waveform generator and a highly sensitive biosignal amplifier to investigate pacing threshold (minimum amount of energy needed to trigger depolarization), refractory time, and signal propagation of bladder and ureter. A camera with a custom made software is used to gain time synchronized tissue movement information.

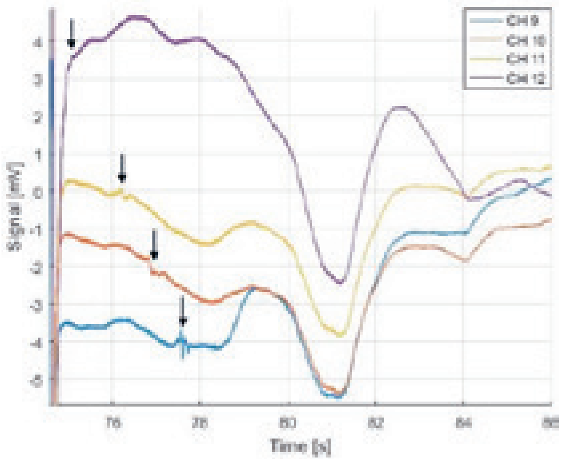

Figure 1 Electrophysiological signals of a pig ureter after induced electrical stimuli. Depolarization spikes are marked with arrows on the different needle electrode channels which are placed one centimeter apart from each other. Stimulation happens right before the first triphasic spike appears (marked with an arrow on CH 12).

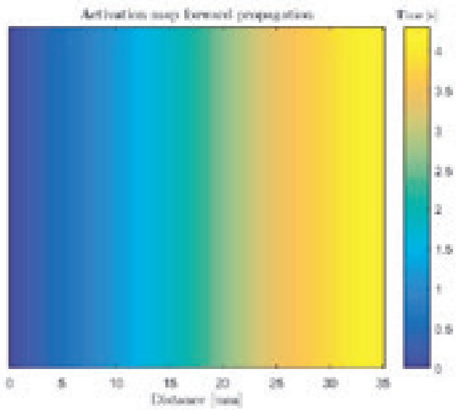

Figure 2 Activation map of detected tissue depolarization spikes shown in Figure 1. X-label is propagation distance, color bar symbolizes elapsed time until tissue depolarization signal arrives. Observed propagation velocity is not uniformly throughout the ureter sample.

Results

Refractory time and pacing threshold in the ureter have been identified. Moreover, signal propagation in the ureter was investigated. Propagation velocities between 5.2mm/s and 33.3mm/s could be observed with needle electrodes. Activation maps were drawn which show signal propagation starting from different origins. Induced electrical stimuli triggered anterograde as well as retrograde signal propagation within the ureter, with heterogeneous propagation velocities across the tissue.

Discussion

The developed setup enables investigation of bladder and ureter electrophysiology. First obtained results are well in the range of what has been reported previously and interestingly indicate non-uniform conduction throughout the ureter [1].

References

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I would like to thank the ARTORG Cardiovascular engineering group for their support.

Influence of Freezing Cycles and Enucleation on Multiaxial Intervertebral Disc Compliance

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Examiners: Prof. Dr. Philippe K. Zysset, Marc Stadelmann

Introduction

Intervertebral disc (IVD) degeneration is linked with chemical, morphological and mechanical alterations that may induce chronic back pain. In particular, drying of the nucleus pulposus affects the IVD's height and compliance. If properly validated, finite element (FE) analyses may help relating degeneration to altered mechanics [1]. Yet, for logistical reasons, experiments on the IVD involve often several freezing-thawing cycles, which may affect its mechanical properties [2]. It is unclear if freezing overshadows the impact of degeneration. Accordingly, our objectives were to investigate how repeated freezing cycles and enucleation influence IVD compliance and determine if the impact of the latter can be captured by FE models.

Materials and Methods

Six bovine and five porcine fresh IVDs were dissected. T_2-weighted MRI images were acquired before mechanical testing was conducted in flexion, extension, lateral bending, axial rotation, tension, and compression within 12h after sacrifice. Next, the IVDs were frozen (-20°C) for two weeks, thawed at room temperature for four hours, and tested again. The procedure was repeated four times with two intermediate freezing cycles without testing. The resulting load-displacement curves were compared to those from the fresh and enucleated IVDs. Extra mechanical tests were done on three human IVDs, intact and after enucleation. Data from two human specimens was used to calibrate the corresponding MRI-based FE models [1].

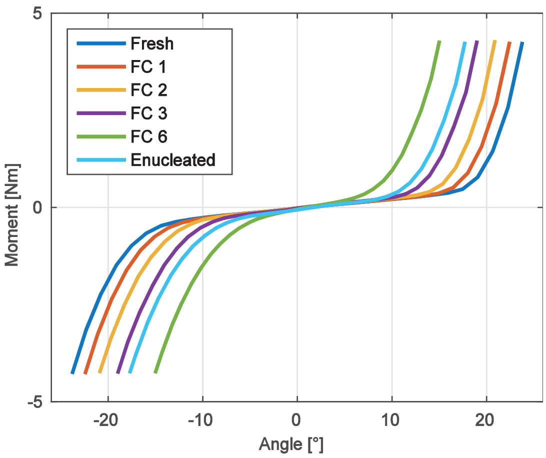

Fig. 1 Averaged moment-angle curves of a bovine specimen in flexion-extension obtained from fresh, after freezing, and after enucleation.

Results

Freezing cycles showed stiffening effects of the IVDs in all loading scenarios. The enucleation had opposite effects by inducing a more compliant behavior compared to the intact IVD. While the stiffening due to freezing was more prominent with bovine specimens, porcine IVDs showed a more pronounced rise in compliance after enucleation (Fig.1). The specimen-specific FE model could qualitatively reproduce the mechanical behavior of the intact and enucleated human discs (Fig.2).

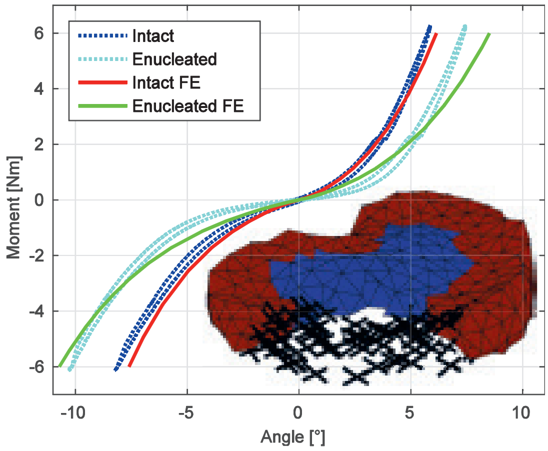

Fig. 2 Simulation of FE human disc model compared to measured load-displacement curves for flexion-extension.

Discussion

The stiffening due to the freezing cycles appeared to be species dependent. Based on this outcome, a broader study would be desirable before extrapolating our finding to human IVDs.

While the FE model could reproduce intact human IVD mechanical behavior, eneucleated disc properties were more difficult to reproduce numerically. Enriching the FE model with sectional fiber angle dependency might help to overcome this issue.

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Acknowledgement

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Master's Thesis in Biomedical Engineering

Building Online Mosaics for Low-Cost Intra-Ocular Imaging

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Examiners: Prof. Dr. Raphael Sznitman, PD Dr. Stavroula Mougiakakou

Introduction

High-definition fundus images are a decisive factor when diagnosing eye diseases like glaucoma, diabetic retinopathy or age related macular degeneration. However, devices to create these images are rarely present in third world countries, leading to high rates of blindness, due to untreated diseases. With the introduction of a smartphone based fundus imaging adapter, a solution to this problem was shown. These devices allow creating a funduscopy image, only using a regular smartphone and a small portable adapter. Despite the advantages, low-cost devices come with the main drawback of creating a small field of view.
The aim of this project is to develop a technique to produce fast mosaics that are accurate enough to provide guidelines as to what regions still need to be imaged. The mosaics created need to be shown on the screen in order to produce a real-time guide for the user during recording of the fundus.

Materials and Methods

The proposed method consists of a Convolutional Neural Network (CNN) that is used to segment the single frames, a landmark based registration, to align the images, and a blending to create the final mosaic.
The CNN was trained using labeled data that were previously recorded with a low-cost smartphone adapter and manually segmented. By using data augmentation, the dataset was further increased. The architecture used is based on a U-Net but was further adapted to be able to run on a smartphone in real-time. Also, the effect of adding dropout, batch normalization and residual connections was analyzed.
Feature based tracking was accomplished in real-time using ORB features. To increase robustness, a RANSAC algorithm was used to estimate the frame to frame transformation.

Fig. 1 The smartphone application created, consisting of a live preview (left) and the mosaic (right), which is updated in real-time.

The images are blended using an adapted feather blending algorithm, taking the segmentation mask into account, that is predicted by the CNN. This helps to compensate for differences in illumination and creates an overall smoother image.
The method proposed was implemented as an Android application, making use of a multithreading pipeline to be able to run this very calculation intense task in real-time. The user interface is composed of a live view, showing the current camera frame and the constantly updated mosaic created so far.

Results

The method proposed was tested using an eye phantom, and the mosaics created this way were compared to the synthetic fundus. All of the mosaic created include the most important structures of the retina. The application achieved an overall framerate of 20 frames per second on a recent smartphone.

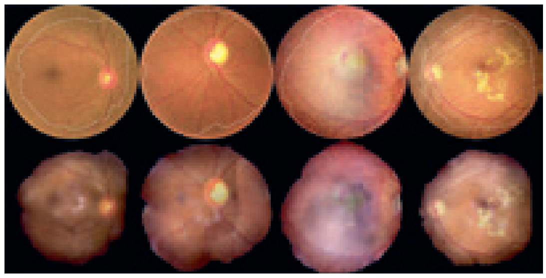

Fig. 2 The synthetic fundus (top) and created mosaics (bottom). The created mosaics have a similar size to the original fundus images as indicated by the dotted outline.

Discussion

These results show, that it is possible to create real-time fundus mosaics using a recent smartphone. However, more labeled data will be needed to train a CNN, that is applicable to a more general set of patients.

Acknowledgements

Firstly, I would like to express my sincere gratitude to my supervisors, Prof. Dr. Raphael Sznitman and Sandro De Zanet for the continuous support. Further, I would like to thank everyone from the OTL group for their help and motivation.

Fast and Accurate Brain Cortex Modeling Using Machine Learning Techniques

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Introduction

Morphometry information such as thickness and curvature provide biomarkers for neurodegenerative diseases. Well-established tools to extract morphometry data from MR images, such as FreeSurfer, are computationally expensive and therefore rarely used in the clinical practice. The goal of this thesis is to develop a fast uncertainty-aware machine learning approach based on random forest (RF) regression [1].

Materials and Methods

A pipeline for random forest regression and evaluation was implemented. About 300 MR images from healthy subjects, recorded on two different scanners with 4 different MR protocols were used for training and testing. Already available FreeSurfer outputs were used as "silver-standard" ground truth. Uncertainty-awareness is achieved on a voxel-level by approximating a normal distribution using the variance of the predictions across individual trees. The output was assessed directly on the cortex volume, the white matter surface and on the parcellations of the Desikan-Killiany atlas.

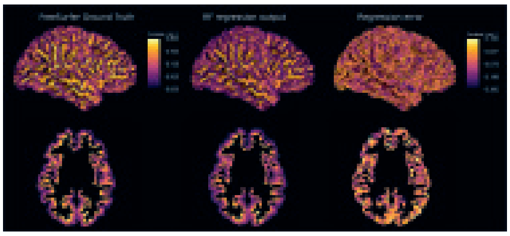

Fig. 1 Ground truth, estimation, and error for the curvature of an example subject. Bottom: Volume output of the RF model, top row: projection onto the white matter surface.

Results

Thickness and curvature estimations both suffer from a large bias. The curvature is consistently underestimated, while the sign of the thickness bias is different between parcellations.

Apart from the bias, the model succeeds in detecting inter-subject differences and correctly maps thickness and curvature values between gyri and sulci. Abrupt changes in thickness or curvature get smoothed during the estimation.

The outputs of a model learned with mean morphometry values for each parcellation are more accurate than the prediction for the voxel-based data.

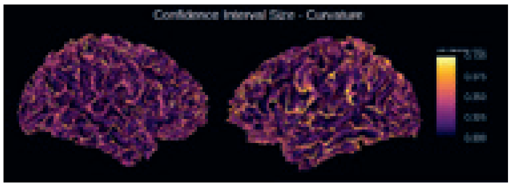

Fig. 2 Confidence interval sizes for the curvature estimation for a selected subject, projected onto the white matter surface for visualization.

Discussion

The random forest regression approach needs much improvement until it can be used in the clinical practice. Future research should go into bias reduction. Resampling of the volumetric RF output shows more promising results.

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I would like to thank my supervisors Prof. Mauricio Reyes and Dr. Christian Rummel for the great support during this project and the whole Medical Image Analysis Group for the valuable inputs.

The Importance of Plasmin in Synovial Fluid for the Healing of ACL Ruptures

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Introduction

Injury to the anterior cruciate ligament (ACL) is one of the most common injuries to the knee. The annual incidence in Switzerland is estimated between 10’000 to 12’000 [1]. As the ACL has a poor self-healing ability, the current gold standard treatment is reconstruction with a tendon graft. It has been shown that there is no fibrin clot formation after an ACL injury which bridges the ends of the ruptured tissue. Murray et al. hypothesized that the high plasmin concentration in the synovial fluid might be a key factor to delay or even prevent wound healing [2]. The aim of this project was to verify this hypothesis by analyzing scratch wound assays using human ACL (hACL) cells and state of the art live cell microscopy.

Materials and Methods

Cells from hACL were cultured in multi-well plates with low glucose-Dulbecco's Modified Eagle Medium (LG-DMEM) + 10% fetal calf serum (FCS). Once confluent, 700 – 800 µm wide scratches were induced with the IncuCyte® WoundMaker™ 96-pin tool (Figure 1). During the experiment, the serum concentration was lowered to 5% FCS to reduce wound closure due to cell proliferation. Plasmin derived from human plasma (Sigma Aldrich, USA) was added in different concentrations (0, 0.01, 0.1, 1, 10, 50 µg/ml) to the media. The wound scratch assays were analyzed with the IncuCyte® S3 Live-Cell Analysis System (Essen Bioscience, LTD., UK). The wound closing rates of the first 24h were compared with a one-way ANOVA.

Fig. 1 Left: IncuCyte® S3 Live-Cell Analysis System. Right: WoundMaker™ 96-pin tool [3].

Results

50 µg/ml plasmin delayed wound closure significantly in three out of six hACL donors. For one donor the wound closing rate increased for 50 µg/ml plasmin. Two donors did not show a significant difference between the high plasmin concentration and the no plasmin control.

However, the combined results of all six donors indicated no significant decrease in wound closing rate with increasing plasmin concentration (Figure 2).

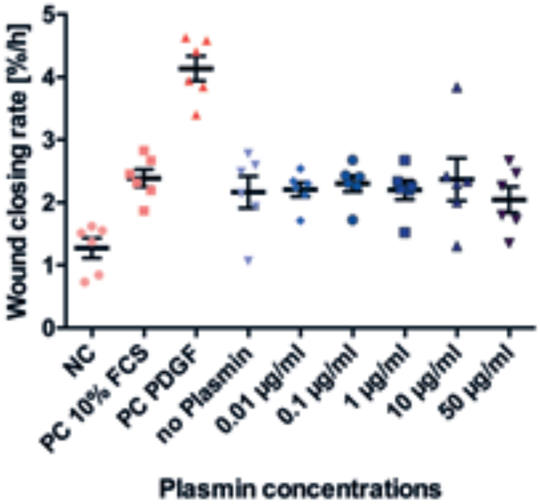

Fig. 2 Wound closing rates of six hACL donors treated with different plasmin concentrations. Values are presented as single donor outcome with ± SEM. Negative control (NC): serum free media. Positive control (PC): culture media with 10% FCS or platelet-derived growth factor (PDGF).

Discussion

The results suggest a donor dependent effect of plasmin on ACL wound closure. Additional experiments with more hACL donors are necessary to determine the influence of plasmin in the synovial fluid on ACL wound healing.

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Development of a Contact-less Physiological Monitoring Solution for Ambulatory Sleep-Wake Assessments

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Introduction

Sleep disorders are a group of syndromes characterized by disturbance in the individual's amount of sleep, quality or timing of sleep, or in behaviors or physiological conditions associated with sleep. An estimated 45 million persons in Europe are annually subjected to sleep-wake disorders. State-of-the-art polysomnography provides sophisticated insights into sleep (patho)physiology. A drawback of the method, however, is the obtrusive setting dependent on a clinical-based sleep laboratory with high operational costs. An unobtrusive and cost-effective sleep monitoring system which can objectively measure long-term sleep-wake patterns can be instrumental in the clinical decision-making process and in providing effective, patient-tailored treatment.

Materials and Methods

This thesis describes the development, testing, and validation of a contact-less prototype to monitor limb movements and vital signs during sleep. A dual channel K-Band Doppler radar transceiver captured limb movements and periodic chest wall motion due to respiration and heart activity. A wavelet transform based multi-resolution analysis (MRA) approach isolated limb movements, respiration, and heart rate from the demodulated signal.

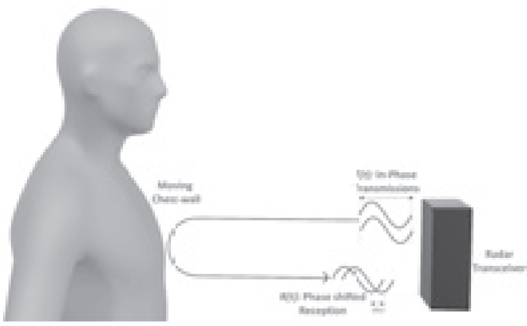

Fig. 1 Doppler radar for physiological sensing.

of the prototype was validated in overnight comparative studies, involving two healthy volunteers, with polysomnography as the reference. The prototype has successfully classified limb movements, with a sensitivity and specificity of 88.9% and 76.8% respectively, and has achieved accurate respiratory and heart rate measurement performance with overall absolute errors of 1 breath per minute for respiration and 3 beats per minute for heart rate.

Fig. 2 Test Bench setup: Exciter with the vibrating surface mounted on top (Panel A) and the Prototype positioned (Panel B).

Discussion

This thesis work shows that K-Band Doppler radar and wavelet transform MRA seem to be valid for overnight sleep marker assessment. The contact-less approach might offer a promising solution for home-based sleep monitoring and assessment.

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Tribology of the Bone Implant Interface

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Introduction

In orthopedics surgery and dental cares, primary mechanical stability of an implant is crucial to ensure bone healing, osseointegration, and thus long-term stability. In cementless implants, primary stability relies partly on the friction between bone and implant. The lack of knowledge in this field limits the prediction of the postoperative stability of new implant designs.
The aim of this master thesis is to investigate the effects of speed, load, implant material, and fiber direction on the friction coefficient between bone and implant, using tribology experiments.

Materials and Methods

Cortical bone samples were extracted from bovine tibiae, machined into hexaedra (~35x20x5mm) and polished. In parallel, pins with a polished spherical end (ø20mm) were manufactured with stainless steel 316L, Ti-6Al-7Nb, and commercially pure (CP) Titanium grade 4. For the latter, two additional surface treatments were applied: sandblasting and one typically applied to dental implants.
Tribology tests were realised with a standard tribometer (TRB, Anton Paar TriTec SA, ball-on-flat and linearly reciprocating mode) with the bone samples immersed in saline. Five load levels (1-50N), 5 materials/surface treatments and 2 directions (parallel/perpendicular to bone fibers) were tested. For each, the maximum linear speed was varied by 3 orders of magnitude (10^2-10^5µm/s). Each test lasted 14 minutes with a sampling frequency of 30Hz and was repeated on 5 samples.

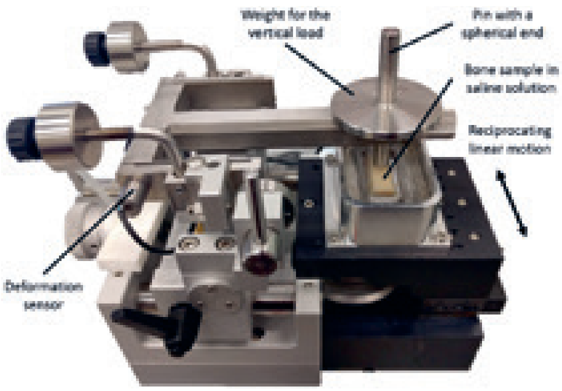

Fig.1 Standard tribometer (TRB), Anton Paar TriTec SA

Mixed statistical models were created for the fixed effects of the logarithm of load, the logarithm of speed, material and fiber direction, taking into account the pairwise interactions. Samples were set as random effects.

Results

The friction coefficient decreases significantly* when the load or the speed increases. The interaction between both load and speed shows that for higher loads, the friction coefficient varies significantly* less with the speed and vice versa.

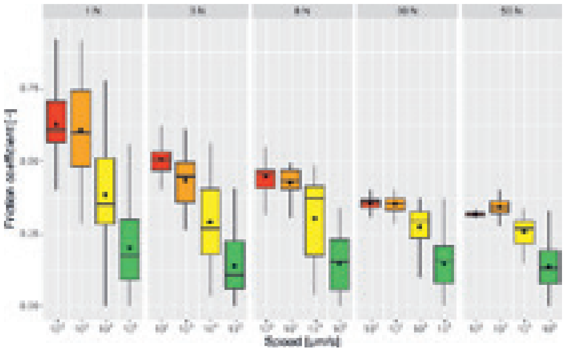

Fig.2 Friction coefficient for stainless steel 316L with respect to speed for each tested load.

At low speed, the coefficients are all significantly* different, except for the two groups stainless steel 316L/Surface treatment and CP Titanium grade 4/Sandblasting/Ti-6Al-7Nb. The variation with the speed is significantly* different for each material.
Concerning fiber direction, the mixed model does not show any significant* difference at low speed. The variation with speed however is significantly* different, being more important for the direction parallel to fibers (*$p < 0.05$).

Discussion

Effect of speed and load may be explained by mixed lubrication with elastohydrodynamic effects and surface effects. As the speed increases, the shear force and fluid pressurization increase, which decreases the force supported by asperities and thus the friction. As the load increases, asperities are flattened and pressurization of the fluid also increases. This again reduces friction. Speculations can be made, but what exactly happens at the micro-scale remains to be clarified.
In conclusion, effects of different parameters corresponding to physiological conditions on the friction coefficient between implant and cortical bone have been assessed. These results will be relevant for the evaluation of primary stability of new implant designs.

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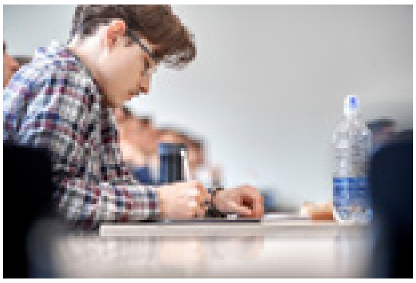
Impressions



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