UNIVERSITÄT
BERN

Master Biomedical Engineering

Annual Report 2013

MASTER OF SCIENCE IN BIOMEDICAL ENGINEERING

Contents

Introduction

Thirty-seven master degrees were awarded in 2013 and it was a real pleasure to celebrate them in the classical atmosphere of the more than century-old Kulturcasino in the city of Bern. At this ceremony, Dr. Beat Gasser as a representative of the Robert Mathys Foundation, awarded for the first time the prize of the highest average score in the master program. I wish to gratefully acknowledge here both the initiative and the financial support of the Robert Mathys Foundation for this award. It reflects the esteem of our long-standing partner and promotes the spirit of excellence that should prevail in our privileged academic environment.

A substantial remodeling of the curriculum was undertaken to balance the foundations in engineering sciences, refocus the mandatory part of the three major modules and improve the complementary skills. New elective courses were introduced to benefit from local expertise in research and clinical practice. All these innovations are described in the pages of the present report. The updated curriculum became operative for the new wave of students in the fall and previously enrolled students have the opportunity to switch to the updated curriculum until March 2014.

From the administrative point of view, the study regulations were updated to better match the organization of the faculty of medicine and I wish to thank the legal department and the office of the dean for their essential contribution towards this endeavor.

This year again, the BME day was a frank success, fresh companies presented their activities and contributed to exchange ideas, discuss projects and seed future collaborations. I look forward to continuing this valuable experience and to attracting further participants interested in the biomedical industry.

The standard teaching evaluations managed by the university of Bern revealed a globally positive feedback from the students and was instrumental in recognizing and resolving isolated difficulties. Clearly, the interest for our themes is confirmed, the resources match the expectations, the communication channels are open, and the content adapted to the profile of the audience and the current state of the art.

The unique cooperation between lecturers/research supervisors in medicine and engineering achieved in this program is now complemented by a constant strive in redefining and raising the quality of the transmitted knowledge and skills. Although important steps were taken in the appropriate direction this year, I look forward to introducing further improvements not only in content but also in the organization of the program in the next semesters.

To conclude, I would like to express my thanks to the teachers, the members of the study commission, the study coordination team and my colleagues from the University of Applied Sciences, Prof. Volker Koch and Prof. Lukas Rohr, for the highly appreciated collaboration and ongoing support.

Enjoy this 2013 snapshot of the master program!

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

BME First Year Students 2013, University of Bern.

Structure of Courses in the Master's Program

The Curriculum
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 the clarity and reduce the complexity of the curricular structure. A main idea was to guide the students through their studies in a better way by adding an elective part to the major modules, which formerly had consisted exclusively of mandatory courses. Besides, the curriculum was expanded by a number of new specialized courses as well as an additional major module called "Image-Guided Therapy".

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

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

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

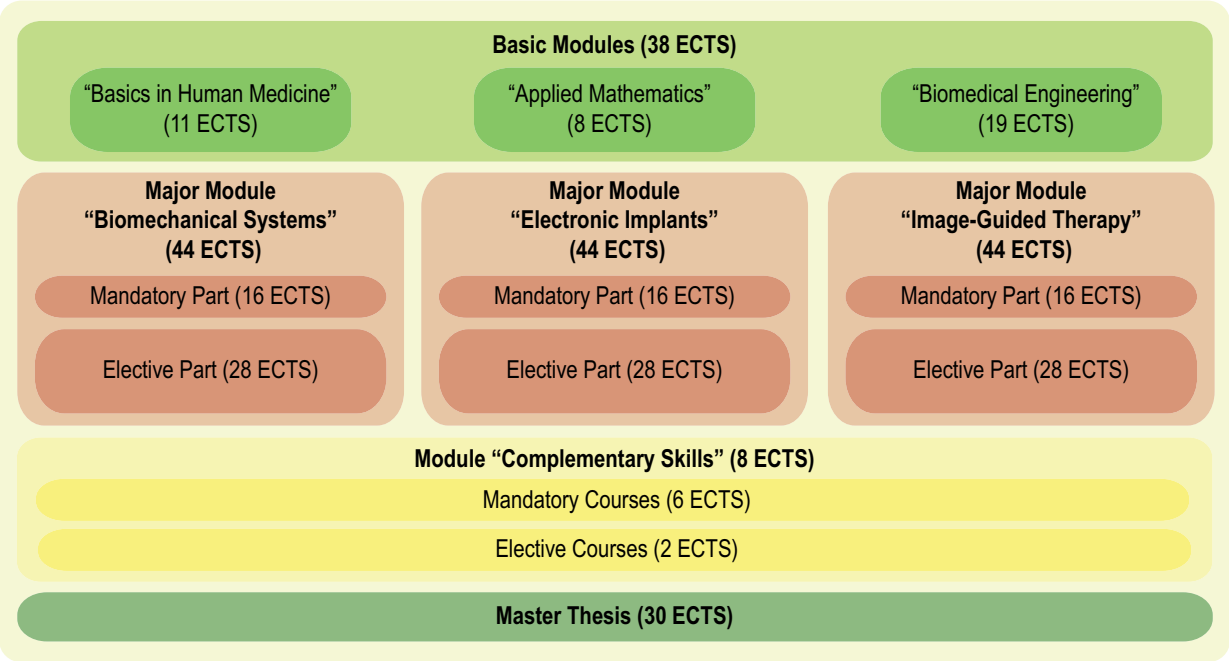
Major Modules
The choice of one of three major modules Biomechanical Systems, Electronic Implants, or Image-Guided Therapy after the first semester constitutes the first opportunity for specialization. The former major module "Musculoskeletal System" has been adapted and renamed "Biomechanical Systems".

Approximately one third of the major modules consists of mandatory courses. In the elective part of the major module, the student is allowed to select any 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 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 is 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 (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 report, 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

Biological Principles of Human Medicine
Biomaterials
Biomedical Acoustics
Biomedical Instrumentation
Biomedical Laser Applications
Biomedical Signal Processing and Analysis
BioMicrofluidics
C++
Clinical Applications of Image-Guided Therapy
Computer Assisted Surgery
Computer Graphics
Computer Vision
Cutting Edge Microscopy
Design of Biomechanical Systems
Engineering Design
Engineering Mechanics I
Engineering Mechanics II
Finite Element Analysis I
Finite Element Analysis II
Functional Anatomy and Histology
Functional Anatomy of the Locomotor Apparatus
Health Technology Assessment
Image-Guided Therapy Lab
Innovation Management
Intelligent Implants and Surgical Instruments
Introduction to Medical Statistics
Introduction to Signal and Image Processing
Machine Learning
Medical Image Analysis
Medical Image Analysis Lab
Medical Robotics
Microelectronics
Microsystems Engineering
Modeling and Simulation
Molecular Biology
Numerical Methods
Ophthalmic Technologies
Osteology
Physiology
Principles of Medical Imaging
Programming of Microcontrollers
Regulatory Affairs and Patents
Rehabilitation Technology
Scientific Writing in Biomedical Engineering
Technology and Diabetes Management
Tissue Biomechanics
Tissue Biomechanics Lab
Tissue Engineering
Tissue Engineering - Practical Course

Major Modules

Biomechanical Systems

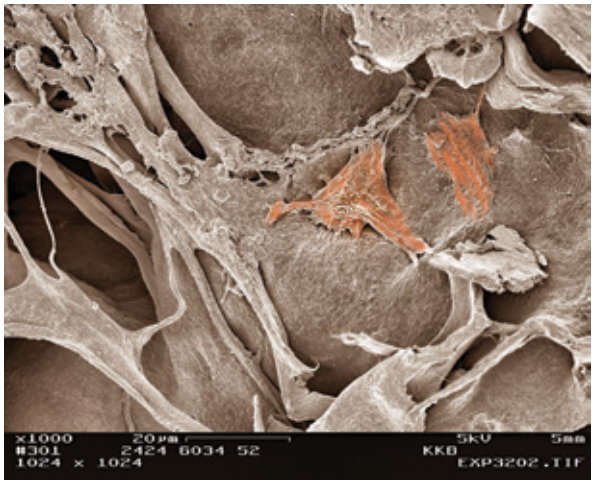
Prof. Dr. Philippe Zysset

The 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. Cardiovascular diseases, musculoskeletal injuries and pathologies are the most costly ailments facing our health care systems, both in terms of direct medical costs and compensation payments related to loss-of-work.
In this module, students will gain a comprehensive understanding of the multi-scale organisation of the cardiovascular and musculoskeletal systems, combining knowledge from the cell, tissue, organ to the body level. They will learn how to apply engineering, biological and medical theory and methods to resolve complex problems in biomechanics and mechanobiology. Students will learn to draw connections between tissue morphology and mechanical response, and vice versa. Students will also gain the required expertise to apply their knowledge in relevant, practice-oriented problem solving in the fields of cardiology, vessel surgery, orthopaedics, dentistry, rehabilitation and sports sciences.

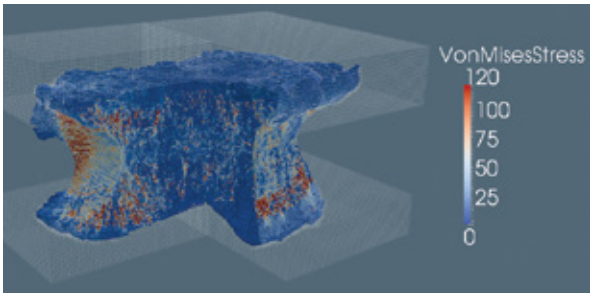
The mandatory courses in this module provide the student with fundamental knowledge of fluid and solid mechanics, tissue engineering, tissue biomechanics and finite element analysis. This provides an overview of the functional adaptation of the cardiovascular or musculoskeletal system to the demands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

Knowledge gained during the coursework highlights the multidisciplinary nature of this study focus area, encompassing the cell to body, the idea to application and the lab bench top to the hospital bedside. This knowledge is applied during the final thesis project, a project often with a link to a final diagnostic or therapeutic application. Examples of recent thesis projects include the analysis of rotodynamic blood pumps, the development of a monitoring tool for screw insertion in bone or the investigation of collagen scaffolds towards anterior cruciate ligament repair.

Career prospects are numerous. Many students proceed to further post-graduate education and research, pursuing doctoral research in the fields of biomechanics, tissue engineering or development of biomaterials. Most of the major companies in the fields of cardiovascular engineering, orthopaedics, dentistry, rehabilitation engineering and pharmaceuticals are strongly represented within the Swiss Medical Technology industry and continue to experience growth, therefore driving a 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.



A mesenchymal stem cells (MSC) grown on Novocart® collagen patches (B.Braun) for 7 days to test their cyto-compatibility for the application of repair of the anterior cruciate ligament of the knee joint. The picture shows MSCs spreaded onto the novocart collagen matrix.



Stress distribution in µCT based FEM model of a human vertebral body.

Electronic Implants

Prof. Dr. Volker M. Koch

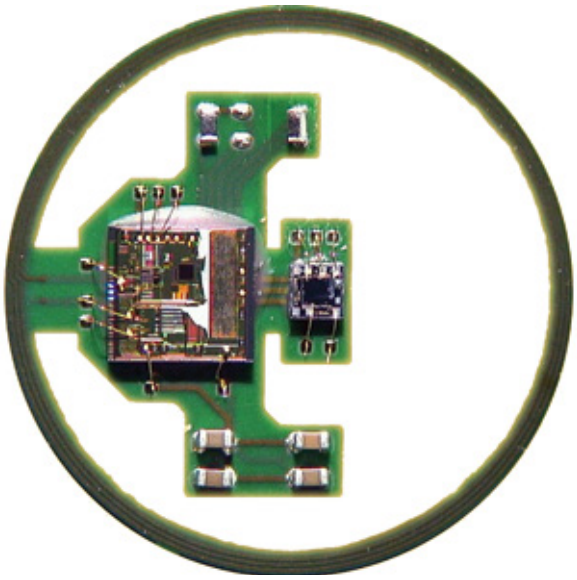
Electronic implants are devices like cardiac pacemakers and cochlear implants. Due to miniaturization and other developments, many new applications become feasible and this exciting area is growing rapidly. For example, cochlear implants provide already approximately 200'000 people a sense of sound. These people were previously profoundly deaf or severely hard of hearing. Recently, researchers demonstrated that electronic retinal implants allow the blind to read large words.

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

In this module, students will learn about the basics of electronic implants. This includes: sensor and measurement technology, signal processing and analysis, microcontroller programming, actuator technology, and miniaturization of micro-electro-mechanical systems. Application-oriented topics are also taught, e.g., cardiovascular technology and biomedical acoustics.

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

Students may already apply their knowledge as a part-time assistant in a laboratory and/or during their master's projects. After finishing the degree program, a wide variety of career paths are available, ranging from research and development to project and product management. Many well-known companies in Switzerland work in this field, e.g., Codman and Phonak Acoustic Implants. This list is, of course, not complete. For example, many "traditional" implants manufacturers have recently become interested in electronic implants, e.g., to measure forces in knee implants.



Glaucoma disease is normally associated with fluid pressure in the eye. The photo shows a miniaturised sensor system used for 24 hours measurements of the intra-ocular pressure and wireless RFID transmission of energy and data. The electronics, bonded on a 10 mm diameter flex print, is ready for integration into a dedicated eye lens. Photo: BFH, Institute for Human Centered Engineering - microLab, CTI project dynamic contour tonometer (industrial partner: Ziemer Ophthalmic Systems).

Major Modules

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 various means of determination of the spatial instrument-to-patient relationship and by suitable visualizations. 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 be introduced to the fundamentals of the above-mentioned clinical and technical aspects of image-guided therapy. They will receive an overview of currently applied clinical standards as well as an overview of latest advancements in research (check out the recently introduced course on Clinical applications of IGT as well as the IGT Lab). Successful students will be able to develop novel clinic-technological applications for complex medical procedures as well as improve existing approaches to IGT. This will enable further 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.

Preclinical validation of a precision robot system for cochlear implantation.
(Photo © ARTORG Center Bern and Inselspital Bern)

New Courses

C++

Prof. Dr. Björn Jensen

The course "C++" was held for the first time during the winter semester 2013/2014. The main aim of this course is to familiarize students who have already experience writing code with C++ and novelties offered by the new C++11 standard.

As a common programming environment an Ubuntu-based virtual machine with Eclipse and a GNU C++ compiler were used. This compiler in its most recent version provides near complete support of the C++11 standard. Even though this standard has been ratified in 2011, it is not yet completely supported by all major compilers.

From disussions with students it became clear that in many areas C++ programming skills are considered an advantage, and sometimes are even mandatory, e.g. for a number of projects proposed as Master theses.

The course "C++" was not intended as an introductory course, but is a course for programmers. However, to cope with the heterogeneous programming background of the huge number of students and to provide a level playing field to all participants, a short introduction into programming paradigms, syntax of C++ and object oriented programming was needed and provided.

C++ offers programmers speed and fine-grained control of the system. However, this control needs to be exercised either by good programming practices and / or software patterns and structures which reduce the risk of memory leaks and undefined behaviour.

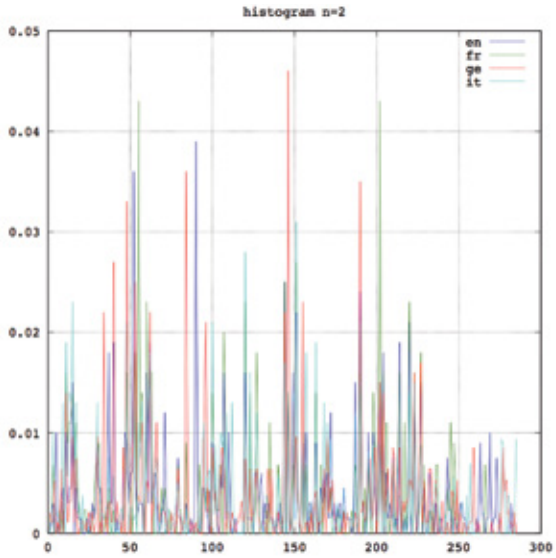
With the recent language improvement C++11 a number of new features have been provided making the language more robust and easier to code for. The new features covered in this course were among others: initialization, low-level programming, tools for writing classes, and new standard library components. More advanced topics such as smart pointers, template programming, exception handling and container classes were presented during the course and then used in a number of exercises.

These exercises form the hands-on part of the course and aim at practicing particular language features. The questions are designed to be independent of each other and of reasonable size and complexity.

For example, students created their own vector type and their own complex number type. They computed histograms of letter frequencies and frequencies of co-occurrences and later wrote code that used this simple information to infer the language of a text.

They used smart pointers and reference wrappers to store elements in container classes and with the help of the OpenCV library students could not only compute but also display fractals such as Mandelbrot sets.

The range of complexity and sophistication of the code written varied significantly and reflects also the spread in programming experience among the students. All participants deserve respect for the considerable amount of time devoted to completing and discussing the coding exercises. It is testimony of their enthusiasm to master C++11 and made "C++" a course which was fun to teach.



Example distribution of a 2-gram for English, French, German and Italian.

New Courses

Two new courses in the IGT module

Prof. Dr. Stefan Weber

Computer assisted therapeutic devices are imperative in modern medicine. Their application ranges from virtual image based planning of surgical and interventional procedures to stereotactic image-guidance and to robot-assistance. The term "image-guidance" encompasses a large variety of technological implementations in various clinical domains. While studying "Image-Guided Therapy", students shall be introduced to the various technologies underlying such computer-assistive devices and also study the availability and advancement of computer-assisted systems within various clinical disciplines. To this end, in 2013 two new courses, Image Guided Therapy Lab and Clinical Applications of Image Guided Therapy, have been introduced to the module "Image Guided Therapy".

Image Guided Therapy Lab
Within this practical course, participating students are required to actively participate in ongoing research projects within various research groups active in the field of Image guided therapy. Students undertake a component of a larger research project and produce a written project report outlining their research aims, methods, and findings. At the completion of the course, students present their work to their peers in a short oral presentation. Project work is carried out on a one to one basis with each student being paired with an experienced researcher who guides them through the completion of a small research project and through the writing of research report. Project work is carried out en-bloc during a suitable time slot and the final project defense takes place in peer-organized workshop towards the end of the semester. During the beginning of the semester, students together with the group representatives identify and define a suitable project amounting to around 20 hours of lab work. Project work includes engineering activities such as software programming, data processing and visualization, designing and production of hardware components and the conduction of experiments in the framework of ongoing scientific and clinically oriented research projects. Students gain insight and participate actively in advanced research projects and identify suitable future topics of interest. By participating in this course, students are able to not only connect with the various research groups and identify a potentially suitable scientific topic of interest for their master's thesis but to also train formal elements of scientific work such as the preparation of reports and the delivery of oral presentations in front of a professional auditorium.

Clinical Applications of Image Guided Therapy
To assist students in gaining an overview of the advancement of computer assistance within the various clinical disciplines a new clinically oriented lecture series has been introduced to the IGT module in 2013. Participating students are introduced to clinically relevant and applicable solutions in image guided therapy throughout various clinical disciplines. Medical topics discussed in classes range from Ear-Nose-Throat, to neuro, to orthopedic surgery, interventional procedures, to oncologic liver surgery, pneumology and also cardiac interventions and robotic abdominal surgery. Students gain insight into specific clinical procedures and how they are carried out with the aid of modern technology. Each of the lectures in this series is taught by an internationally renowned expert in the field, typically clinicians with distinct know-ledge not only about the specific medical background but also with vast experience in applying IGT technology in day to day routine.

Student and advisor evaluate a tablet computer based 3D medical image viewer.
Photo: ARTORG Center

Preclinical evaluation of a new surgical robot system for minimally invasive cochlear implantation.
Photo: ARTORG Center

Innovation Management

Dr. Alexander Mack

After several years, it was time to adapt the former course in management and to focus its content more specifically on the importance of innovation. Indeed, innovation has become the major source of a company's success in a strongly competitive environment. Moreover, the early 21st century is characterized by the emergence of a new generation of innovation process models whose key features are systems integration, networking, flexible and customized response, and continuous experimentation and testing.

The new course "Innovation Management" offers an introduction to the theory and applied practice of management as a discipline and process under the guiding principles of innovation. Therefore, the implications of the innovation economy for business companies and more specifically for strategic management and strategy dimensions are first presented and discussed. A special focus is put on the strategic advantages through innovation and their mechanisms. In parallel, examples of innovation, e.g., based on the 4Ps model (product, process, position, paradigm), illustrate the different types of innovation. Difficulties but also advantages for small firm innovators are discussed, and the core abilities needed in managing innovation highlighted.

The course also presents the major principles of the classical management process – planning and decision making, organizing, leading, and controlling. In this context, the importance of the organization's internal and external environments is illustrated, and several modern tools for planning and decision-making are discussed. Additionally, the course introduces related major topic areas including management of innovation and technology, managerial economics, marketing, and quality management. Indeed, quality is another major determinant of business success or failure and thus has become a further central issue in managing organizations. The whole course is accompanied by case studies on innovation and practical exercises.

The purpose of the course is to give students the skills and knowledge set necessary to ethically manage today's business operations for innovation, productivity, and performance. It introduces different concepts and tools that are relevant to achieve leadership and organizational goals while advancing the strategic objectives of the organization. Finally, the course introduces several quantitative techniques to analyze a firm's numerical data and make efficient and effective decisions.

New challenges for management: high-tech and precision manufacturing. Photo: Alexander Mack

Combining innovation, performance, and team building. Photo: Alexander Mack

New Courses

Modeling and Simulation

Prof. Dr. Norman Baier

A major drive of the scientific progress in the last few decades was the availability of ever increasing computing power. This allowed scientists to carry out experiments virtually, in the computer. Alternatives to simulations are conventional laboratory experiments on the one side, and the derivation of exact mathematical solutions on the other side.

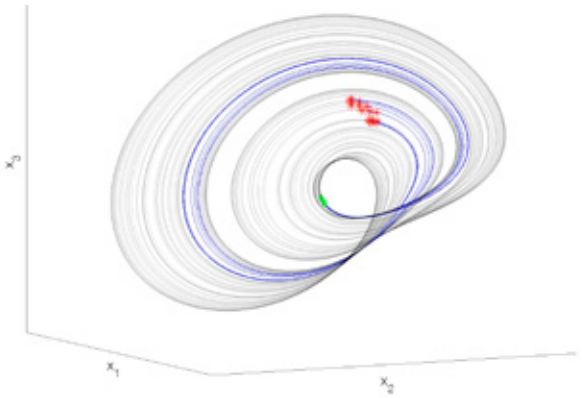
Fortunately for the simulation enthusiast todays problems are almost always of such a complexity that an exact mathematical solution can rarely be given. Sometimes even the mode of action of the system being analysed is not completely understood or is not accessible for measurements. Analysing processes running within the human body lead to situations of that kind.
Slightly less desperate is the situation when the mode of action is known but when the solution is very complex. This is the case when chaotic behaviour is involved then simulations are often the only way to get reproducible data.

So much is said for the general reasons that lead to the formulation of this elective course. The content can roughly be divided in three parts. During the first part mathematical solvers for simulating dynamic systems are employed to get acquainted with the possible qualitative behaviour of dynamic systems. The considered dynamic systems are in the general form of ordinary differential equations.

One major insight imparted is that even simple systems and differential equations can exhibit chaotic dynamics and in this case simulation can help in understanding the qualitative behaviour. Figure 1 shows the trajectory of the model of a simple electronic circuit (Colpitts oscillator) studied in this course. The figure also illustrates the chaotic nature of this circuit. During the evolution of the system initially nearby points in the state space diverge from eachother: The green asterisks are initially nearby and then diverge along the trajectories in blue.

The second part of the course is dedicated to the application of simulation to hypothesis validation. As a training object the saccadic eye movement is employed. This model has been developed and used to explain a certain number of lesions affecting eye movement. Lesions that can be analysed or explained with this model include for example nystagmus, ophtalmoplegia or strabismus. The models are built upon "first principles" which are, in occurrence, the laws of Newton. The model leads also through the area of conflict when gathering data for a model can be problematic for ethical reasons.

The third part focuses on the situations mentioned in the beginning, when the mode of action is not known or necessary measures cannot be performed, but when, nevertheless, the dynamic behaviour of the system has to be described. This is the application field of "black box" models. It is an aim of this elective course to show applications of the most widely used concepts of black box models: ARX, ARMAX and a representative of the neural networks, the NARX-model.



Trajectory of a simple 3rd order model showing chaotic behaviour.

Ophthalmic Technologies

Prof. Christoph Meier

PD Dr. Jens Kowal

The field of ophthalmology has always been strongly interrelated with the development of new diagnostic means and advanced surgical procedures. This course raises awareness of the students for innovative diagnostics and surgical treatments in ophthalmology. The course tries to link the pathological conditions on one side with diagnostic possibilities and treatment options on the other side. That way the attempt is made to develop a thorough understanding why diagnosis and treatment have been developed the way they are today.

The course starts with an introduction of eye anatomy and physiology. Then pathological conditions such as age related macular degeneration, glaucoma, or diabetic retinopathy are introduced to the students. Emphasizing the socio economic impact of these diseases should help the students to put those into perspective and raise the awareness for the challenges in this field. Symptoms of pathologies, diagnosis, and treatment options are illustrated.

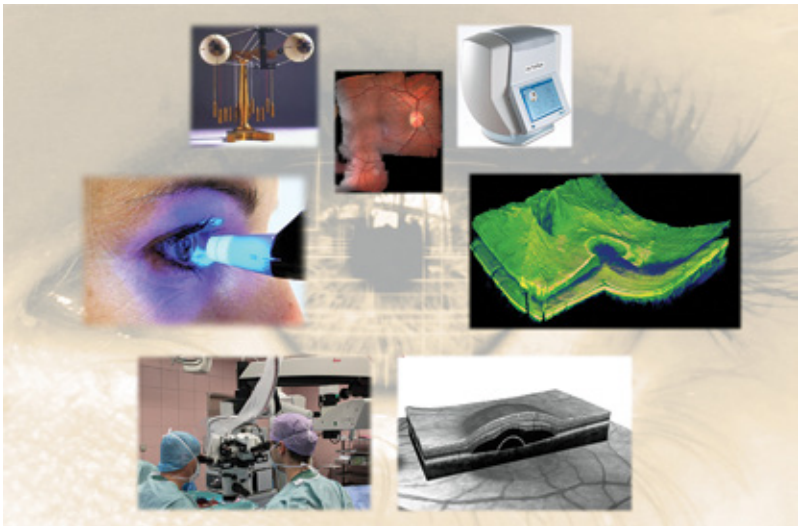
Because an understanding of optical principals is somewhat essential to ophthalmology the basics of geometrical and physical optics are repeated as part of the course.

Subsequently a comprehensive overview of diagnostic tools is presented. Specific emphasis is put on new imaging technologies such as optical coherence tomography (OCT). Functional principles like Michelson interferometry are explained in more detail because they are fundamental to understand and interpret OCT images. Different implementation alternatives of OCT imaging are discussed highlighting their individual advantages and disadvantages. The students get the chance to learn more about the OCT's during a lab session held in Biel at the University of Applied Sciences. In a laboratory environment they gain knowhow in using this new and fascinating imaging modality.

In addition to OCTs other regular diagnostic principles such as Slit-Lamp imaging, Fundus Photography or Corneal Topography are also introduced to the students. They learn about the challenges and possibilities of the individual imaging techniques. The overview is designed in a way to always make links to pathologies and how these pathologies manifest itself using the presented diagnostic tools.

During a visit at the Ophthalmology Department in small groups the students get a hands-on experience in using diagnostic tools such as OCTs, Fundus cameras or corneal topographer. Under guidance of experienced users they can learn how to use these systems. By this they develop a deeper understanding of how to deal with artifacts and challenges during the diagnostic procedure.

A little excursion to surgical treatments of ophthalmic diseases complements the overview of ophthalmic technologies. In particular interventions such as Laser-Assisted in situ Keratomileusis (LASIK) or Epiretinal Membrane Peelings with their associated problems are discussed.



Diversity in ophthalmic diagnostics.

New Courses

Scientific Writing

Dr. Simon Milligan

This course on scientific writing in biomedical engineering took place for the first time in 2013. The course is intended to provide support most immediately to students preparing to write their theses in the MSc Biomedical Engineering Program. In almost every case, this is the longest and most ambitious text the students have ever attempted, so support in this effort is essential. However, the broader aims of the course also include fostering effective communication practices which can be put to use long after the MSc has been awarded. Since a large proportion of the Program's graduates go on directly to pursue professional careers rather than to further study, the techniques included in the course were selected for their adaptability to a range of academic, industrial, commercial and other settings.

The course was designed and delivered by the University of Bern's Academic English Services, a unit of the Vice-Rectorate Development. Half-day workshop-style classes were scheduled at fortnightly intervals to allow time for writing assignments, and class sizes were limited to allow detailed individual feedback and questions. Assessment was by a portfolio of work completed over the course and self-edited by the students, and the lecturer's final assessment was returned to the students individually along with advice for future development.

Even within a single field such as biomedical engineering, written styles vary widely. Computer engineers, for instance, produce research articles which are quite different in several clearly observable characteristics from those produced by materials scientists or by imaging technologists. The single greatest influence on the form and language of an effective text comes from its intended readership, so each student is asked to locate some examples of texts from within his or her particular specialism before the course begins. Throughout the course, generic information about, for instance, the presentation of graphs and diagrams or the structure of introductions is used to guide an examination of the corresponding sections of these model texts. In this way, the students each focus on how functions and strategies common to texts in many fields are realised in their specific discipline. Having identified the phrases, structures and techniques used in their model texts, the students then put these into practice in assignments. Individual feedback on these seeks to ensure not only that the grammar and vocabulary are appropriate but that the mechanics of the text, such as patterns of citation and punctuation, can also be corrected to meet the expectations of the target readerships.

All the students who attended passed the course, which was oversubscribed. Their feedback on the course was enthusiastically positive, and their results indicate that they are well equipped to communicate effectively in a range of industrial and academic settings as well as to produce successful MSc theses in completion of their studies.

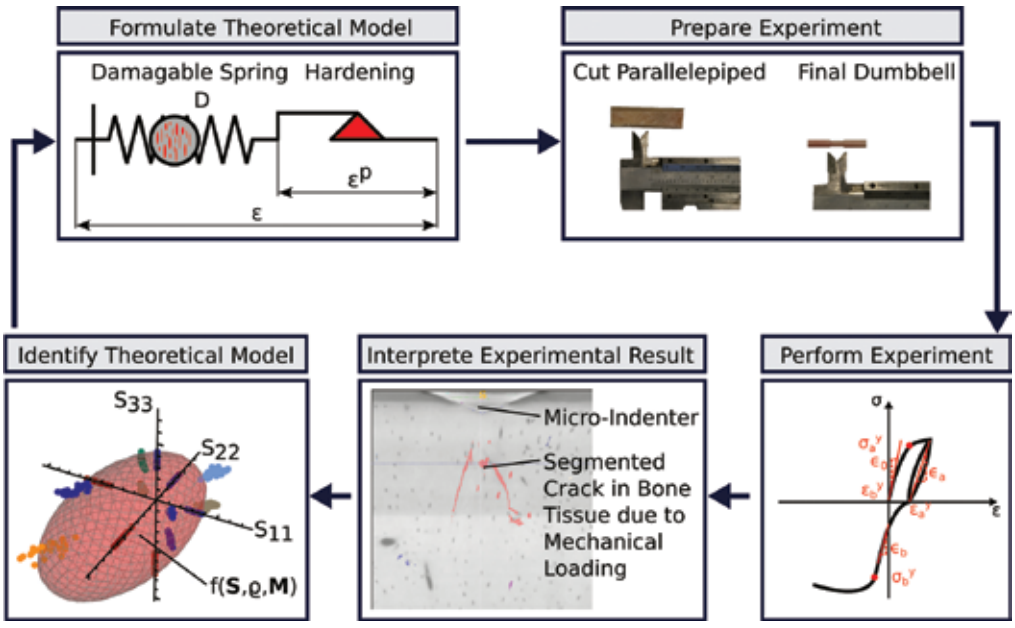
Tissue Biomechanics Lab

Dr. Uwe Wolfram

All biomedical application are usually theory driven developments. Be it the invention of a novel theory to represent the physical behavior or to the design of a novel implant system. From an engineering point of view, this poses a set of challenges that have to be met. Theories representing the physical behavior of, for instance, biological soft tissues need to be identified with experimentally determined material parameters. For novel developments, on the other hand, it is necessary to experimentally verify their functionality. Finally, it is of outmost importance to validate any new development against an independent set of experiments throughout all fields of biomedical engineering, since they are eventually meant to be beneficial for the patient.

Biomedical engineering offers a cornucopia of applications and unites the most different research fields. Surprisingly, the basic strategies on how to setup, manage, evaluate, and present an experiment are very similar for fields of research so different as experimental tissue biomechanics and microsystems technology (Figure). Owing to the focus of the lecturer, the course will be focused on tissue biomechanics. This field of research is investigates the intimate relationship between the hierarchical structure and mechanical function of skeletal tissues and the formulation of the basic principles for their characterization, modeling, replacement, and regeneration. As mentioned before, the characterization and identification of the specific behavior of a tissue is almost exclusively the subject of experiments which can be performed in vitro, in silico, or even in vivo. Furthermore, theoretical descriptions of tissue behavior need to be justified by a proper set of experiments before they can be used in applications as for instance the patient specific computation of the load bearing capabilities of bone-implant structures.

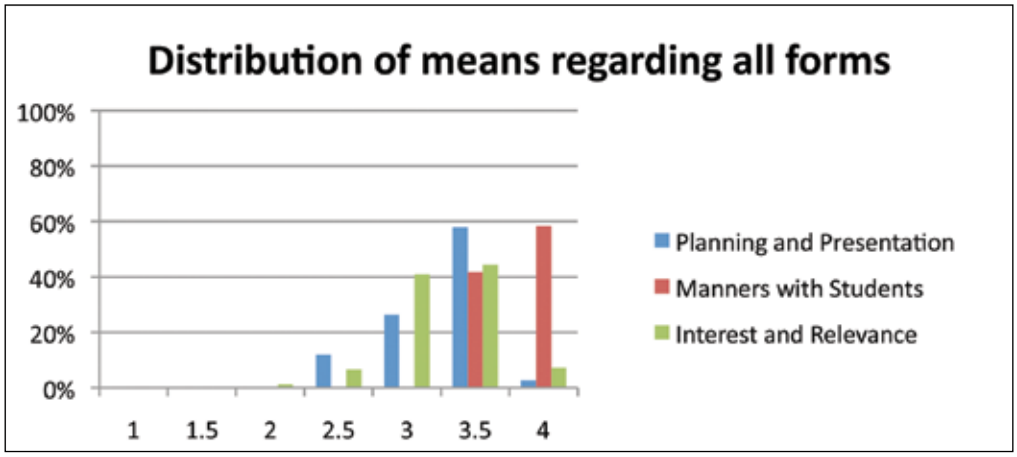
Typical mechanical features of the major tissue types such as linear and non-linear elasticity, plasticity, and active fiber contraction are taught in the course in an experimental fashion. In a virtual laboratory, students will learn how to perform experiments. Specifically, they will acquire knowledge of how to define and conduct mechanical experiments to identify specific tissue behavior. They will gain experimental understanding of the relationships between the structure and function of musculoskeletal tissues and develop the ability to obtain parameters to identify constitutive material models. Finally, they will acquire the knowledge to statistically evaluate experimental results and present them in a concise way.



Representative experimental work-flow illustrating the identification of material parameters for a biological tissue. The strategies taught in the course can be adapted to other fields of biomedical engineering.

Evaluation of Courses in 2013

Like in the previous year, a centralized evaluation was performed in the Master's program in 2013 according to the guidelines of the University of Bern. Both spring and fall semester were considered leading to 45 course evaluations involving more than 1000 forms in total. The results regarding all forms (see below) reveal that the students are satisfied with the course program and that the courses are interesting and demanding at the same time.



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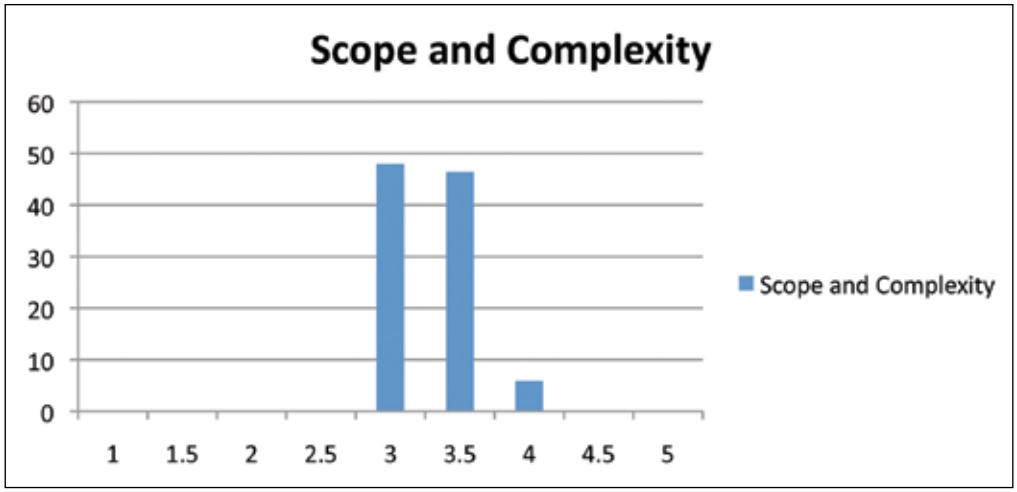

1: far too narrow/narrow 3: just right 5: far too high/wide

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Baier Prof. Dr., Norman
Baum PD Dr., Oliver
Bell Dr., Brett
Buchs Dr., Nicolas
Büchler PD Dr., Philippe
Burger PD Dr., Jürgen
Busato Prof. Dr., André
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Zysset Prof. Dr., Philippe

Biomedical Engineering Day 2013

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

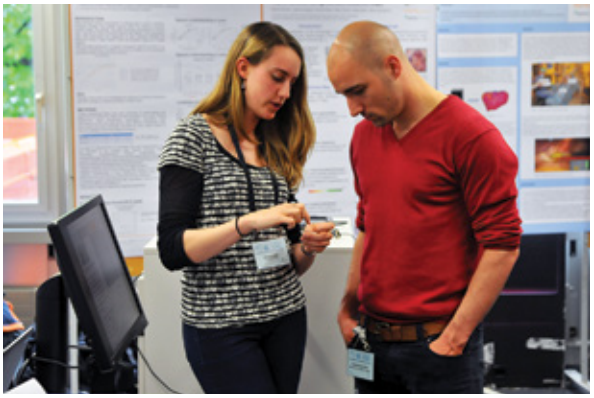
On May 24, 2013, the Biomedical Engineering Day took place in the auditorium Ettore Rossi at the Inselspital in Bern. The Master in Biomedical Engineering program of the University of Bern organized this event for the fifth time.

Attentive participants in the auditorium.
Foto: Tom de Bruyne

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

Two UniBe students discuss the latest BME newsletter.
Foto: Tom de Bruyne

The BME Day offered great opportunities for the Bernese biomedical researchers, too. The ARTORG Center for Biomedical Engineering Research and the Institute for Surgical Technologies and Biomechanics as well as the Bern University of Applied Sciences, a partner within the Master program, used the possibility of presenting current research projects to more than 250 participants. Interestingly, Master and PhD students play an important role in many of these projects. Thereby, this event was a demonstration of scientific achievements, too. Besides company representatives, scientists, researchers, and young academics, many medical doctors participated in this year's event as they had the chance for intensive communication with the biomedical engineers.



A student from the Lung Regeneration Technology Group at the ARTORG Center describes the principle of a microfluidic lung-on-chip to a BFH student. Foto: Tom de Bruyne

One highlight of the day was the successful live liver surgery by Professor Daniel Candinas, Head of the Department of Visceral Surgery and Medicine, Inselspital Bern. Illustrative explanations in the auditorium were given by Stefan Weber, head of the ARTORG Center for Biomedical Engineering Research, and a close scientific collaborator of Daniel Candinas.

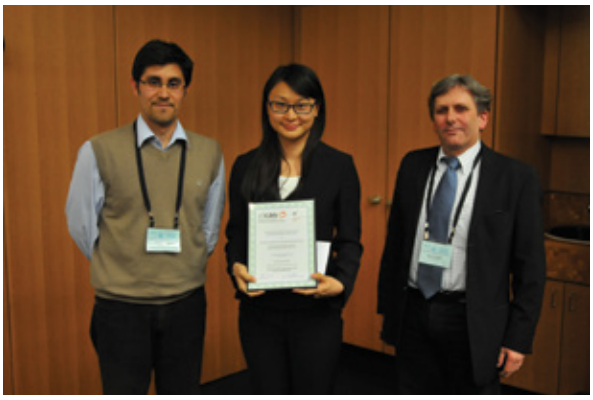
Lunch time: a great networking opportunity.
Foto: Tom de Bruyne

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

Juan Ansó received the SICAS Award 2013 for the best Master thesis for his work "Integrated Facial Nerve Monitoring for Functional Control of Robotic Assisted Drilling in the Mastoid".

Juan Ansó receives the SICAS Award 2013 for the best Master thesis in the Biomedical Engineering Program of the University of Bern from Mauricio Reyes (left; ISTB, University of Bern) and Bernard Reber (right; Director of the SICAS Foundation). Foto: Tom de Bruyne

The SICAS Award 2013 for the best PhD thesis was given to Samantha Chan for her work "Evolution of In Vitro Organ Culture Models for the Intervertebral Disc".



Samantha Chan receives the SICAS Award 2013 for the best PhD thesis in the field of Medical Engineering at the University of Bern from Mauricio Reyes (left; ISTB, University of Bern) and Bernard Reber (right; Director of the SICAS Foundation). Foto: Tom de Bruyne

The SICAS Poster Award 2013 was given to Patrick Steiner. His poster "Image Enhancement Algorithms for OCT Imaging of Subthreshold SRT Laser Lesions" convinced the jury.

Mauricio Reyes (left; ISTB, University of Bern) and Bernard Reber (right; Director of the SICAS Foundation) congratulate Patrick Steiner, winner of the SICAS Poster Award 2013, for his excellent work. Foto: Tom de Bruyne

We thank our sponsors and exhibitors

- Amgen
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- Nobel Biocare
- RMS Foundation
- SICAS Foundation
- Stryker Trauma
- Ziemer Ophthalmic Systems

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. Our members represent a growing network of biomedical engineers, scientists, past and present students and medical technology corporates who all desire 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, by facilitating attendance of international conferences and by organizing touring visits of various industrial plants and laboratories. The BME club is recognized as an official alumni association of the University of Bern under the umbrella organization – Alumni UniBe. A dedicated executive committee follows the principles of our constitution.

We are an enthusiastic and versatile group with diverse activities:

- bi-monthly "Stammtisch" in a local restaurant as an amiable platform to network, brainstorm or simply chat
- visits to Swiss medical and engineering companies
- providing information on career opportunities (including job offers)
- organizing annual welcome event for new students of the BME Master program
- organizing an annual alumni gathering
- participating in the annual BME day (co-organized with Master Study Coordination)
- publishing annual BME Newsletter
- rewarding two students each year with student travel award
- providing access to the Medical Cluster events
- joint membership with SSBE (Swiss Society for Biomedical Engineering)

BME alumni who join us will automatically become a member of Alumni UniBe, the alumni association of the University of Bern. Among other benefits this includes receiving a lifelong UniBe email address.

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 seeing you!

The BME Club Board in 2013


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A group of BME Club members after their visit to MPS AG in April 2013.

The BME Club team at the Grand Prix in Bern, May 2013.
Top from left to right: Christian Gueder, Jorge Sague, Gregor Spreiter, Constanze Hofmann, Juan Anso, Andreas Vollenweider, Tom De Bruyne.
Bottom from left to right: Matthias Peterhans, Jochen Walser, Lukas Kohler, Andreas Renggli.

The BME Master alumni meet for the already legendary annual barbeque on the top floor terrace of Murtenstrasse 50 in August 2013.

BME Club members have lunch at the World Medtech Forum in Lucerne in September 2013. The event was co-sponsored by the Precision Cluster and the Bern University of Applied Sciences for celebrating the success of VoiSee, a viewing aid for elderly patients with age-related macular degradation (AMD).

BME Club Stammtisch at Restaurant Beaulieu in fall 2013.

A group of BME Club members is enjoying a hot Glühwein at the traditional Bernese Onion Market in November 2013.

Graduation Ceremony

On 16th March, the graduation ceremony of the master students of the Biomedical Engineering program took place at the Grosser Saal Kultur Casino in Bern. It was organized by the Faculty of Medicine of the University of Bern.

This was a moment in which we could share memories of the past two years with all of the friends that we had made during the program. We were all happy to achieve a goal set long ago, but more important was the opportunity to share this special day with our mothers, fathers, siblings, and partners. We were all highly rewarded for the many hours spent studying text books and for all the stress of the exams.

During the ceremony, we were reminded that this moment is the key that opens the door to a larger part of life: working life. Of all of the words and messages that were said during the ceremony, one important message will remain with us; that society gave to us this enormous opportunity to study. With this message we take the responsibility of giving back to future generations the possibility of receiving higher education by encouraging research investments. As former students we will, with humility, carry the responsibility of contributing to education and highlighting its worth to society.

After the speeches, diplomas were presented to each student by Prof. Dr. Philippe Zysset, our program director. We would like to take advantage at this point, to say thank you to all of the professors for their efforts in teaching and for sharing with us their knowledge and experience.
The RMS Foundation prepared a special award this year. Two students with the best grades received a price from Dr. Beat Gasser for their dedication during the studies. Congratulations to Damien Maurer and Jörg Wagner.
At the end of the ceremony, a photograph of all the graduates was taken. It was a little difficult because we were so many this year. Fortunately we got a nice shot that will stay forever in our memories.
Lilibeth Brogna (Salas Téllez), BME alumna

RMS Master Award
In 2013, the RMS Foundation established the RMS Master Award for students graduating from the Master in Biomedical Engineering program at the University of Bern. The annual award is bestowed in recognition of excellent academic achievements. It is presented to the student with the highest grade point average.
This year, Damien Maurer and Jörg Wagner shared the award. The laureates were honored at the graduation ceremony of the Medical Faculty in March 2013.

Our alumni and alumnae.
bottom (from left to right): Jonas Guerdat, Patric Eichelberger, Andreas Waldmann, Simon Wüest, Anton Schärer;
top (from left to right): Dawei Chen, Jörg Wagner, Kaspar Jäggy, Thomas Fejes, Silje Ekroll Jahren, Adrian Derungs, Fanny Arcolino, Peter von Niederhäsuern Tina Furtwängler (before Frühauf), Patrick Vogt, Martin Vogt, Ben Hausammann, Lilibeth Brogna (before Salas Téllez), Damien Maurer, program director Philippe Zysset, Rosablanca Paez, Sébastien Gelin.

From left to right: Beat Gasser (CEO, RMS Foundation), Jörg Wagner, Damien Maurer, Philippe Zysset (Program Director, Master Biomedical Engineering).

Graduate Profile

Marc Stadelmann

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

MS: After compulsory school I did an apprenticeship as electronic technician at the Fribourg Technical and Art School. Followed by a short break due to military service and language school, I studied electrical engineering with a focus on control electronics at the University of Applied Sciences of Fribourg.

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

MS: In the last semester of my undergraduate studies, I started to look around what I would do next. I wanted to pursue a career in engineering, however, was looking for a program in which I could expand my horizon and apply some of my knowledge as an electrical engineer. I then found the University of Bern's Master's program in Biomedical Engineering. It offers a focus area Electronic Implants and, therefore, I subscribed to that program. During the first semester, in which all students take the same basic courses, I discovered my interest in muscles and bones. So I ended up taking Biomechanical Systems instead of Electronic Implants as initially planned.

BME: You went abroad for your Master's Thesis. Where did you go and how was this experience?

MS: I already went abroad for my undergraduate thesis and had a very good experience at that time. Therefore, from the first semester on I had it in mind to do another exchange if possible. I started to look around for universities that would do research in the same field and finally found a spot in Calgary, Canada. In summary, I can say that it was a great experience which I would recommend to everybody. It was certainly more work to get everything organized for the project than if I had stayed in Switzerland. However, I could benefit in so many ways, professionally and socially, that it was definitely worth the additional effort.

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

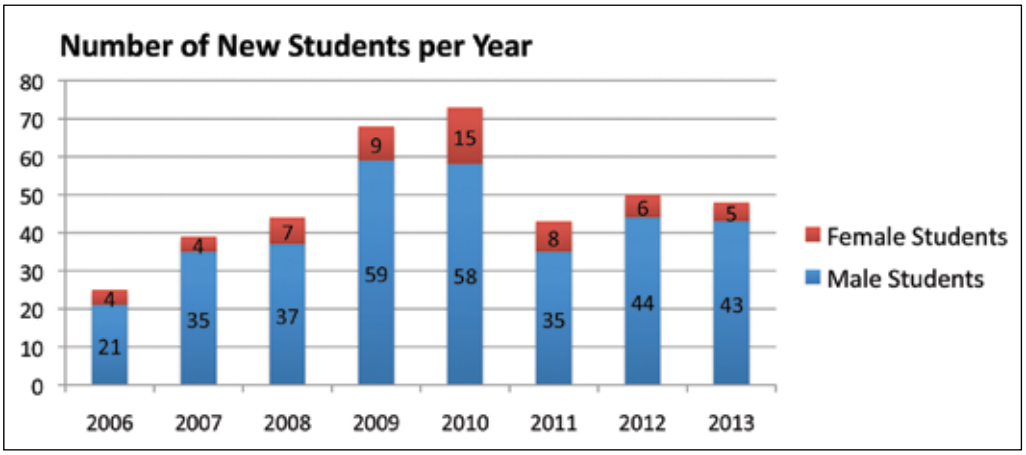
MS: I have just recently completed my degree. The qualifications I obtained during my Master's allowed me to perform my remaining service days as an engineer in a hospital instead of in the military. The first thing that I will do now is work for four months at the University Hospital Basel. After that, I will either start working in the medical industry or continue in academia towards a PhD.

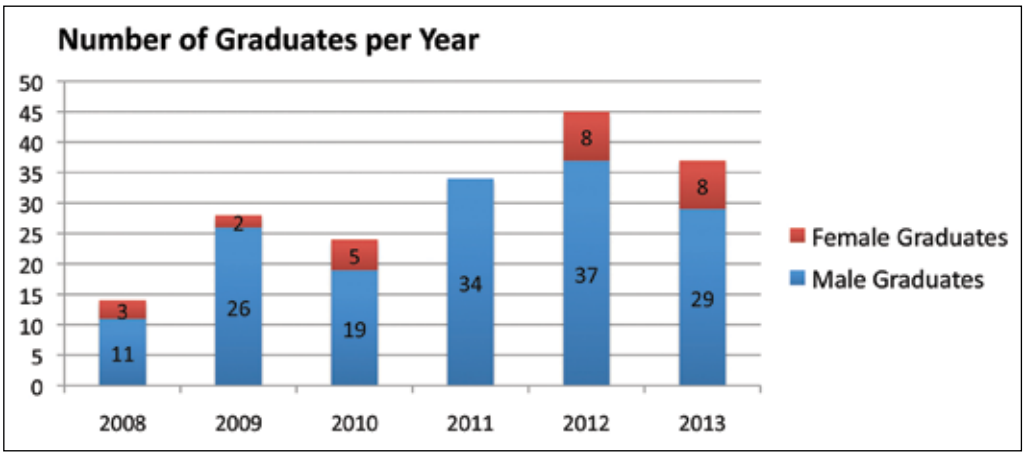
BME: What is the benefit of the Master studies with regard to your current professional activity?

MS: Since I have not really started working yet this is not very easy to tell. But for now, it allowed me to find an excellent placement to fulfill my remaining service days. For the future, I think, it will open many doors to jobs in the industry which I would not have access to without these Master studies.

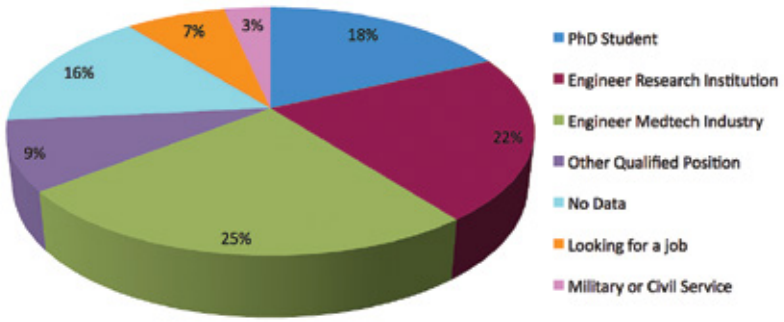
Statistics

Number of Students and Graduates per Year





BME Alumni: Career Directions
Profession after Graduation



Master Theses 2013

Please visit our website at http://www.bme.master.unibe.ch for an online version with full page Master Theses summaries.

Simulation of Soft Tissue Deformation for CranioMaxilloFacial Surgery using Cone-Beam CT Imaging and Inverse Planning Modeling

Salman Alaraibi, M.D

Supervisor: Dr. Kamal Shahim
Institutions: Institute for Surgical Technology & Biomechanics, Universität Bern
Examiners: Dr. Mauricio Reyes, Dr. Kamal Shahim.

Introduction

CranioMaxilloFacial (CMF) corrective surgeries have aesthetic and functional elements which surgery intends to restore or improve. As in other types of invasive intervention CMF surgery carries tremendous risks. Computer simulation system in CMF surgery enables precise and interactive manipulations of 3D reconstructed tissues to predict the changes and visualize the post-operative appearance. The reduced image quality and the presence of many different artifacts made the integration of cone-beam CT (CBCT) in this planning pipeline very difficult. Statistical shape models (SSM) proved to be robust in segmenting noisy and incomplete data, hence it could be suitable as a shape prior for segmenting CBCT. In a computer aided planning solution, patient's concerns about disfigurement can be easily addressed prior to the use of scalpel. The surgeon would still need to modify his plan several times to reach a facial appearance that would be equally pleasing. Instead if the desired appearance was set as a goal, an inverse approach would find the plan that can produce this result while being restricted by the functional aspect.

Materials and Methods

In this thesis, SSM ability to segment CBCT data is evaluated. SSM segmentation is tested on several CBCT data with certain modification to enhance its robustness. Two methods of fitting are compared one that constrains the model variance base on anatomical landmarks and the second where the model is independently fit to overlapping local regions.

In the second part of the thesis the ideal method to calculate and predicted post-operative plan while accounting for the functional limitations is examined. To formulate a solution for the multi-object registration problem a modified implementation of Iterative Closest Point (ICP) is used.

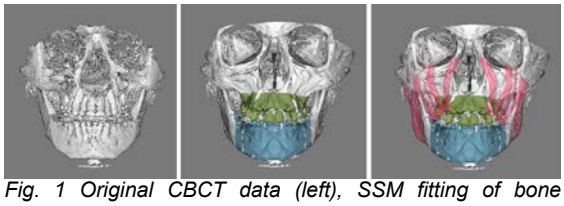


Fig. 1 Original CBCT data (left), SSM fitting of bone (middle) and the propagated muscles and osteotomy planes from a template to the mean model (right).

Results

SSM and using different fitting methods was able to segment CBCT data with a mean distance error in the range 0-1mm in the majority of cases. Both constrained and local fitting schemes produced comparable results.

Using the Constrained ICP implementation shows promising result in finding the ideal occlusion for a specified facial appearance. The constrained penalization value that produced the best results was in the range (0<k<=0.5).

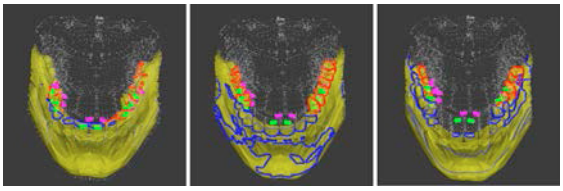


Fig. 2 The figure on the left was generated using the constrained ICP with a collision penalizing value (K) of 0.005. The Middle figure shows the same implementation with a K= 0.5. The right figure show the results with constrain K = 10. Depth of collision shown as of mesh intersection (blue outlines) between bone and soft tissue, and (red outlines) for dental arches.

Discussion

The results have proven SSM to be a fast and reliable tool for segmenting CBCT data. Most of the mean error was below 1mm. To enhance the model ability for describing pathological cases, a partitioned model was used. SSM performed better in the mandibular region in comparison to the maxilla.

Constrained iterative closest points (CICP) proved to be robust in optimizing this multi body registration problem. In less than 10 iterations CICP would converge to a solution. And by setting the constrain value to a range between 0<k<=0.5 the collision between the involved parts was at its minimum

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Integrated Facial Nerve Monitoring for Functional Control of Robotic Assisted Drilling in the Mastoid

Juan Ansó

Supervisors: Prof. Dr. Brett Bell
Institutions: ARTOR for Biomedical Engineering Research, Universität Bern
Department of ENT, Head and Neck Surgery, Inselspital, University of Bern
Examiners: Prof. Dr. Stefan Weber and Prof. Dr. Kai Rösler

Introduction

Minimally invasive direct cochlear access (DCA) aims to eliminate the need for a mastoidectomy by drilling a small tunnel through the facial recess to the cochlea with the aid of stereotactic tool guidance. Because the procedure is performed in a blind manner, structures such as the facial nerve are at risk. Neuromonitoring is commonly used as a tool to help surgeons identify the facial nerve (FN) during routine surgical procedures in the mastoid. The objective of this study was to determine if this drilling system could be used to warn of an impending collision with the FN during robot assisted DCA. This work describes the integration of a neuromonitoring enabled drill with a robot system designed specifically for image guided surgery of the lateral skull base followed by an in vivo feasibility test in a sheep model.

Materials and Methods

The sheep was chosen as a suitable model for this study due to its similarity to the human ear anatomy. The same surgical workflow applicable to human patients was performed in the animal model. First, four bone screws, serving as reference fiducials were placed in the skull near the ear canal. Second, the sheep head was imaged using a computed tomography scanner (0.75 × 0.5 × 0.5 mm^3 voxel size). Segmentation of facial nerve, Mastoid and other relevant structures as well as planning of drilling trajectories (1, 0.5 and 0 mm distance to the facial nerve) was carried out using a dedicated software tool (Otoplan). During the actual procedure

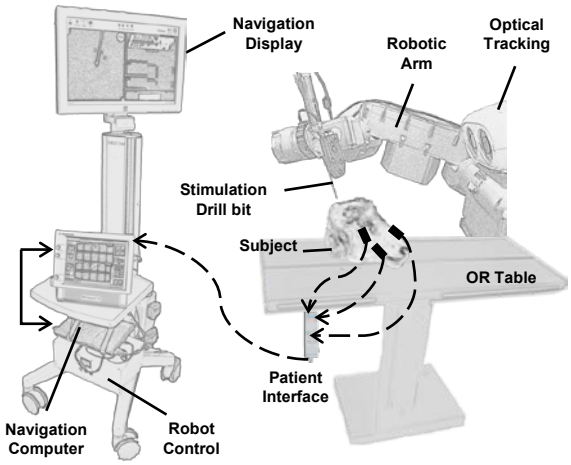

Fig. 1 Sketch of the experimental set up.

a surgical drill system was connected to a NIM 3.0 nerve monitor (both Medtronic, USA) and guided by a custom built robot system (Figure 1). As the planned trajectories were drilled, stimulation and EMG response signals were recorded.

Results

Using the drill position synchronized with EMG signals, the precise relationship between distance to FN and EMG intensity could be determined for each drill case.

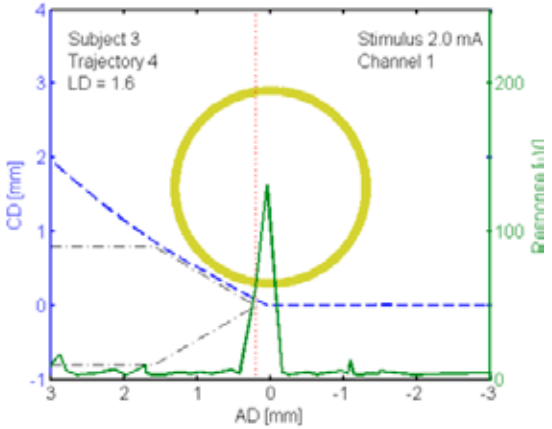

Fig. 2 The EMG response, the FN, the drill bit and the closest distance depicted relative to the axial distance (AD) for one of the trajectories in Subject 3.

Discussion

From the results of 11 trajectories from three sheep, it was determined that the current system lacks sensitivity and repeatability necessary to be used as a warning device in robotic DCA. Electrically isolated drilling tools will be tested in the future to determine if the sensitivity of the system can be improved.

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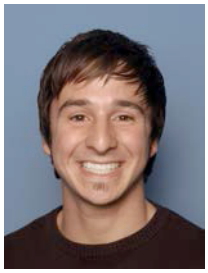
Acknowledgements

This project was supported by the Swiss National Science Foundation (Co-Me). The contributions with the EMG equipment from Medtronic (Switzerland) and the support from Christina Stahl and members of the Veterinary Faculty and Tierspital of Bern are greatly appreciated.

Statistical Shape Model-Based Articulated 2D/3D Reconstruction

Steven Balestra

Supervisors: PD Dr. Guoyan Zheng and Dr. Steffen Schumann
Institution: Institute for Surgical Technology & Biomechanics, Universität Bern
Examiners: PD Dr. Guoyan Zheng and Dr. Steffen Schumann



Introduction

For diagnosis and treatment of hip related pain, the acquisition of conventional X-ray radiographs is still the standard imaging procedure, although X-ray images provide only two-dimensional (2D) information about a three-dimensional (3D) problem. Recent studies have shown the benefit of 3D models over 2D images in clinical routine. Existing 2D/3D reconstruction techniques usually reconstruct single anatomical structures based on statistical shape models. Such techniques could fail to correctly reconstruct the hip joint, because they do not consider the joint relationship between the structures, which may lead to penetrating surfaces due to the narrowness of the joint space. To address this problem a novel 2D/3D reconstruction algorithm using an articulated statistical model was developed.

Materials and Methods

In a first part, the articulated statistical shape model (aSSM) was constructed. The training shapes were built based on a non-rigid deformation of a template mesh in order to establish the correspondences. To perform principal component analysis (PCA) the training shapes were aligned, such that the aSSM only exhibits true shape variation. Therefore the joint posture was explicitly defined by a parametrized rotation around the joint center.

In a second part, a novel 2D/3D reconstruction algorithm was investigated. Contours and landmarks semi-automatically assigned on the X-ray images served as *a priori* information. Based on 2D/3D correspondences [1] the rotation of the hip joint, as well as the patient specific models of the joint structures, i.e. the proximal femur and the pelvis were estimated by optimally fitting the aSSM to a limited number of calibrated X-ray images.

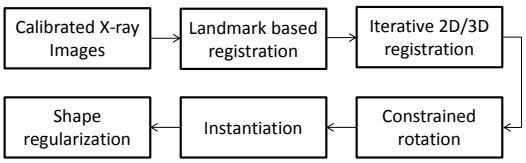


Fig. 1: 2D/3D aSSM-based reconstruction pipeline

Results

X-ray images and CT-scans were acquired for cadaveric and plastic bone models. The segmented CT models served as ground truth and the X-ray images were used as input for the reconstruction algorithm. Qualitatively, the results demonstrated the feasibility of the developed 2D/3D reconstruction framework with respect to hip joint space preservation, as no penetrating surfaces were observed. Quantitatively, average reconstruction errors of 1.9mm and 1.1mm were found for the pelvis and the proximal femur, respectively.

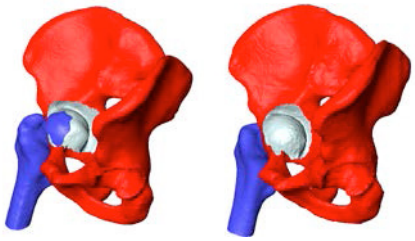


Fig. 2. Comparison of reconstructed hip joint models. Surface models obtained with the conventional single SSM-based 2D/3D reconstruction algorithm (left) and aSSM-based 2D/3D reconstruction algorithm (right). The aSSM-based reconstruction has the advantage of preserving the hip joint space and thus representing a true hip joint model, while the conventional algorithm leads to surface model penetration, which should not happen for a true hip joint.

Discussion

It has been demonstrated, that the novel 2D/3D reconstruction framework using an articulated statistical shape model is able to preserve the hip joint and can further be used for, i.e. femoroacetabular impingement diagnosis or planning of total hip arthroplasties. The novel method was validated on a relatively small number of cases. Therefore its performance needs to be further investigated using clinical datasets.

References

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Acknowledgements

I would like to thank the members of the radiology department of the Inselspital, Bern, for their support during the X-ray acquisitions. Further I appreciate the effort of Urs Rohrer, who was always helpful in construction issues.

Development of a Portable System for Perfusion of Isolated Porcine Hearts

Stefan Brun

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Department für Gefäss- und Herzchirurgie Inselspital, Bern Universitätsspital und Universität Bern
Examiners: Prof. Dr.-Ing. Justyna Czerwinska and Prof. Dr. Hendrik Tevaearai

Introduction

Demand for heart transplantation currently exceeds supply; the number of transplants performed is currently limited by donor organ availability. *Ex vivo* perfusion of cardiac grafts may help to improve donor organ availability by facilitating graft evaluation and enabling treatment to optimize post-transplant cardiac recovery. The goal of this thesis project was to develop and test a portable heart perfusion system suitable for the perfusion of large animal hearts.

Materials and Methods

A portable heart perfusion system, designed to perfuse and/or store a cardiac graft under a variety of conditions was designed, built and tested. Key components of the perfusate circuit included a pressure-control module, incorporating either a peristaltic or centrifugal pump, and a heating/cooling module. In addition, a heart-support container was developed, as was a quick-connect cannula, and a rapid and easy cannulation method was established for attaching the heart to the system. An independent power supply was created to provide autonomy during heart transport. The system was developed and tested in accordance with pre-defined system requirements.

Fig. 1: The portable heart perfusion system comprising electric, perfusate, oxygen and heart modules. The system includes a touch-panel for parameter control and monitoring, and is mounted on a trolley for easy displacement.

Results

The portable heart perfusion system is shown in Figure 1. The heart module provided full access to the heart and aortic cannulation was rapid and secure. Both peristaltic and centrifugal pumps successfully fulfilled system requirements; perfusate pressure could be varied between 0 and 120 mmHg with adequate speed and accuracy. The supply of perfusate to the heart was sufficient with a pump flow range of 0 to 2 l/min. Perfusate temperature could be increased from 23°C to 37°C within 10 min. Introducing 100 ml ice-cold solution into the perfusate circuit at 37°C had a small effect (-1.2°C) on system temperature at the level of the heart. Subjecting the system to vibration, expected during transport, caused interference in the pressure signal that could be resolved with a low-pass filter. The system can function for at least 4 hours in an autonomous manner and is sufficiently compact for easy transportation. The system controller runs in a stable manner.

The system was tested with five porcine hearts from experimental animals. All hearts were successfully resuscitated with the perfusion system, and potential evaluation parameters, such as Troponin-T could be measured (Figure 2). Three hearts were transported with continuous perfusion.

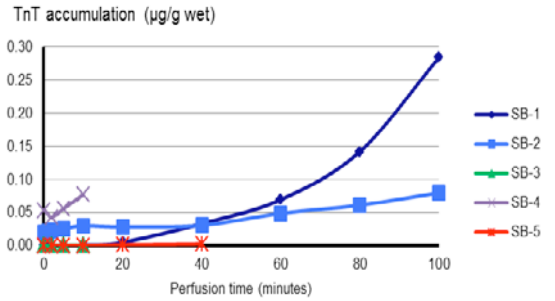

Fig. 2: Troponin-T (TnT) accumulation during the heart experiments. Hearts SB1 and SB2 were perfused after cardioplegic arrest and storage. Hearts SB3, SB4, SB5 were directly perfused upon procurement (without cardioplegia).

Discussion

A portable heart perfusion system, designed to perfuse and/or store a heart under a variety of conditions, was built and tested. Testing of the system demonstrated that both the peristaltic and centrifugal pumps successfully fulfilled most system requirements. Heating and cooling capabilities of the temperature regulating component were also examined; heating was rapid and sufficient, while cooling requires further refinement. Promising results were obtained with for resuscitation of cardiac grafts, stable heart perfusion, and continuous graft perfusion during transport, as well as system autonomy. Finally, a portable heart perfusion system was created, which can be further developed by the Department of Cardiovascular Surgery, and used for future experimentation.

An Integrated Head Holding Device for Robotic Assisted ENT Surgery

Dawei Chen

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Institutions: The Artificial Organ (ARTORG) center for Biomedical Engineering Research, Universität Bern
Examiners: Prof. Dr. Ing. Stefan Weber and Dr. Brett Bell

Introduction

A computer assisted robotic navigation system for the direct cochlear access (DCA) surgery was develop by the image guided therapy group at the ARTORG center at the University of Bern. The target application for the robotic system is minimally invasive implantation of hearing devices in the cochlea, which requires extremely accurate placement of a drill trajectory to avoid damaging vital structures. The DCA can reduce the trauma to the patient, save surgical intervention time, and make cochlear implantation more widely available.
Nowadays, the patient's head is immobilized with an invasive head clamp which uses at least three pins penetrating into the skull to hold it in place. The goal of this project is to develop an integrated solution for holding the head in a non-invasive way, and attaching the robot to the OR table.

Materials and Methods

The many different types of immobilization devices were researched and evaluated for use in the robot system. Advantages and disadvantages of the various fixation methods were contrasted with the requirements of this project. After this evaluation, it was determined that a combination of a rigid shell structure and granular bead filled fixation bags. As seen in Fig. 1

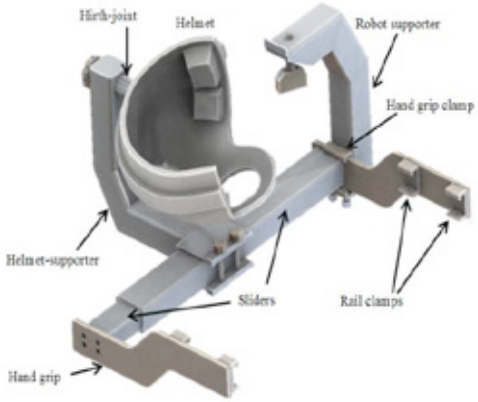

Fig. 1 The end design of the new non-invasive head holder with the name of the most important parts in this system

A solid model of the proposed solution was then designed and constructed. Mechanical testing was performed to evaluate stiffness of the holding device in comparison with the currently used invasive fixation system. This stiffness testing was performed by applying loads in magnitude and direction similar to the actual drilling forces by the robot system.

Results

The results of the stiffness test show that the prototype achieves better stability than the current device (maximum stiffness of the prototype: 25.49 N/mm; maximum stiffness of the current device: 16.08 N/mm). In addition to improved stiffness, the installation of the robot to the OR table was much faster than previously. The total weight of the fixation system (6.4 kg) means that it can be easily installed by a single person in the OR. Radiolucency was deemed less important for this first prototype, and was not addressed at this time.

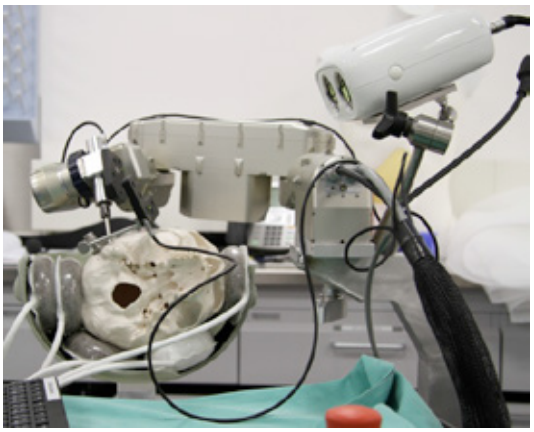

Fig. 2 Setup for the stiffness test with the prototype

Discussion

The first non-invasive head holding device with the integration of the robot and OR table was manufactured. Through the stiffness test of both head holding systems, the technical and practical requirements were evaluated. Improvements to the structure and materials are foreseen to add one degree of freedom to adjust the head height.

Acknowledgment

The entire team of image guided therapy of ARTORG center, Thomas Müller from Pearltec AG for the product information

A Framework for Medical Image Analysis of Brain Tumor Studies

Thomas Fejes

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Institutions: Institute for Surgical Technology & Biomechanics, Universität Bern
Examiners: Mauricio Reyes, PD and Dr. sc. nat. Johannes Slotboom

Introduction

A brain tumor is a seldom, but very serious and life threatening disease. An important part of the treatment is a regular magnetic resonance imaging (MRI) examination. The acquired images need to be analyzed, sometimes manually segmented, to get an impression of the tumor location and shape. This is a very tedious and time consuming work. To support the neuroradiologists, a graphical user interface (GUI) was developed in collaboration with the Department of Neuroradiology, Inselspital, Bern that follows the user to control of a fully automated segmentation algorithm [1]. Furthermore, several approaches to define the size of a tumor were investigated and compared.

Materials and Methods

The GUI was completely written in C++. Open source libraries like Qt [2], Insight Segmentation and Registration Toolkit (ITK) [3] and Visualization Toolkit (VTK) [4] were used. The GUI contains four viewers, so that all four modalities can be examined at the same time. Different views, sagittal, coronal and transversal, on the data series are possible as well.

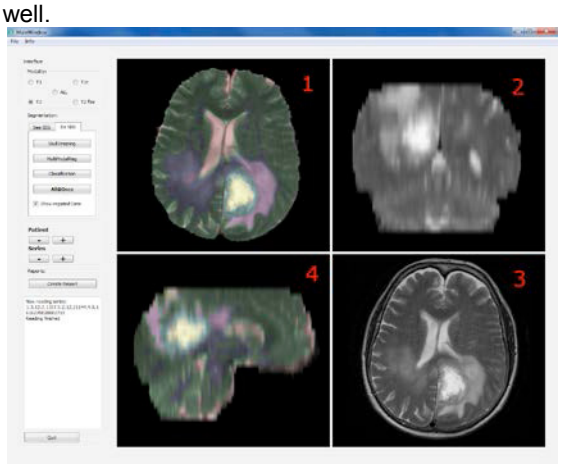

Fig. 1 Screenshot of the GUI. The four screens show a registered image in three different views (1, 2, and 4) and one original image (3) of the same patient. The colored overlay of the classifier output helps the user to distinguish between healthy and tumor tissue.

With the automated segmentation software, the volume of a tumor and its surrounding tissue, could be quantified and compared with a regular manual method [5], which is a diameter-based approach that measures the enhanced part of a tumor by finding the two longest diameters which are perpendicular to each other. The comparison between the volumes, and the sum of the diameter products of each observer (SDPO), was performed and is shown as a scatter plot.

Results

The GUI is easy to use for a clinician. The comparison of the absolute values, SDPO and volume, showed no correlation between those two approaches. Beside, the relative changes, from one MRI record to the next, had a higher correlation, Spearman coefficient: 0.5034, Figure 2.

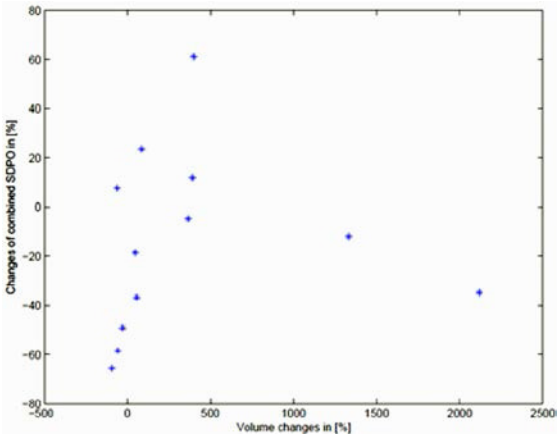

Fig. 2 Scatter plot of the volume (evaluated by the software) and the combined SDPO of two observers.

Discussion

The graphical user interface can show and perform analysis of several datasets. It is easy and straightforward to use. A report file is available as well. The comparison of the two methods indicated a correlation, although the 3rd dimension was not taken in account. It should be mentioned that the number of samples is rather small to make any general assumption.

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[3] http://www.itk.org/, ITK, 6. January 2013
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Design of Miniaturized Electrospray Instrument for Gene Therapeutic Treatment of Idiopathic Pulmonary Fibrosis

Prosper A. Fiave

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Institute for Medical and Analytical Technologies
University of Bern, Department of Pulmonary medicine and University Hospital
Department of Clinical Research
Examiners: Prof. Dr. Schittny and Prof. Dr. Thomas Geiser

Introduction

Electric field accelerated plasmid droplets to permeate tissues has been demonstrated on cell culture and ex-vivo lung tissue of rats using enhanced green fluorescence protein reporter gene for transfection. This opens a window of opportunity to design an electrospray instrument usable within the working channel of bronchoscope to noninvasively treat idiopathic pulmonary fibrosis (IPF).The aim of the present study is to design an electrospray device using a single access port to the lung taking into account restrictions within typical bronchoscopy procedure.

Materials and Methods

Technical, biological and medical specifications which are critical during bronchoscopy procedures were explored. These specifications were evaluated to realize a flexible tubular instrument providing high voltage and fluidic drugs to be delivered to the lung. Finite Element Methods (FEM) using COMSOL Multiphysics® was employed to verify the electrical compatibility for the miniaturized device. Materials selection for the design of the device was done so as to conform to regulatory standards regarding medical devices. Regulatory issues were explored to keep the device as close as possible to a medical device. The fabricated device is as shown in Figure1.

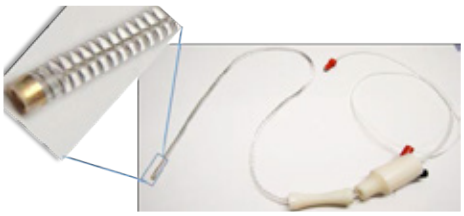

Figure1. The electrospray device

To test the device we sprayed a plasmid (pCMV-GFP) (Plasmid Factory GmbH) on sections of the lung tissue of a rat (Fischer rat) which have been placed in a DMEM growth medium. The plasmid was electrosprayed at voltages between 2.5-3.5kV at a flow rate of 5µl/min and current between 100µA-200µA for 1-3minutes. 0.03% of ethanol was mixed with some of the plasmids to compare the differences in transfection. The electrosprayed tissues were kept in an incubator for 24hours at 37°C with 5% CO_2 environment and microscopic analysis perform on them. In order to evaluate the DNA integrity, the plasmid was electrosprayed at 2.5kV and collected in an eppendorf tube placed at the tip of the device. The collected plasmid was run on 1% agarose gel to check the DNA quality by determination of its size compared to the standard DNA ladder of 1kbp (Promega USA) using electrophoresis.

Results

Figure 2 shows the confocal microscopic image of a tissue which has been sprayed with 50µg/ml with 0.03%ethanol, without ethanol and a negative control.

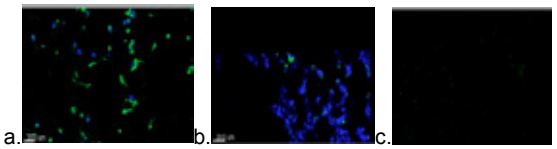

Figure2. Confocal microscopic image of sprayed tissue 50µg/ml with 0.03%ethanol (a), without ethanol (b) and a negative control(c).

Discussion

Transfection has been successfully demonstrated by the newly designed electrospray device. The addition of small concentration of ethanol has greatly improved the transfection efficiency. However since the intention of the design of the electrospray system is to treat IPF which occurs in humans, the implication of using ethanol for electrospraying has to be greatly explored

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Study of Magnetic Resonance Imaging Sequences of the Brain: Segmentation of MPRAGE and MP2RAGE in Early Degenerative Brain Diseases

Sébastien Gelin

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Examiners: Prof. Dr. Ing. Philippe Cattin.

Introduction

To diagnose neurodegenerative diseases is quite difficult due to an absence of known causes, an insidious and gradual evolution. Magnetic Resonance Imaging (MRI) has become of great interest to diagnose Alzheimer's disease in its mild or early stage. Therefore, significant efforts have been made to develop robust and accurate brain tissue segmentation methods that aim at quantifying loss of GM. To this end, the recent use of high-resolution MR imaging (e.g MP2RAGE) has allowed detecting lesions degeneration (volumetric measurement) of structures affected in the earliest clinical stage of AD, Nowadays, existing tissue segmentation methods are particularity optimized for conventional MR image (e.g MPRAGE). However, their applicability on novel MR sequences remains unknown.

Toolboxes and Methods

We used two atlas-based methods (Segment (S) and New Segment (NS) in SPM8) and an in-house free-atlas method Multivariate Bayesian Image Segmentation Tool (MBIS) on novel MRI sequences to automatically segment white matter (WM), gray matter (GM) and cerebrospinal fluid (CSF) from MPRAGE and MP2RAGE, see Fig.1, images using control (young and elderly) and mild cognitive impaired (MCI) patients. S and NS use priori probability maps registered from an atlas and each class modeled by a mixture of Gaussian distributions. MBIS uses a 5-class model (3 pure tissues plus CSF-GM and GM-WM partial volume) a one Gaussian distribution per class. As methodological contribution, we proposed a method to merge partial volume classes into the three pure tissues classes with both MRI sequences. In order to identify situations in which MP2RAGE could be better than MPRAGE, voxel-wise statistics analyses were performed using SPM8 and global as well as regional-based analysis were performed with the aid of FreeSurfer .

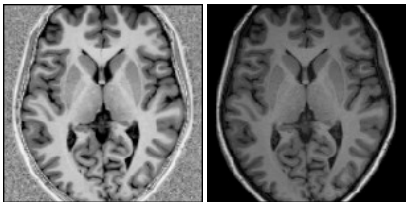

Fig.1: Axial slice. Left to right: MP2RAGE and MPRAGE

Results

Fig.2 shows a paired t-test on tissue probability maps of WM according to S and GM according to MBIS. The age is as covariate and a 6 mm spatial smoothing was used. Segment succeeds in finding significant differences in region such as the putamen, the hippocampus, and the amgydala which are used as biomarkers in order to predict the evolution of neurodegenerative diseases (i.e. Alzheimer's disease). Concerning MBIS, it showed a significant difference in the cortical GM. Indeed, due to a good contrast in MP2RAGE, the cortical GM appears thinner and better delimited in MP2RAGE than in MPRAGE.

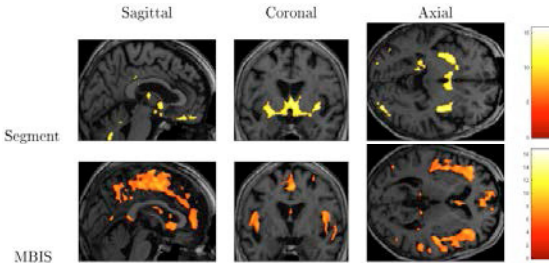

Fig.2: Voxel-wise analysis. Regions where significant differences appear according to Segment (WM_{MPRAGE}>$WM_{MP2RAGE}$) and MBIS (GM_{MPRAGE}>$GM_{MP2RAGE}$) in MCI subjects.

Discussion

Results show that all previously mentioned methods can be applied to MP2RAGE. Moreover, with current segmentation methods applied to MP2RAGE, we are able to detect volume variations, such as atrophy of the hippocampus or the cortical GM, increase of the CSF and loss of WM in the central nuclei, at least as good as with MPRAGE in MCI subjects. Our contribution, as it is the case for the atlas-based methods, completely succeeds in segmenting healthy subjects. However, some issues arise for the pathological subjects for all methods. Further development is needed in tissue model and segmentation methods.

Acknowledgment

This work was supported by CIBM of the UNIL, UNIGE, HUG, CHUV, EPFL and the Leenaards and Jeantet Foundations.

Simulations towards the optimal esophageal lead system

Pedro Antonio González Pérez

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Institutions: University of Bern
Examiners: Prof. Dr. Josef Götte and Prof. Dr. med. Rolf Vogel

Introduction

Heart rhythm disorders like atrial fibrillation might have serious consequences and increase the risk for stroke, heart failure or even death. The standard and most effective approach to detect arrhythmias is the Electrocardiogram (ECG). In particular for paroxysmal arrhythmias long-term ECG registration is crucial. Esophageal leads are a good candidate to record long-term ECG, and could be the base of an implantable eECG monitor. The anatomical relation of the esophagus to the left atrium allows us to obtain more detailed information on supraventricular electrical activity. However, the optimal lead configuration and eECG signal morphologies are still under investigation. Thereby, a mathematical model may improve the basic understanding of eECG signals The aim of this work is to derive such a model, to suggest the optimal esophageal lead configuration from a theoretical viewpoint and study ECG waveforms for a normal and a pathological electrical heart excitation.

Materials and Methods

The source model of electrocardiography was implemented by rewriting Ohm's law with the help of Green's identities. The basic equation for a volume conductor derives to:

$$\varphi(\vec{r}) = \frac{2\sigma_s}{\sigma_-^l+\sigma_+^l}\varphi^{\infty} - \frac{1}{2\pi}\sum_{k=1}^{K}\frac{\sigma_-^k-\sigma_+^k}{\sigma_-^l+\sigma_+^l}\int_{S^k}\varphi(\vec{r'})\frac{(\vec{r}-\vec{r'})}{|\vec{r}-\vec{r'}|^3}\vec{dS'}.$$

Boundary element method techniques are used to discretize the basic equations and set up a transfer matrix relating the electrical activity in the heart to potentials observed on different surfaces, e.g. the esophagus. The model was implemented in MATLAB and fed with the anatomical model (Fig. 1) and reference data exported from the ECGsim software.

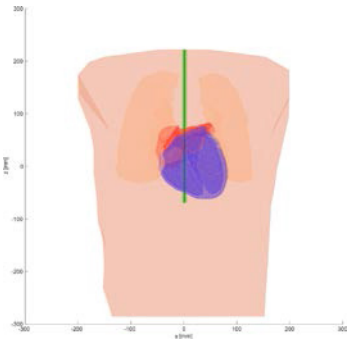

Fig. 1 Anatomical model used for the computations. The atrial cavities are shown in red, ventricles in blue, and the artificial esophagus in green.

Results

The highest peak-to-peak atrial signal amplitude obtained with a bipolar esophageal lead was observed with an inter-electrode distance from 15 to 30 mm as shown in Fig. 2. At such distances, steep atrial signals (0.5-1.7 mV/s) can be obtained. Specific ectopic activity was successfully identified on the esophageal channel using the proposed lead. The standard 12-led ECG was calculated with much higher accuray than the eECG.

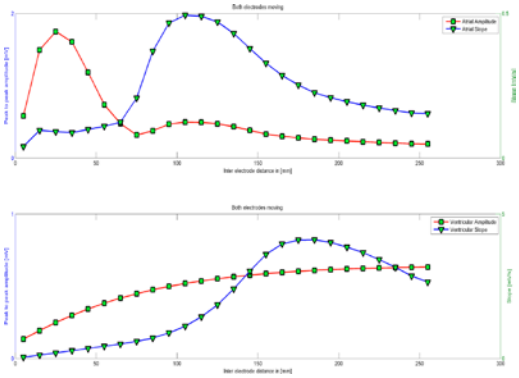

Fig. 2 Peak to peak signal amplitude and maximal slope of bipolar ECG signals for different inter-electrode distances.

Discussion

The source model is a powerful numerical technique which enable to model ECG signals at different surfaces, particularly in cases of arrhythmic episodes. Our Results suggest that unnoticeable arrhythmias for conventional surface ECG might be unmasked using an esophageal lead with selected inter-electrode distances. The registration of more anatomical models and ECG measurements can improve the results and enable more electrical activation sequences on the heart to be researched.

References

T. Niederhauser et al. *High-resolution esophageal long-term ECG allows detailed atrial wave morphology analysis in case of atrial ectopic beats.* Med Biol Eng Comput 2012;50:769–72.

Acknowledgements

Special thanks to Dr. Matti Stenroos whose publications and open-source library about biomedical oriented boundary element methods form the cornerstone of this work.

User Interfaces for Automated Knee Rehabilitation

Constanze Hofmann

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Institutions: Institute for Laboratory Technology ILT, University of Applied Sciences Rapperswil
Examiners: Prof. Dr. Kenneth Hunt and Prof. Dr. Agathe Koller

Introduction

The knee is the biggest and most complex joint in the body. Due to its complexity it is vulnerable to injuries and diseases. Knee surgery and knee injury cause tissue injuries within and around the joint. These can lead to scar tissue formation and tissue adhesions. This is why the rehabilitation of the knee is a crucial part in maintaining joint movement. The patella (kneecap) is the small sesamoid bone in the front of the knee articulating with the femur (thigh bone). Tissue adhesions usually occur around the patella. Therefore patellar mobilization as part of the rehabilitation process of the knee is essential.

The University of Applied Sciences Rapperswil, Switzerland developed a robotic device to mobilize the patella called the Knee Rehabilitation Device (KRD). The most critical part of the KRD is the patella gripper which is in direct contact with the patient. A measurement system has not been implemented yet.

The aim of this thesis was to develop new patella grippers and a measurement system to measure patella deflection and the force to mobilize the patella during therapy sessions.

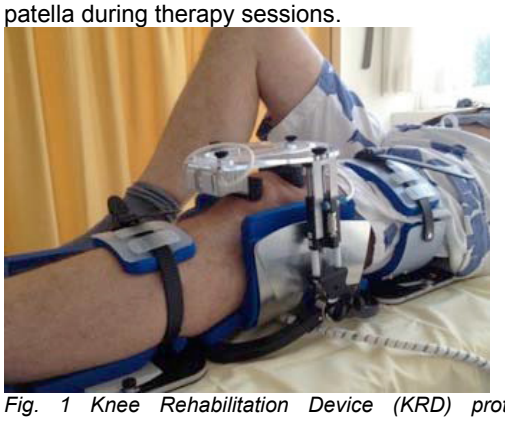

Fig. 1 Knee Rehabilitation Device (KRD) prototype developed by the ILT, University of Applied Sciences Rapperswil

Materials and Methods

The new patella grippers consist of a metal base gripper connected by a screw joint to the KRD and a soft material fixed on the metal gripper. The soft material ensures a comfortable interface to the patient`s patella.

The measurement system consists of two foil potentiometers which measure the distance, two force sensitive resistors as force sensors, a microcontroller board, a display and a switch to start the measurement. The sensor values are displayed on the display and the data is written to a text file which can be selected for analysis if connected to a PC.

Results

The patella grippers and the measurement system was integrated into the existing prototype and tested. The force transmission of the new patella grippers was superior to the previous grippers. The new patella grippers were reported as very comfortable and they could adapt easily to different sized and shaped patellas. Initial tests could be performed at the Medical Center Bad Ragaz. But the measurement system could not be tested with adequate methods to prove its precision. The realized 9V battery supply is not sufficient as it lasts only for a few hours.

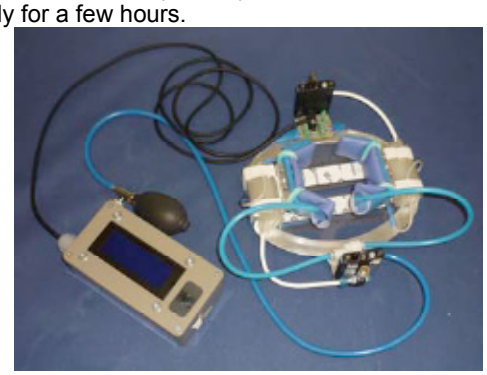

Fig. 2 Newly developed patella grippers and newly developed measurement system installed on the KRD

Discussion

The patella grippers need to be tested with more patients to ensure that the new design is suitable for many patella sizes and shapes.

The measurement system needs to be revised as the power supply is not secured. The circuit chosen for the force sensor allows a current that is too high for the force sensors. This must be changed before the measurement system can be used for force measurement. Another concept to transmit force on the sensor has to be considered as well.

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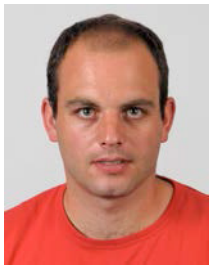
Characterization of Human Mesenchymal Stem Cell Clones for Intervertebral Disc Regeneration

Clément Huguenin



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Examiners: Prof. Dr. Benjamin Gantenbein-Ritter and Dr.Jivko Stoyanov

Introduction

The occurrence of back pain, the related loss of quality of life and the related costs are huge. Back pain is mostly due to intervertebral discs degeneration. Regenerative medicine is a promising field of research to develop treatments against intervertebral disc degeneration. Mesenchymal stem cells (MSC) have a therapeutic potential which could be used on this purpose. Nonetheless, the state of the art methods of isolation of MSC lead to heterogeneous cells populations composed of multipotent stem cells, progenitors cells and fibroblasts. It is known that the therapeutic efficacy of mesenchymal stem cells is positively correlated with their content in multipotent cells. The methods of purification and isolation need to be improved to augment the fraction of multipotent cells in the harvested cells population. It implies work in the characterization of mesenchymal stem cells namely in term of proliferative properties, genes expression profile and surface marker profiles. Moreover, in the perspective of therapeutic use of MSC for IVDs regeneration we wanted to investigate the differences and the interactions between MSC and nucleus pulposus (NP) cells.

Materials and Methods

We cultured NP cells, MSC and bi-gender co-cultures of them for tri-lineages differentiation (osteogenic, chondrogenic and adipogenic). We investigated the presence of multipotent cells or of precursors cells with adipogenic or osteogenic potential in the NP. We compared the expression and the accumulation of specific cartilage molecules in NP cells and MSC cultures and in NP cells-MSC co-cultures. On this purpose, the cells were cultured in chondrogenic media in 3D matrix (collagen). We measured the fraction of NP cells and MSC in the co-cultures after osteogenic and chondrogenic differentiation. It was done quantifying by qRT-PCR the relative quantity of Y chromosomes marker genes in the genomic DNA extracted from the co-cultures. We compared the proliferation dynamic of bi-gender MSC co-cultures along expansion and during differentiation, on this purpose the fraction of each cells population were measured with the Y chromosomes marker based method at the end of the differentiation and at 3 passages of the expansion.

Results

We didn't find cells with adipogenic or osteogenic potential in the NP. We showed that the MSC cells population which proliferate the faster during expansion proliferates also the faster during differentiation. We showed an high expression and accumulation of collagen type II in MSC and none in the NP and we showed that the fraction of NP cells in the NP cells – MSC co-culture is augmenting during differentiation

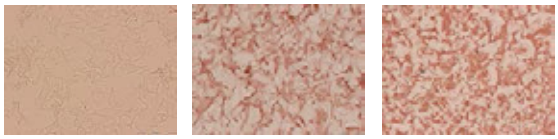

Fig. 1 Immunohistological staining for collagen type II after 28days of culture in 3D collagen matrix. The left sample corresponds to 100%NP cells, the middle one to 50%NP cells-50%MSC and the right one to 100%MSC.

Discussion

The very important differences between NP cells and MSC in the genes expression and in the accumulation of collagen type II is contradicting with the literature and open questions.

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Acknowledgements

Thanks to my supervisor, the Dr.Jivko Stoyanov and to his team for their counsels and their support. .

Novel Approach for a Control Loop for Piezo Motors

Matthias Hutter

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Institution: Institute for Human Centered Engineering, Bern University of Applied Sciences

Introduction

A device of the industry partner of this project uses ultrasonic, piezo linear motors to actuate optical elements guiding laser beams used for imaging and machining applications. For precise actuation, PID controllers with extended, piezo-specific functions are used.

The optics must be precisely actuated at high velocities with good repeatability in order to achieve a clean dissection of the tissue. The current state of the art requires tedious manual tuning of the controllers to reach satisfactory performance.

The goal of this master thesis was to develop a toolkit to assess the performance of different mechanical and electronic setups and controller settings. The toolkit could then be used to automate the tuning process or to evaluate novel approaches to control the piezo motors.

Materials and Methods

The test setup used for most experiments consists of the main controller board as used in the device and the optomechanics including the piezo motors. The electronics controlling the device include an ETX form factor computer-on-module and multi-axis motion controller cards.

The test setup was connected to a dSPACE MicroAutoBox II system. A model was then developed in Matlab/Simulink and run on the MicroAutoBox II to monitor in real time the position and controller output of the piezo-actuated axes.

A test method to evaluate system performance was developed based on circular motion patterns. To evaluate the trace files obtained in the test, a performance prediction model was developed. This model calculates an estimated precision value based on the trace files. The model focuses on the repeatability of the motion, as this is the key problem for the actual usage of the device.

The device's software running on the ETX computer-on-module was extended with the functionality required to autonomously perform motion test runs, using pre-programmed trajectories and controller settings. This allowed for automated data collection.

To test the developed prediction model, two series of experiments were conducted which allowed to tune the model parameters by comparing model prediction to actual outcome.

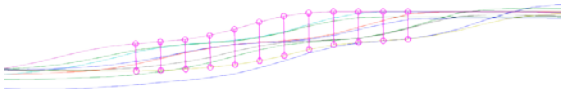

Fig. 1 Visualization of motion paths at an axis turning point. The magenta markers highlight lateral deviations between subsequent passes that are above threshold.

Results

Most elements of the envisaged toolkit were realized. Testing of alternative control approaches or adding an appropriate optimizer algorithm to automatically tune the existing controller is now feasible. However, the performance prediction model still has its limitations, see our discussion below.

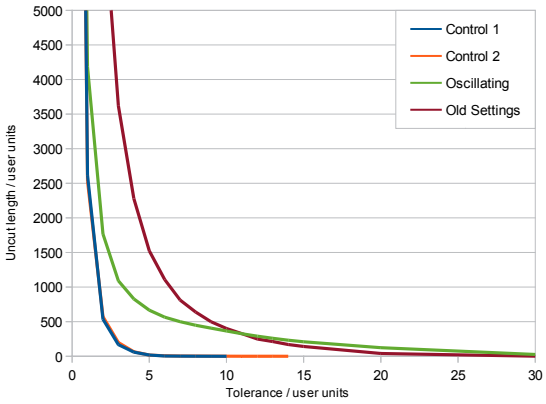

Fig. 2 Prediction model result of several test runs, depending on allowed tolerance. At 5 user units, Control 1 and Control 2 are essentially zero whereas the Oscillating sample (incorrectly) and the Old Settings sample (correctly) indicate insufficient cutting precision.

Discussion

Due to the complexity of piezo linear motor control, as well as the lack of literature on control of the exact type of piezo motor used in the device, efforts to evaluate novel control approaches had to be deferred in favor of research on the methods and models needed for evaluation.

The performance prediction model is promising, but still not fully satisfactory because it cannot correctly handle certain motion patterns. The current model can tolerate lateral path deviations below a threshold, but is unable to tolerate them if they occur only over a short distance (see Fig. 2).

Further refinement of the model is required, as are experiments to validate the model.

Acknowledgements

The project was supported by the industry partner.

Use of Electrical Stimulation of Hepatic Neurons to Improve Glucose Homeostasis

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Examiners: PD Dr. Jürgen Burger and Prof. Dr. Josef Goette

Introduction

Overall glucose homeostasis is maintained by regulating liver glucose production and peripheral glucose uptake. Insulin, a hormone secreted from the pancreas, has historically thought to be the major regulator in this process.

Type 2 diabetes mellitus (T2DM) is a disease characterized by insulin resistance which leads to increases in glucose levels. However, the genesis of this disease is multifactorial and indeed, accumulating evidence suggest that the brain's ability to regulate hepatic glucose production is also a key player in the dysregulation of glucose homeostasis in T2DM.

The textbook description of the central nervous system regulating blood glucose has historically focused on the sympathetic innervation of the liver. It has been shown that electrical stimulation of the hepatic sympathetic nerves does lead to an increase in glucose. The role of the parasympathetic innervation in glucoregulation has been mostly established via denervation studies. Here we hypothesized, that electrical stimulation of parasympathetic nerves to the liver will improve glucose homeostasis. The aim of this thesis was to verify this assumption, by stimulating the common hepatic branch in rats and simultaneously observing the blood glucose level.

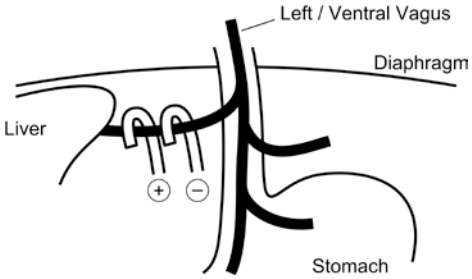

Fig. 1 Placement of the electrode around the common hepatic branch. of the vagus nerve.

Materials and Methods

Study 1. Acute electrical stimulation was performed for 1 hour in anesthetized lean and obese rats. Together with the initiation of the electrical stimulation, 1.5 ml of 50% dextrose or saline was injected into the stomach, in order to mimic postprandial conditions. Blood samples were taken prior to and during the study for glucose, insulin, and assessment of gastric emptying rate.

Study 2. In 4 rats an electrode was implanted to study the impact of acute electrical stimulation on glucose tolerance in conscious chow-fed rats. The glucose tolerance test involved an intraperitoneal dextrose injection, followed by 2 hours of electrical stimulation while the animal remained unrestrained in their home cage. The same study was repeated after one week of 60% high-fat diet feeding.

The lean animals were used to study the impact of the electrical stimulus in the healthy animal. Obese rats were used to discover the possible influence of the stimulation in diabetic patients. Rodents unlikely develop T2DM, however they become glucose intolerant when put on a high-fat diet over a certain amount of time.

A signal with 0.3 ms wide 4 mA peaks every 71 ms, an on-time of 0.1 s and off-time of 4.9 s was applied to all animals that received stimulation, except for 5 animals, on which different frequencies and currents were tested.

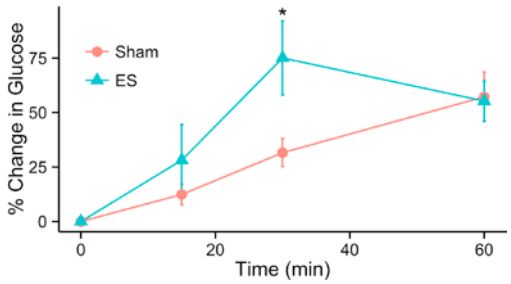

*Fig. 2 Effect of electrical stimulation (ES) on blood glucose level in obese rats compared to non-stimulated control animals (Sham). Dextrose was injected into the stomach together with the initiation of the stimulation at the 0 min time point. *P < 0.05 vs. sham.*

Results & Discussion

The results from the studies in lean unconscious or conscious animals did not show any significant change in blood glucose levels, insulin secretion or gastric emptying. However obese animals had significantly increased glucose and insulin levels after a dextrose injection and 30 minutes of stimulation under anesthesia. These data suggest that the used stimulation paradigm would not be effective as a therapy for T2DM. Further studies are needed to determine if different stimulation signal may alter glucose homeostasis in a positive manner.

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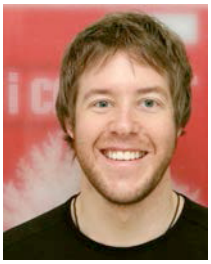
Novel Sensor Belt Connector for an Electrical Impedance Tomography Device

Roger Infanger



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Bern University of Applied Sciences, Biel
Swisstom AG, Landquart
Examiners: Prof. Dr. Volker M. Koch and Dr. Pascal O. Gaggero

Introduction

The company Swisstom AG is currently developing an electrical impedance tomography (EIT) heart-lung monitor. One of the major obstacles for the production of the final product was the electrically unreliable connector of the active electrode sensor belt, the SensorBeltConnector (SBC). The goal of this master thesis was to develop a novel SBC with the following requirements:
The single-use part "DockingStation" must have a durability of 50 connection cycles, despite its low-price requirement. The correspondent multi-usage part "MatchBox" must endure 11'000 connection cycles. Contact resistances of the 14-pin SBC should remain smaller than 1 Ω during the whole life span.

Materials and Methods

Multiple shortcomings of the initial SBC design were identified. Redesigning tasks were implemented in CAD for the DockingStation part as well as for the MatchBox part. Three prototypes with alternative designs were built and verified.
A test suite was developed to evaluate conformance of the final SBC prototype with the requirements. Fig. 1 shows the implemented mechatronic system, which allows repeated connection and disconnection of the MatchBox from the DockingStation and measurement of the contact impedance. The control of the actuators and the impedance measurement system was realized by an Arduino microcontroller board. Impedance measurement data of the SBC contacts is transmitted to a host PC and processed in Matlab.

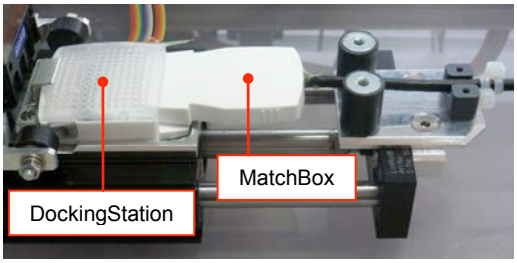

Fig. 1 *Test suite with DockingStation and MatchBox*

A sample size of 20 final DockingStation prototypes underwent contact quality tests on the test suite. 50 connection cycles, followed by 72 hours service life storage and again 50 connection cycles were performed. The contact impedances of each of the 14 pins were measured after each cycle.

The MatchBox part was cycled in a durability test for 22'000 connections and disconnections while monitoring the contact impedances after each 100th cycle.

Results

Mean contact impedance remained below 0.25 Ω before and after the 72 hours service life storage (see Fig. 2). No disconnections could be detected on any contact of the test sample lot. Mechanical interlock of the MatchBox with the DockingStation remained fully functional after completion of the 22'000 cycles. The galvanic hard gold layer of the contact pads has remained intact. The rise of the mean impedance on the SBC contacts was minimal and remained below 10 mΩ during 1'000 connections and disconnections.

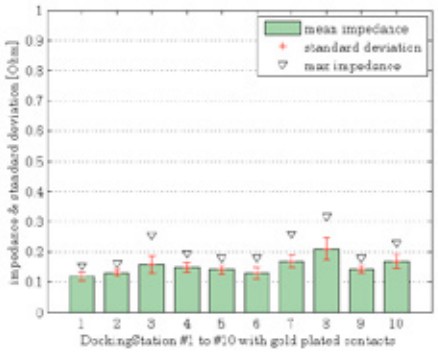

Fig. 2 *SBC contact impedance measurements of 10 DockingStations. Results shown for 50 connections and disconnections. Each bar includes the results of all 14 pins per DockingStation.*

Discussion

Reliable functionality of the developed connector type has been successfully demonstrated on the implemented test suite. The contact quality and the durability requirements are met by the implemented SBC. Thus, the usage of the novel SBC can be recommended without any restrictions. The work done in this thesis substantially helps Swisstom to market a high quality product.

Acknowledgements

The author thanks Swisstom AG for the opportunity of working on such a multidisciplinary project. The received support throughout the master thesis was highly appreciated.

Analysis of HQ loops of Rotodynamic Blood Pumps

Silje Ekroll Jahren

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Institute for Dynamic Systems and Control, ETH Zürich
Examiners: Prof. Stijn Vandenberghe and Prof. Dr. Hendrik Tevaearai Stahel, MD

Introduction

Pulsatility is a recurring topic in mechanical circulatory support. There is evidence of reduced risk of adverse events caused by the lack of vascular pulsatility, enhanced myocardial perfusion, and heart recovery [1-3]. A commonly used method for restoring pulsatility with rotodynamic blood pumps (RBPs) is to apply a sinusoidal speed profile, synchronized to the cardiac cycle. This introduces two additional parameters that influence the (un-)loading of the heart: the timing between the heartbeats and the pump pulses (i.e. the phase shift), and the pump speed amplitude.

Materials and Methods

In this study, the impact of these parameters on the heart-pump interaction was examined using the pressure head-pump flow (HQ) diagram. The first measurements were conducted using a model of the Levacor ventricular assist device (VAD) (WorldHeart Inc., Oakland, CA, USA) in a cardiovascular simulator modified from the ViVitro Model Left Heart System (ViVitro Systems Inc., Victoria, Canada). The second measurements were conducted to evaluate the effect of heart contractility upon the HQ diagram of pulsatile pump speeds, using a turbodynamic Deltastream DP2 pump (Medos Medizintechnik AG, Stolberg, Germany) in a validated hybrid mock circulation with baroreflex function.

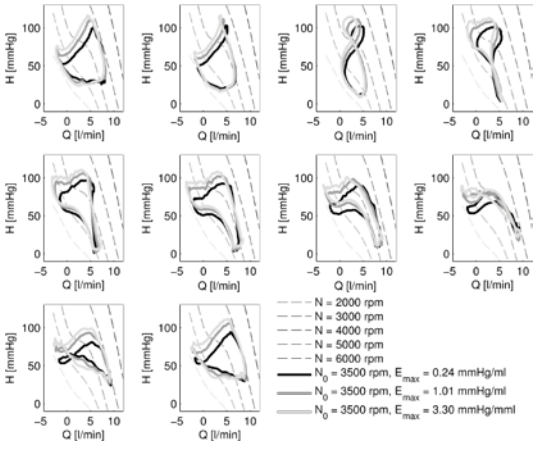

Figure 1: The effect of phase shift and increasing contractility upon the HQ loops.

Results

The level of (un-)loading and the shape of the HQ loops strongly depend on the phase shift. The HQ loops revealed a characteristic shape for each phase shift, and increased heart contribution (increased stroke work, W_S) resulted in a broadening of the loops (Figure 1). It was found that the previously described linear relationship between W_S and the area of the HQ loop A_{HQ} for constant pump speeds does not exist for pulsatile pump speeds, but that A_{HQ} additionally depends on the phase shift and the pump speed amplitude (Figure 2a). However, it was found that there exists a linear relationship between W_S and A_{HQ} for each phase shift (Figure 2b).

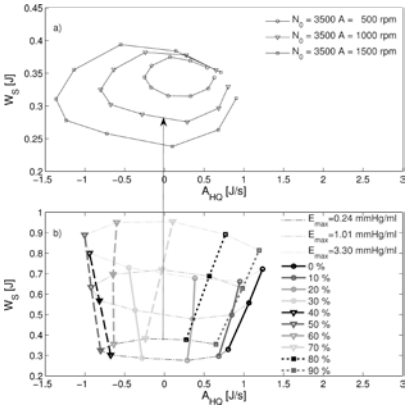

Figure 2: Panel a) shows W_S versus A_{HQ}. Panel b) shows W_S versus A_{HQ} for different contractilities and different phase shifts.

Discussion

The phase shift strongly influences the loading of the left ventricle, and can therefore be used to fine tune the load of the ventricle to the need of the patient. A linear relationship between W_S and A_{HQ} exists for each phase shift, which could be used to predict W_S. The shape of the HQ loops could be used for live tracking of the ventricular load. This can be a useful tool to discover if the ventricle is recoverable or not. The results of this study need to be validated with in vivo measurements.

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Acknowledgements

This study was funded in part by the Swiss 3R Research Foundation, by the NIH grant R01 HL086918 and by a grant of the Swiss National Science Foundation (project #32003B_127443/1).

An In-Vitro Model for the Characterization of Immiscible & Nonlinear Multiphase-Flow in Porous Media

Patrick Käppeli

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Examiners: Prof. Dr. Stephen Ferguson and René Widmer

Introduction

Damages to the spine highly affect the quality of life. Illnesses like osteoporosis and fractures of vertebrae can lead to an impairment of the patients range of motion and cause pain. Vertebroplasty is a minimally invasive treatment option for spinal fractures that can promote a better spine function and thereby increase the patient's well-being. However complications related to uncontrolled flow of the augmenting biomaterial remain a concern. The main objectives of this study were to develop and verify experimental methods for the generation of data for the validation of computational flow models. Prior studies have used metallic foam and dairy butter to emulate the real bone / marrow. (Loeffel, 2008) In this study, a new approach is made by using models produced with rapid prototyping technology and a polyethylene glycol mixture as marrow and biomaterial substitutes.

Materials and Methods

An experimental set-up was designed and every element of it has been verified to be working as intended. For the production of a physiologically-relevant specimen using rapid prototyping (RP) technologies, segmented clinical CT data had to be adapted for manufacturing. The models then have been qualitatively examined for their suitability for the planned experiments. In a similar way, appropriate liquids had to be found to substitute bone marrow and bone cement as the use of real bone cement was not possible due to the time-frame needed for image acquisition, and the desire to re-use the RP specimens. The injection process was also extensively tested. Images were made from 180 angles with a step increment of 1°. This was achieved by using a high- precision step motor as a positioning tool for the syringe and the connected specimen. The generated data then can be used for 3D – reconstruction.

Fig. 1 Experimental set-up for fluoroscopy measurements during bone cement substitute injections

Results

The manufactured specimen had an acceptable level of accuracy to perform well in the experiments. There is room for improvement, however, as the delicate structures of osteoporotic cancellous bone were either printed too thick or not at all.

Positioning and injection accuracy were suitable for the experiments. Positioning errors only occurred due to the minimal step widths. The relative error for positioning is at 0.111%±0.008%. Injection experiments with water in 0.5 ml steps resulted in an average of 500.69 µl being injected.

The main experiment resulted in a complete data collection for each injection step. The following images in figure 2 show processed samples.

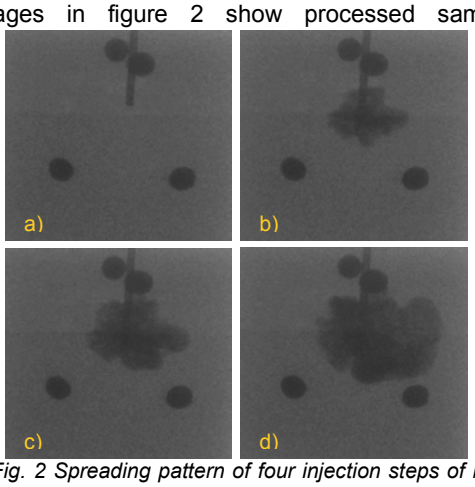

Fig. 2 Spreading pattern of four injection steps of bone cement substitute. a) 0.0ml b) 2.0 ml c) 4.0 ml d) 9.0 ml

Discussion

The results show a flow pattern that can be expected in comparison to patterns occurring during vertebroplasty. An interesting discrepancy between measurements with rapid prototyped specimens and metal foam is shown, with a more diffuse heterogeneous filling in the RP specimens, as is also observed in natural bone. While the manufactured specimens were acceptable for testing, the use of rapid prototyping in biomechanical experiments is still limited, as accuracy and material properties are not yet suitable in every case.

References

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Study of the Electrical Conductivity of Tissues and Organs for Electrical Impedance Tomography

Anna Khimchenko

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Institutions: Institute for Human Centered Engineering - BME Lab, Bern University of Applied Sciences
Examiners: Prof. Dr. Volker M. Koch and Dr. Stephan H. Böhm

Introduction

The literature about conductive properties of biological tissues is very controversial and large value differences are being found. The challenge faced in present thesis was to master the measurement of impedance of biological tissues within the electrical impedance tomography (EIT) frequency range from 1 kHz to 1 MHz. Moreover, the clinical effectiveness of EIT is often tested in expensive animal studies. In this work, we propose a possible surrogate for in-vivo animal experiments based on the use of ventilated excised pig lungs placed in a saline tank.

Materials and Methods

The impedance measurements were performed by an impedance spectroscope HF2 from Zurich Instruments (Zürich, Switzerland). Based on analytical and numerical analysis, we developed a dedicated measurement probe. The measurement head of the probe was composed of an linear horizontal Wenner electrode array with four gold-covered stainless-steel electrodes (diameter: 0.49 mm, inter-electrode spacing: 1.91 mm, height: 3 mm). The measurement set-up was calibrated using saline solutions of various known molarity.

The tissue samples, from pigs, were acquired at a local slaughterhouse. The fresh samples were examined between 1 and 14 hours after death.

The imaging of the lung's ventilation using the 32 active-electrode EIT system "Pioneer Set" from Swisstom (Landquart, Switzerland) was realized within a saline water tank. The lungs were kept open, even under water, by closing the upper part of the tank with a tight cover, which in some extend mimic the physiology of the thorax. In this way, the lungs can be kept open and ventilated with pressures in the physiological range.

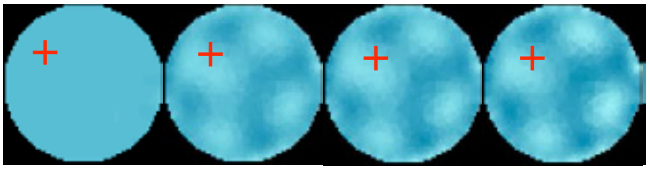

Fig. 1 EIT images of pig lungs placed into the EIT test tank filled with a saline solution with 9 g/l NaCl. Pressures in the trachea (a) 0 cmH_2O, (b) 34 cmH_2O, (c) 43 cmH_2O and (d) 144 cmH_2O. The cross is the test pixel.

Results

From the analytical and numerical analysis the minimal sample size, which satisfies the infinity assumption, is given by minimal width 16a, height 5a and spacing between the sample's border and the nearest electrode 8a, where a is the inter-electrode spacing. For liver, heart and lungs the specific impedance results are found in the same value range as the one reported in the literature. Nevertheless, we observed differences of 2% between the references and the measurements for the liver two hours after death. In the second part of this work, we were able to ventilate excised lungs within a saline water tank. The lungs exhibited the expected hysteresis curve in the impedance versus pressure plot, reported in Fig. 2.

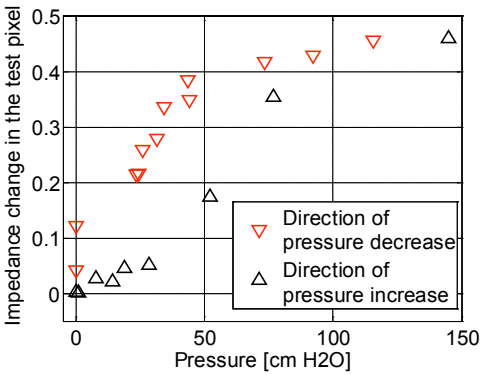

Fig. 2 Impedance change of the pig lungs placed into the EIT tank filled with a saline solution in function of the air pressure at the trachea. The impedance was taken from the pixel marked by the cross on Fig. 1.

Discussion

In this work, we developed a robust and well documented method to measure the specific impedance of biological sample; the results correspond to the findings of similar studies. The differences could be explained by 1) the sample water content, 2) the sample freshness (time degradation of the tissue after death), 3) the room temperature and 4) the localization of the measurement spot. For the later this is especially true for highly heterogeneous organ such as lungs.

The developed experimental set-up for ventilating excised pig lung shown promising results. A similar set-up could potentially be used as a surrogate for in-vivo animal studies and/or for the pre-clinical testing of EIT instruments.

Simulation of Air-Guiding in a Respiration Therapy Device

Birgit Lehretter

Supervisors: Prof. Bernard Schmutz, Damien Maurer, Diego Stutzer
Institutions: Institute for Human Centered Engineering – BME Lab, Bern University of Applied Sciences
Examiners: Prof. Dr. Volker M. Koch, Prof. Bernard Schmutz

Introduction

Respiratory therapy devices are used for patients suffering from lung disease with breathlessness. A state-of-the-art system (not further specified here due to a non-disclosure agreement) has the disadvantage that it can only be used in a horizontal position during the therapy. Furthermore, it is only possible to train at rest. The optimization includes on the one hand the improvement of the gas mixture control and on the other hand an included variable breathing resistance. This will allow a more flexible respiratory therapy.

Materials and Methods

This master's thesis supports the optimization of the device in the area of breathing resistance. The final goal is simulation and analysis of the air-guiding in the optimized therapy system (Fig. 1). The analysis covers both the interaction of the different components and the mixing ratio of the gas-mixing module. Also the ratio of pressure, volume flow and cross section is analyzed. Therefore, the system is simulated for several volume flows. The simulation of the air-guiding through the device is done with the software Comsol Multiphysics Version 4.3a.

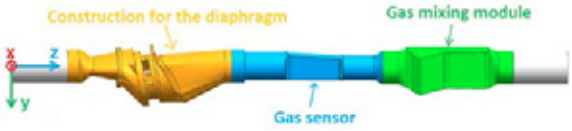

Fig. 1: CAD air-guiding model of the respiratory therapy device

To become acquainted with CFD simulations, the diaphragm was simulated first. This was done according to the standard EN ISO 5167-1, which uniquely defines the structure and the constraints of the diaphragm. Furthermore, the diaphragm is a possible breathing resistance. The gained knowledge and experience was the basics for the subsequent simulation, analysis and optimization of the therapy system.

Results

The oval shape of the inlet pipe to the diaphragm influences the mass flow distribution through the openings of the diaphragm. Therefore, also the streamwise orientation of the openings plays an important role: The orientation influence the dissipated power over the system. The influence can be even around 20 %.

The examination in the field of static pressure measurements shows that the difference in the measured pressure between the measuring tube (Fig. 2a) and the measuring ring (Fig. 2b) simulated at a positive volume flow is in the range of 0.2 %. The advantage of the measuring ring is the homogenous pressure distribution in the ring. The complicated cleaning of the ring supply channels is a disadvantage.

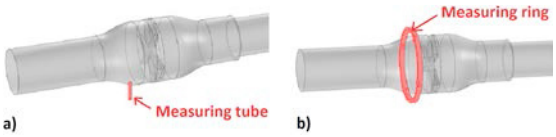

Fig. 2: Pressure measurement with a) measuring tube, b) measuring ring

Problems occurred with the gas-mixing module: it was not possible to simulate the mixing ratio. With this model, the limitation of the k-epsilon turbulence model of Comsol was reached. Also the turbulence model k-omega seemed not very suitable for solving these problems. Therefore, further research has to be done to solve these problems.

Discussion

The analysis of the air-guiding in the optimized therapy device model gave important information about the interaction of the various components and the influence of diaphragm shape. This supported the project in the design optimization.

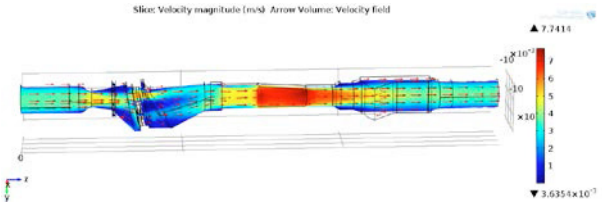

Fig. 3: Velocity magnitude and the vector plot of the velocity field through the device with the software Comsol

The graphical comparison of results between simulations and initial experiments shows a good match. But deviations occur since the simulation does not take certain real effects into account (such as leakage, different inlet velocity profile etc.).

Future work includes further investigations into turbulence models, mesh-quality and CAD geometry polishing.

Decision Forests for Multimodal Brain Tumor Segmentation

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Examiners: PD Dr. Mauricio Reyes, Prof. Dr. Paolo Favaro

Introduction

Brain tumor segmentation is considered to be one of the most challenging tasks in medical image analysis. It plays a major role in different clinical areas such as radiology, radiotherapy planning and surgical planning.

The present thesis focuses on machine learning-based approaches for solving the problem of segmenting brain tumors from multimodal magnetic resonance image data. In medical science, answers to questions are mostly beyond a simple “right or wrong” and thus should be expressed in terms of a degree of belief (probability) we hold in them. Machine learning techniques have in common that they learn a hypothesis from training data which is able to perform a prediction about the true state of interest on new testing data. An integral part of the thesis are a class of machine learning methods called decision forests.

We hypothesize that the generalization and thus performance of machine learning-based models for brain tumor segmentation can be improved by addressing the representation of the input data, the complexity of the model and the amount of training data. The aim of this thesis is to verify this by improving a baseline model [1] with regard to these three aspects.

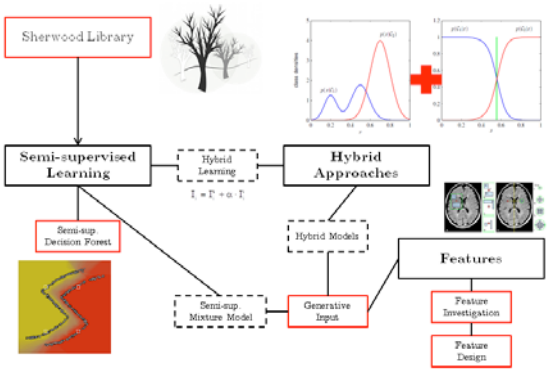

Fig. 1 Structure of master thesis.

Materials and Methods

In a first part, current and novel features for brain tumor segmentation were investigated. In doing so, feature importance measures derived from the structure of decision forests were employed to gain insights about their role for the task at hand. Consequently, the baseline model was enhanced by an optimized feature set.

In a second part, a novel generative-discriminative hybrid algorithm was developed. The main motivation behind this endeavor was to utilize complementary properties of generative and discriminative models regarding generalization.

In a final part, a semi-supervised modification of the decision forest model was explored with the purpose of studying the effect of additional unlabeled data on the performance of the baseline model.

Results

By experiment, it has been shown that a modified feature set can lead to an improved generalization given an intermediate amount of training data. In case of the hybrid algorithm, a consistently improved segmentation of the tumor core has been observed (see Fig. 2). In contrast, performance degraded for the semi-supervised model.

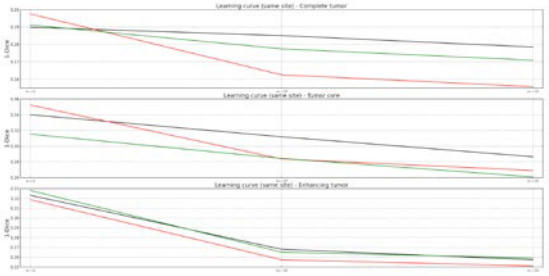

Fig. 2 Learning curves (error in Dice coefficient) of baseline model (black), discriminative model with new feature set (red) and novel hybrid algorithm (green) for varying amounts of training data (x-axis).

Discussion

We showed experimentally that both approaches *can* lead to an improved generalization and therefore segmentation performance. We could not show that a similar argument applies for semi-supervised learning. Due to computational hurdles, experiments for the semi-supervised model were performed with a simplified version of the model. Consequently, the role of semi-supervised learning in brain tumor segmentation remains an open question to be answered in future research.

References

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Laser Head Calibration

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Examiners: Prof. Dr. Philippe C. Cattin and PD Dr. Guoyan Zheng

Introduction

Osteotomy is a surgical procedure to cut bone for various purposes. Mandibular or maxillary osteotomy is performed to restructure the jaw by cutting and repositioning the bone. The bone heals slowly while the jaw is kept in place with wires or plates and screws. The conventional method to perform such an osteotomy is by cutting the bone with surgical tools like chisels or saws. The CARLO device is an approach to facilitate the procedure and to raise its accuracy by robotic guided laser osteotomy. A laser beam is redirected with a 2D mirror onto the surface of the target.

Materials and Methods

To calibrate the laser head a simple setup consisting of a CMOS camera, a 2D steering mirror and a laser diode has been used. In later experiments the laser head has been mounted on a robotic arm. The foundation of the laser head calibration is the camera calibration process. During the camera calibration additional images are acquired with laser dot corresponding to different combinations of voltages. The established camera calibration parameters allow calculating the 3D coordinates from the detected 2D laser dot coordinates in the image. These coordinates combined with the corresponding voltage settings allow calculating a mapping matrix that defines the relation between 2D coordinates and voltage settings.

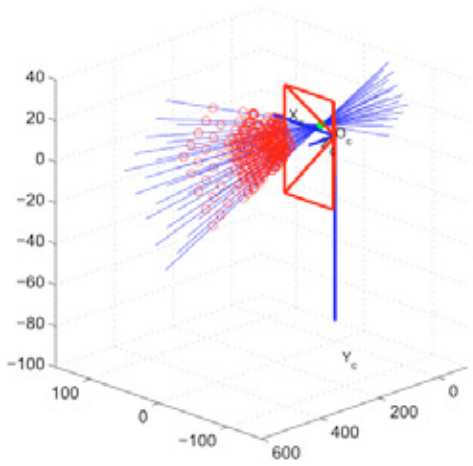

Fig. 1 MATLAB visualization of the detected laser dots and the bundle point transformed into the 3D camera coordinate system.

Verification of the method has been done by calculating the reprojection error and the mean distance of the laser beams to the bundle point.

Results

The calibration of the camera led to a reprojection error of around 0.2 pixel in x- and y- direction. The calibration of the steering mirror increased the reprojection error to 0.4 pixel in x- and y- direction. The mean distance of the laser beams to the bundle point is around 65 µm. Figure 2 shows the mean reprojection error projected on one chessboard compared to the detected points.

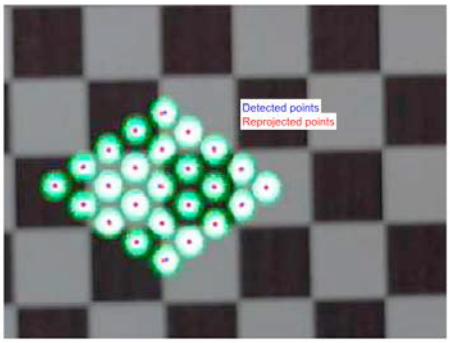

Fig. 2 Visualization of the assembled laser dots on one chessboard comparing the detected to the reprojected coordinates.

Discussion

Based on the calculated results and the visualizations it can be said that the proposed method is capable of calibrating the laser head of the CARLO device. The relevant tasks for a fully automatic calibration have been developed and documented furthermore, an overall improvement of the accuracy with the steering mirror has been shown.

Further improvements can be done regarding detection of the laser dot and the camera calibration. The influence of the camera calibration parameters is significant, attention should be payed when calibrating the camera to achieve the best possible result. The laser dot detection is a crucial part of the calibration and leaves room for improvement.

A future implementation in an existing C++ framework is planned and can be realized and finally implemented into the CARLO device.

References

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Foot-Stimulation Module (FSM) for a Robotic Tilt-Table

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Institutions: 1. Institute for Rehabilitation and Performance Technology, BFH
2. Hocoma AG
Examiners: Prof. Dr. Kenneth J. Hunt and Prof. Dr. Tobias Nef

Introduction

Robotics-assisted tilt-table technology has recently been introduced in the field of neurological rehabilitation. This is applied to patients with a variety of impairments including stroke and spinal cord injury. The Erigo system (Hocoma AG) is a leading product in the market. Erigo is a tilt-table with two actuators which move the legs in a cyclical gait-like pattern. It has been shown that an adequate stimulation during the cyclic movement of the lower limbs activates the relevant sensory-motor areas in the brain. This is very important for the restoration of functional capacity after neurological injury or disease [1]. Therefore, it has been hypothesised that an additional foot-sole vibration module for the Erigo can activate further sensory-motor areas.

Materials and Methods

Firstly, a research phase was undertaken to evaluate the technical state of the art concerning vibration devices as well as the physiological background. The knowledge of the technical, as well as the physiological requirements provided the possibility to combine these two fields. This phase concluded with a design proposal. The design process during the second phase was marked by the evaluation of various actuator systems. After a decision on the basic principle was made, three different stages of functional prototypes were built. These prototypes were based on the results of the prior prototype.

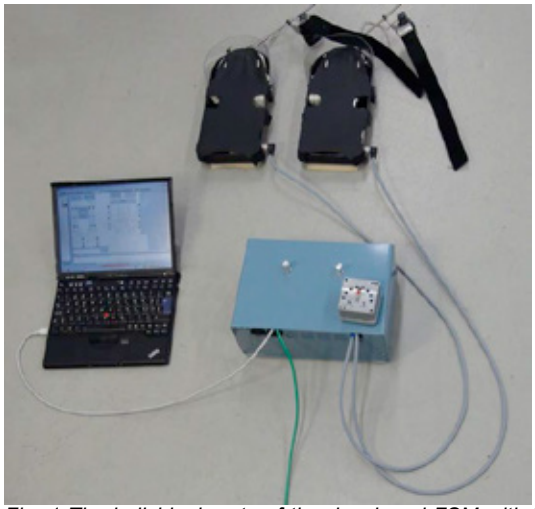

Fig. 1 The individual parts of the developed FSM with the foot shells, control box and laptop.

The final stage was concerned with an analysis of the produced vibration and the modification of the latest prototype.

Results

The research phase showed that variable vibration intensities are more beneficial than permanent vibrations. Due to this finding, a novel vibration device was developed which, despite its compact size, can stimulate three different foot zones. The quantification of vibration showed that the oscillations move in all directions and varied strongly with respect to frequency and amplitude.

Fig. 2 The FSM is combined with the Erigo to stimulate different foot zones individually depending on the actual leg position.

Discussion

A foot stimulation module was developed, which can stimulate various foot zones in accordance with different positions of the leg. Tests showed that there are physical limits for the FSP which cannot be changed easily. Applied mechanical vibrations are powerful enough to stimulate the human body strongly. The developed device is a promising addition to the Erigo. Physiological and clinical studies are planned for the near future.

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Kremneva EI, Chernikova LA, Konovalov RN, Krotenkova MV, Saenko IV, Kozlovskaya IB (2012) Activation of the sensorimotor cortex using a device for mechanical stimulation of the plantar support zones. Human Physiology 38(1):49-55

Development of a new Chemoresistive Microfluidic Chip for Spheroids Formation.

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Institution: ARTORG Center for Biomedical Engineering Research
Examiners: Prof. Dr. Olivier Guenat and Dr. Thomas Marti

Introduction

Spheroids are sphere-shaped (three-dimensional) cell colonies formed by self-assembly that allow various growth and functional studies of diverse tissues. Spheroids are known to provide more reliable and meaningful therapeutic readouts in cancer treatment as they mimic more closely the cells in vivo conditions. We have developed a novel microfluidic chip that enables spheroids formation on chip which will ultimately be used in personalized medicine applications. As in personalized medicine approach the patients own cells will be available in small quantity, the chip is designed to form spheroids with small amount of cells which can later be tested with chemoresistive assays.

Materials and Methods

A microfluidic chip composed of three layers structured by polydimethylsiloxane (PDMS) was fabricated by rapid prototyping using soft lithography. A 70µm thin PDMS membrane sandwiched between the bottom and middle layer is deflected by applying pressure from the top. Once deflected, uncured PDMS is added on the deflected membrane from the bottom end of the chip and allowed to cure on a hot plate to retain its hemispherical shape.

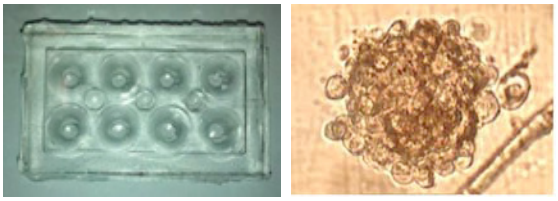

Fig. 1: Left: Image of a 43x25x8.5mm microfluidic chip with 8 microwells for spheroid formation. The distance between two adjacent microwells is 9 mm. Right: Image of a spheroid (diameter 191µm) formed after 48 hours using a cell seeding density of 300 cells per microwell.

Hemispherical shaped microwells of the microfluidic chip are coated with 1% (w/v) Synperonic F-108 preventing cell adhesion. Afterwards, mesothelioma H2052 cells with different cell densities were seeded on the chip. The chip was then centrifuged so that cells aggregate (pellet). Then the chip is placed in an incubator at 37°C and 5% CO_2 to create spheroids from the cell aggregate. The project focuses upon the geometry (in particular the radius or deflection) of the microwells and the formation of spheroids obtained on changing the cell seeding densities.

Results

The size of the spheroids in diameter (µm) obtained with cell seeding densities of 300, 500 and 1000 cells per microwell were 199 ± 18, 254 ± 25 and 367 ± 14 after 48 hours, whereas it increased to 264 ± 11, 296 ± 15 and 421 ± 65 after 72 hours, respectively.

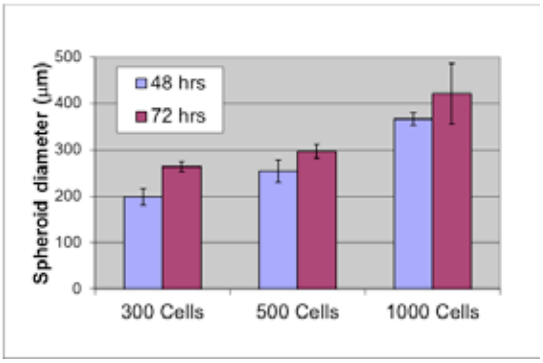

Fig. 2: Growth of the spheroids on chip in function of time and of the cell seeding densities.

Conclusion

We present a novel microfluidic chip, on which spheroids are formed with cell densities ranging from 300 to 1000 cells per microwell. The microfluidic chip allowed the spheroids to be cultured for up to 72h. The clear advantage of this chip in comparison to other microfluidic chips used for spheroid formation is its capability to seed an accurate amount of cells per well. The process of centrifugation of the cells on chip provides a fast way to produce spheroids. It is also possible to individually monitor the morphological changes occurring in the spheroids formation.

References

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PHEMA Based Coating for Sustained Delivery of Antimicrobial Active Compounds in Orthopedic Device Associated Infection Therapies

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Institutions: RMS Foundation, Bettlach.
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Introduction

Temporal implants are often used in two stage procedures to treat devices associated infections (DAI) in orthopedy. They are made of poly(methyl methacrylate) PMMA loaded with antibiotic, such as gentamicin or vancomycin. However, as they are molded during surgery, the mechanical properties and the release kinetics are not reproducible [1].
The aim of this study is to develop a coating system for metallic implants, formed by a hydrogel, which contains the antibiotic. The release should be sustained for 1 to 2 months.

Materials and Methods

The samples were prepared using 2- hydroxyethyl methacrylate (HEMA) and polyethylene glycol (PEG) solution; in a volume relation 1/3 (HEMA/PEG). The influence of lecithin to enhance the drug encapsulation was tested. The polymerization was initiated by a combination of ammonium persulfate (APS) and tetramethylenethylene-diamine (TEMED). The 3D structure of the polymers was characterized using scan electron microscopy (SEM). The effect of the crosslinker concentration, ethylene glycol dimethacrylate (EGDMA), was evaluated with respect to the mechanical properties, which were evaluated as function of the load/displacement under uniaxial compression (MiniZwick, Zwick/Roell). The surface adhesion was calculated using a pull-out test. Metal pins coated with the hydrogels were prepared and incubated in a gentamicin or vancomycin solution of 200 mM for 4 hours. The release rate was measured by UV/VIS spectrometer (Lambda 10, Perkin Elmer).

Results

Figure 1 depicts the internal porosity of the coating. A high interconnected porous structure was observed. The porosity of the samples was calculated and compared with the elastic modulus for hydrogels of 2 basic compositions: HEMA-PEG (H-P) or HEMA-PEG-Lecithin (H-P-L) with 1, 2 or 5 wt% crosslinker (CL) (see Figure 2).

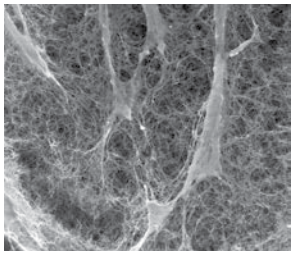

Figure 1. SEM micrograph (50 μm scale) of a cross-section of a p-HEMA coating with 1 wt% crosslink.

The *in vitro* antibiotic release was measured with and without lecithin for both antibiotics. The coating compositions with better release performance for each antibiotic are showed in the Table 1.

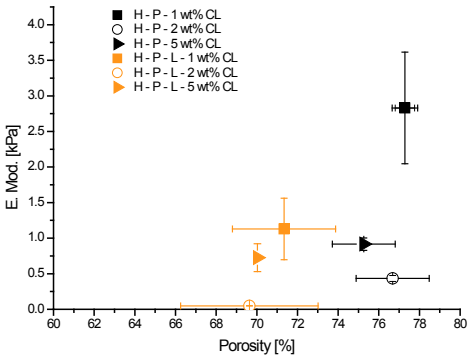

Fig. 2. Mechanical properties of both hydrogels HEMA-PEG and HEMA-PEG-Lecithin.

Table 1. In vitro drug release profiles of antibiotic-loaded coatings.

Gentamicin	H-P-5 wt% CL		H-P-L-1 wt% CL	
Accumulate release (%)	50	100	50	100
Time	0.5h	6.6h	6.0h	7.6h
Vancomycin	H-P-L-1 wt% CL		H-P-L-5 wt% CL	
Accumulate release (%)	50	100	50	100
Time	6h	27 days	19 days	19 days

The adhesion strength results showed values of 0.38 MPa (± 0.127) and 0.32 MPa (± 0.098) for Titanium and Cobalt-Chrome Molybdenum surfaces respectively. The failure occurred in the polymer body and not at the coating-metal interface.

Discussion

Lower concentration of crosslinker leads to higher strength values, due to the 3D porous structure formed by a fiber mesh that restricts the displacement between the polymeric chains. The long-term drug release rate should still be improved. The lecithin did not reflect a drug encapsulation effect. The results of the pull out test evidenced that higher adhesive strength values are required to remove the polymer coating from the metallic surface.

Reference

[1] A.E. Gross, (2005) J. Orthopedic Clinics of North America 36:49-54.

Single-View Augmented Reality Navigation System

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Examiners: Prof. Dr. Philipp C. Cattin
PD Dr. Guoyan Zheng

Introduction

This thesis explores the possibilities of combining and implementing a single-view navigation and augmented reality system based on a low-cost tablet computer. This combination offers interesting applications which are explored on two surgical procedures, namely ventriculotomy and pedicular screw placement.

Methods

Markers are attached to the patient and to the surgical tool. They are identified in the camera image by generating a binary mask which separates the markers from the rest of the image. The 2D-3D correspondence between the markers 2D projection- image positions and the known positions in the markers 3D coordinate space is established using the PRM algorithm. With these known correspondences, the position and orientation of the tool and the patient coordinate system relative to the camera coordinate system can be estimated. Using this relation one can transform the tool coordinate system into the patient coordinate system and its position and orientation in the patient coordinate system can be calculated. To gathered measurement values can then be used to guide the tool to the desired location and orientation in the patient space. At the same time the information about the position of the patient and tool in the camera space can be used to render structures at the anatomically correct position into the image.

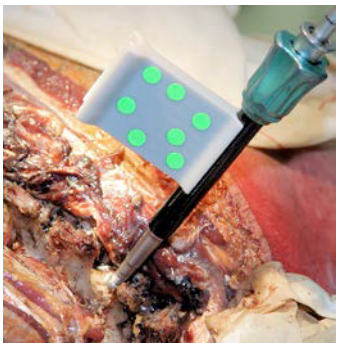

Fig. 1 Marker plate attached to a surgical tool for spinal fusion. The correct insertion direction of the screw can be monitored.

Results

In place rotation in a distance of 350mm from the camera shows a mean absolute error (MEA) of 0.155° with a standard deviation (SD) of 0.080°. Translations in direction of the optical axis in the range of 200 to 700mm show a MEA of 0.397mm and a SD of 0.452mm. Translations orthogonal to the optical axis from -225 to 225mm had a MEA of 0.498mm with a SD of 0.815mm.

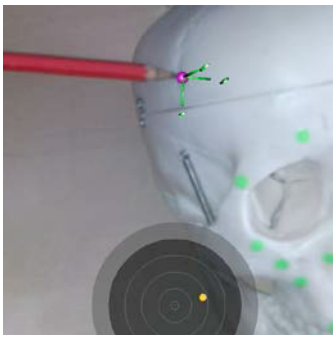

Fig. 2 Navigating a tool to a point and orientation on the patients head by guidance of augmented reality.

Markers can be recognized up to the distance of 1.7meters.
The augmented reality frame rate could be increased by +34.8% to more than 20 frames/s using various optimizations.

Discussion

The proposed single-view navigation system is suitable for intrasurgical navigation. It can be implemented on low-cost consumer hardware using the proper methods. With the addition of augmented reality a basis for a new field of applications is created.

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Model-Based Iterative Reconstruction

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Supervisor: Dr. Tobias Kober
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Siemens-CIBM, École Polytechnique Fédérale de Lausanne
Examiners: Prof. Dr. Volker M. Koch and Dr. Tobias Kober

Introduction

Diagnosis of brain tumors, strokes and multiple scleroses are just a few clinical applications of magnetic resonance imaging (MRI). Currently, MR images are evaluated qualitatively, i.e. by using the relative intensity differences between pathological and healthy tissue. In spite of the huge success of MRI in the last decades, this approach is not optimal in terms of image comparability and traceability (i.e. longitudinal intra-subject comparison). Instead, one could measure the underlying physical properties which generate the contrast differences, having the advantage of directly measuring "hard" physical parameters which are better comparable. One of the few crucial contrast-determining parameters in MRI is the longitudinal relaxation time T1. However, corresponding parameter mapping acquisition techniques are typically very long, impeding their clinical application. The goal of this project was to overcome this limitation by using an iterative reconstruction approach which allows high data under-sampling and thus drastically reduces the acquisition time. The a-priori information used for the image reconstruction is a model of the signal behavior, i.e. the longitudinal relaxation. Using this knowledge and an iterative reconstruction approach allows recovering the non-sampled data.

Materials and Methods

An existing iterative reconstruction framework for T2 mapping was extended to allow for T1 quantification (see Fig. 1). A mono-exponential signal model, which serves as a-priori information, was developed and evaluated by phantom- and in-vivo measurements. A numerical phantom was used to optimize the employed MR sequence parameters, i.e. the number of samples on the T1 relaxation curve required and the different sampling patterns. Furthermore, by using in-vivo measurements, the performance of the algorithm for different sampling schemes was tested and practical limits were investigated. All implementation was performed in Matlab (The Mathworks Inc., MA, USA).

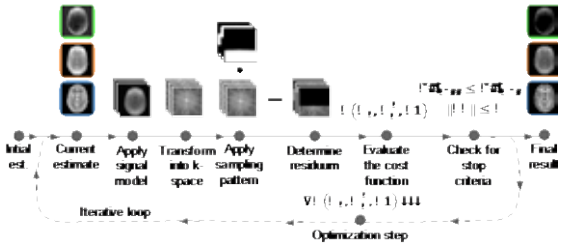

Fig. 1 Illustration of the model-based iterative reconstruction algorithm.

Results

A T1 relaxation model was developed, optimized and implemented in the reconstruction framework. Using acquired phantom and in-vivo data, it was found that randomly distributed sampling patterns yield the best reconstruction results. Furthermore, optimal acquisition parameters were deduced. Obtained T1 maps were compared to a reference mapping technique (MP2RAGE). In conclusion, it was found that clinically usable T1 maps can be obtained with up to 4-fold acceleration (see Fig. 2). This reduces the acquisition time from 12 to 3 minutes.

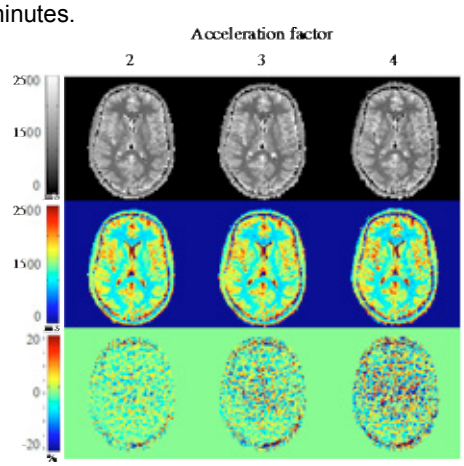

Fig. 2 T1 maps reconstructed from in-vivo measurements are shown for different AFs. The associated difference maps illustrate the dissimilarity to the reconstructed T1 map resulting from a fully sampled measurement.

Discussion

It has been illustrated that, by applying iterative reconstruction techniques and exploiting recent progress in mathematical methods, it is possible to sample the MR signal below the Nyquist limit while retaining good image quality. By further investigating Cartesian- and radial sampling patterns, as well as adding regularization to the optimization problem, acceleration factors >4 may be possible.

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Acknowledgements

The author is grateful to the Siemens AG for the opportunity to conduct this novel and challenging project.

Correlation of Bone Machining Parameters with Image Data for 3D Pose Estimation

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Institutions: ARTORG CENTER – Biomedical Engineering Research, Universität Bern
Examiners: Prof. Dr.-Ing. Stefan Weber and Prof. Dr. Andreas Stahel

Introduction

A serial robotic manipulator, designed to aid in the performance of minimally invasive cochlear implantation, has recently been developed at the University of Bern. The target application for this system involves the drilling of a tunnel from the surface of the temporal bone to the round window for inner ear access; in order to avoid contact with vital structures in the region (Fig.1) the accuracy requirements for the procedure are restrictively high.

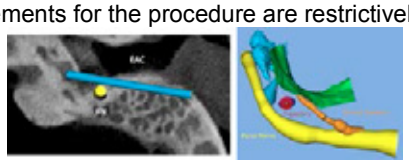

Fig. 1 Trajectory for minimally invasive implantation of cochlear implants.

The published accuracy of the system (0.56±0.41 mm) is not sufficient to safely complete the procedure and the sources of errors cannot be easily identified. It is hypothesized that a combination of optical tracking, registration, tool calibration and tool bending errors is responsible for the resultant inaccuracy. Additionally, during drilling it is essentially impossible to detect if the drill is advancing in the correct direction and that injury of vital structures will be avoided. To overcome this problem, a tool localization method based on the measured drilling forces and the density of bone within a region of interest around the planned trajectory was proposed by Williamson [1]. The goals of this thesis were to identify which components of the algorithm could be improved in order to obtain a more reliable calculation of the pose estimation, as well as the implementation of the algorithm into custom planning (OtoPlan) and navigation software (OtoNav).

Materials and Methods

The algorithm was divided in three parts: Image processing, search space and force-density correlation. An alternative to the original method for each division was proposed, having a total of 8 combinations for the algorithm.

In order to evaluate the effectiveness of each of the alternatives, as well as the final configuration, two studies were carried out. The first was a retrospective study in which a total of 18 data sets were utilized to evaluate each of the 8 proposed combinations. Once a suitable configuration was identified, a prospective study was completed; a total of 8 datasets were tested utilizing the selected combination.

The final selected algorithm was successfully implemented into both planning and navigation phases of the robotic drilling process. Additionally, a method for pre-operatively estimating the effectiveness of the force-density pose estimation algorithm based on the specific patient anatomy was identified and implemented into the planning phase (Fig.2). The effectiveness of this pre-operative "risk map" was evaluated through comparison with the final pose estimation results.

Results

Each of the eight variations of the algorithm demonstrated similar estimation accuracy (Minimum: 0.279 ± 0.145, maximum: 0.320 ± 0.164). The algorithm with the smallest error was applied to the second set of data (n=8) and the target accuracy was 0.3232 ± 0.1429.

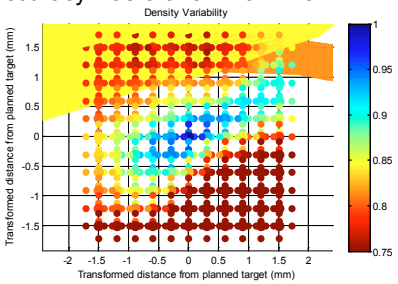

Fig. 1 Preoperative risk map showing high variability between the planned and the alternative trajectories.

Discussion

The mean accuracy of all variants was below the mean drilling error of the robot, with a smaller standard deviation. No significant differences were noted between the variations and further testing needs to be undertaken in order to select a definitive combination between the search space, the density calculation and the force-density correlation.

The preoperative planning was successfully implemented and integrated into OtoPlan and the 3D pose estimation algorithm was implemented into OtoNav. The short computation time (10ms) permits the system to calculate the position in real time. An improvement of the software interface must be done in order to show more clearly the estimated pose and confidence of the calculation in order to help the surgeons to make a decision on when to stop the procedure if one of the vital structures is at risk.

References

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Development of an S100 Protein-Based Assay for Assessment of Human Articular Chondrocytes Re-differentiation in Monolayer

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Examiners: PD Prof. Dr. Dobrila Nesic & Prof. Dr. Benjamin Gantenbein

Introduction

Among cell-based therapies to treat cartilage lesions, autologous chondrocyte implantation (ACI) represents one of the most promising approaches. However, during the expansion phase to obtain sufficient cell numbers for re-implantation human articular chondrocytes (HAC) dedifferentiate and lose their ability to rebuild hyaline cartilage. HAC redifferentiation has been intensively investigated in 3D pellet cultures. These models limit the possibility of large, comprehensive, and well-controlled comparative studies of induction of HAC redifferentiation. S100 has been previously identified as a marker of HAC redifferentiation potential[1]. The aim of this study was to develop an S100-based 2D microplate cell-based assay (CELISA) as a redifferentiation readout and to assess correlation of an increase in S100 expression in monolayer with HAC chondrogenic capacity of 3D cell pellets.

Materials and Methods

S100 cells-based ELISA (S100 CELISA) was optimized using S100-positive A2058 cell line and S100A1/B antibody. Principle of the assay is provided in Fig. 1. S100 expression was studied in MSC and HAC at different stages of dedifferentiation. Stimuli to induce S100 included increased osmolarity, hypoxia (5% O_2) and chondrogenic factors BMP-4 and TGFβ1. S100 induction under different conditions was evaluated via CELISA, RT-qPCR and immunocytochemistry. Neochondrogenesis was evaluated in pellet cultures analyzed qualitatively via histology and immunohistochemistry, and quantitatively via biochemical GAG/DNA measurements.

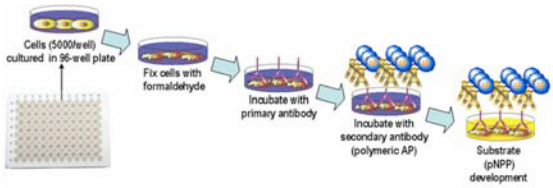

Fig. 1 *Experimental outline of the CELISA procedure.*

Results

S100 CELISA showed high S100 expression in differentiated P0 HAC, lower yet detectable expression in partially dedifferentiated P3 HAC, and no expression in fully dedifferentiated TF HAC, and in MSC (Fig.2A). Incubation with BMP4 but not TGF β1 induced S100 in P3 HAC but not in TF HAC or MSC. S100 in P3 HAC from three donors was induced in response to BMP4 in a dose dependent manner (Fig 2B). The highest concentration was used in further experiments. In addition to CELISA, induction of S100 expression in P3 HAC with 100 ng/ml of BMP4 was demonstrated at the gene expression level, with an increase in S100A1 gene coinciding with increased levels of chondrogenic markers collagen type II and aggrecan. Finally, an increase in percentage of S100A1 positive cells was detected in P3 HAC treated with BMP4, thereby validating S100A1 as a chondrogenic marker at the gene and protein levels. Analysis of pellet cultures from HAC with increased S100 due to induction with BMP4 did not reveal a clear improvement of their chondrogenic potential.

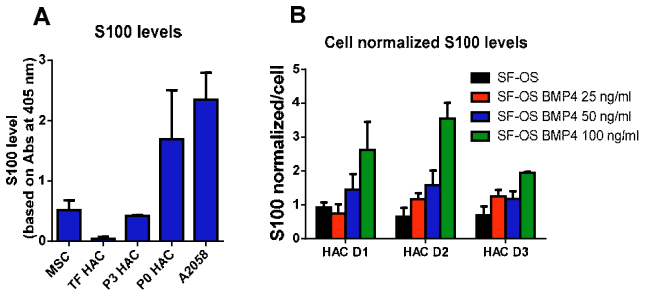

Fig. 2. *S100 in different cell types (A) Induction of S100 in P3 HAC from three different donors with increasing concentration of BMP4 (B). S100 levels were normalized to cell numbers. The results are shown as mean ± SEM (error bars) from triplicate measurements.*

Discussion

In summary, S100-based CELISA was established and validated as an assay assessing HAC redifferentiation potential based on S100 expression in monolayer. The S100-based CELISA could thus offer an advantageous alternative in terms of time and cell amount requirements to 3D pellet culture for testing factors/conditions to induce HAC redifferentiation. Some of these factors/conditions may find clinical application for cell-based cartilage repair treatments.

Reference

Giovannini et al. J.Cell.Physiol. 222:411. 2010

Design of a Haptic Device Mimicking Index Finger Abduction Force

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Introduction

Passive methods like Movement observation and motor imagery could serve as add-ons for motor training especially in early days after injury or during the resting periods between conventional rehabilitation therapy sessions. But the effectiveness of these passive methods has not been proven conclusively. Due to this, question arises whether somatosensory input could induce larger motor training effect given the fact that sensory system is closely interlinked with motor system. The idea of the device is to apply forces by an actuator as a passive somatosensory input and see if it could have an effect on Motor Evoked Potential stimulated by Transcranial Magnetic Stimulation pulses.

Materials and Methods

The first prototype was designed to measure index finger abduction forces in the context of the envisioned sensorimotor task. With this abduction force application we wanted to determine some of the important aspects of human physiology like maximum frequency of force control and maximum rate of change of force. These aspects will be necessary for selecting an actuator in the future.

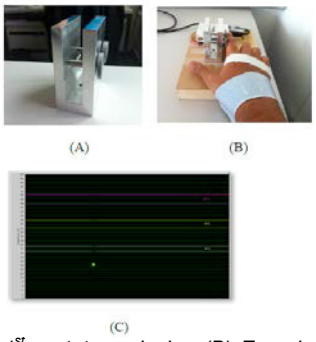

Figure 1: (A) 1st prototype design (B) Experimental setup (C) Visual feedback in LabVIEW

Pilot trials were done with one subject with the experimental set up shown in Figure 1. Force sensor was mounted on the device and specific visual feedback was designed in LabVIEW. The aim was to reach target forces which were 20%, 30% and 40% of the Maximum index finger abduction force at 0.5 Hz, 1 Hz, 1.5 Hz and 2 Hz frequencies. Error would occur if the subject could not reach the target force at a given frequency. Error % and force velocity profile (rate of change of force) were calculated for each frequency.

Results

The upper limit for tolerable error percentage was kept at 80%. This limit was reached at 1.5 Hz trial. So 1.5 Hz could be the maximum frequency for index finger abduction force in context of our experiments. The force velocity profile was calculated at this frequency as rate of change of force would be the highest considering our upper limit. The maximum rate of change of force was 48.437 N/second.

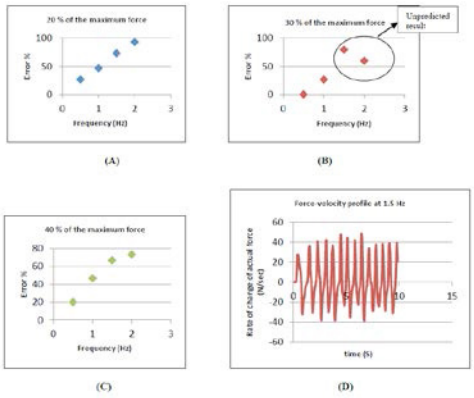

Fig. 2: (A), (B) and (C) shows error% for 20%, 30% and 40% of the maximum forces at different frequencies respectively and (D) shows force-velocity profile at 1.5 Hz.

Discussion

Maximum frequency of 1.5 Hz and maximum force changing rate of 48.473 would be considered to select the actuator in the future. Trials with more subjects will be done to get rid of some inconsistencies in the results shown in Figure 2 (B).

References

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Acknowledgements

I would like to thank Prof. Dr. Nicole Wenderoth for giving me this opportunity to work under her supervision.

Finite Element Simulation to Optimize the Property Distribution of an Iso-Elastic Femoral Stem to Increase Stability After a Cementless Total Hip Replacement

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Introduction

The use of cementless iso-elastic stems in total hip arthroplasty (THA), for the purpose of reducing stress shielding, has briefly been investigated in the literature in the past, but such stems are currently not used in the clinical practice. This may be due to several reasons such as complication in manufacturing of the devices and poor survival rate in the past. However, the advancing of 3D printer technology for production of metal models may open up new possibilities for producing stems with highly variable material properties. This can be done by controlling the variation in the porosity of the bulk material in the stem during production. The aim of the present study was to optimize the property distribution of an iso-elastic femoral stem and compare the strain stimulation in the host bone to that of a host bone implanted with a conventional stiff stem.

Materials and Methods

CT scans of 2 subjects, with different bone mineral density, were obtained and used for constructing a subject specific Finite Element (FE) model of THA patient. The creation of FE model was carried out in several steps; 1) Segmentation in Amira, 2) solid CAD models of stem and bone assembly created in SolidWorks, 3) FE mesh generated in ANSYS Workbench. Walking and stair climbing loads [Heller, 2005] were applied on the proximal femur based on each subjects body weight. The model was fixed at the distal end. Material properties were assigned to each node of the FE mesh of the bone. The implant was divided into 6 parts, which were assigned different material properties. The objective of the optimization was to minimize the volume fraction of non-stimulated bone. Two cases of optimization were carried out. Firstly, the secondary stability case that simulated the contact between the stem and the bone after bone ingrowth has occurred. Secondly, a primary stability case that happens in the initial weeks after surgery, before bone ingrowth has occurred. In this case additional constraint for micro-motion between the stem and the bone were included.

Results

The results show a decrease of non-stimulated bone for all optimized cases, compared to a conventional stiff stem. The optimized stem for the secondary stability case received weaker material properties in the middle of the stem. However, the primary stability optimization resulted in more homogenous material property distribution throughout the stem, due to constraints of micro-motion.

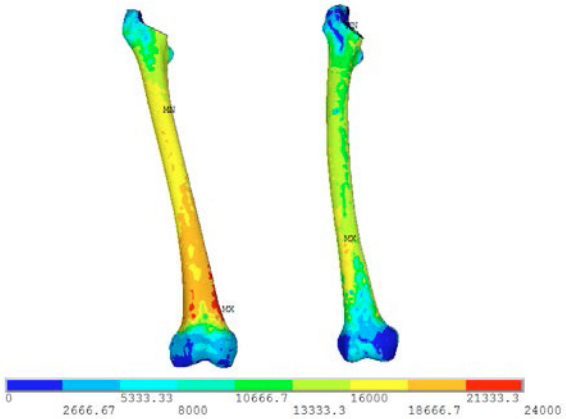

Figure 1: Material properties distribution in femur of subject having normal bone mineral density (left) and osteoporotic subject (right). The values show the distribution of Young's modulus in each node and are given in MPa

Discussion

The study shows that using an iso-elastic stem can increase the volume of stimulated bone compared to a conventional stiff stem. However, the results indicate the same problem for iso-elastic stems as has been shown in clinical studies. The micro-motion between the stem and the bone is a concern. When optimizing with the constraints for primary stability the tendency is always toward a stiffer stem than secondary stability optimization results show.

References

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Acknowledgements

This project is supported by the Icelandic Center for Research (www.rannis.is).

Computed Tomography Image Recycling for Non-invasive Estimation of Bone Strength

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Examiners: Prof. Dr. Philippe Zysset, Dr. Hadi Seyed Hosseini

Background

The current diagnosis method for osteoporosis-related bone quality is based on the measurement of bone mineral density (BMD). However, osteoporosis-related fractures are caused by low bone strength, and it has been shown that strength depends not only on BMD, but also on its 3D micro-architecture.

Computed tomography (CT) data has proven in the past as an ideal input for biomechanical modeling using FEM analysis to provide a patient-specific estimate of bone stiffness and strength. Whereas in-vitro or preclinical µCT scanners possess a resolution high enough to capture bone micro-architecture, clinical CT scanners allow only the measurement of a homogenized BMD distribution. Using these homogenized images as source for FEM models, it is challenging to assign correct elastic parameters for the particular elements.

The objective of this project was to evaluate various published relationships between CT attenuation values and elastic parameters of bone.

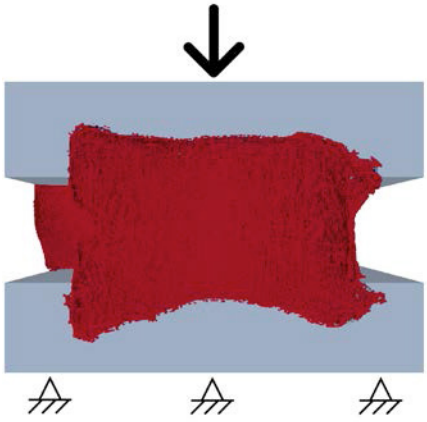

Figure 1: High-resolution FEM model of a lumbar vertebra embedded in PMMA end-caps to simulate a compression test.

Materials and Methods

Human cadaveric lumbar spines were scanned on a clinical CT scanner and µCT scanner. The high-resolution images were segmented and a constant Young's modulus was assigned to all elements containing bone (fig.1). A compressive load resulting in 1% strain was applied to every model.

The resulting reaction forces were computed and used as reference values.

Three different relationships between CT attenuation values and elastic parameters of bone were evaluated and applied to the clinical CT models. The resulting stiffness of these models was then compared to the reference models.

Results and Discussion

Due to the use of linear-elastic constitutive material laws, only stiffness and no strength was computed. A almost five-fold difference in stiffness was found between the vertebrae. This can be explained through the large difference in bone quality. Comparing the µCT derived reference stiffness to the clinical CT model stiffness, a high correlation (R^2=0.84) was found for one of the evaluated relationships (fig. 2).

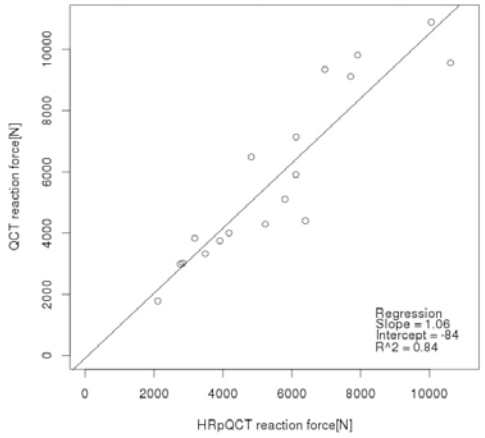

Figure 2: Linear regression between the reaction forces derived by clinical CT images and high resolution µCT.

On the other hand, if these same reference stiffness values are compared the their average BMD, a lower correlation was found (R^2=0.66). This suggests that clinical CT based FEM models are a better predictor of fracture strength than simple BMD measurements.

Acknowledgements

Thanks to Prof. Dr. Steven Boyd and all members of the Bone Imaging Laboratory, University of Calgary for their support during the project.

Towards Personalized Medicine: Homogeneous Cell Distribution on a Microfluidic Chip to Form Tumor-Spheroids

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Introduction

One of the objectives of personalized medicine is to test the own cells of the patient's tumor to optimize the chemotherapeutic treatment. To investigate the cell response to specific drugs, these assays are usually done in 2D cell cultures, which poorly mimic the in-vivo environment of the cells. It was recently shown, that by culturing three-dimensional cell aggregates (spheroids) in a perfused environment, the chemoresistance of these spheroids was highly increased. The objective of this project was to design and fabricate a microfluidic device aimed at forming tumor spheroids of homogeneous size from a solution of suspended cells. Furthermore, in the perspective of personalized medicine applications, for which only a very small number of cells are available, the device should be able to efficiently handle low number of cells. The aim of the platform is then to perfuse and expose these spheroids to chemotherapeutic drugs.

Materials and Methods

A microfluidic network aimed at distributing cells homogeneously in eight microholes was developed. The cells were loaded by hydrostatic pressure and trapped by gravitational sedimentation in microholes with a tiny continuing microchannel working as sieve. The microfluidic chip was fabricated using PDMS (polydimethylsiloxane) soft lithography of a SU8 photoresist structure on silicon, which was fabricated using photolithography. Different concentrations of suspended H2052 cells, a cell line from an aggressive malignant pleural mesothelioma, were loaded on the chip and cultured for three days, with daily renewal of media containing growth factors. The homogeneity of the spheroid size was investigated for the different concentration of loaded cells. In a last step, the chip was fabricated in gas impermeable Cyclic Olefin Copolymer (COC), in view of performing the chemotherapeutic assays under hypoxic conditions.

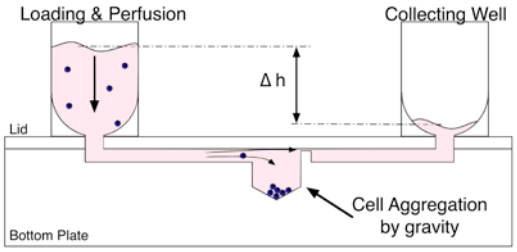

Fig. 1 Principle of cell trapping on the microfluidic chip.

Results

The loaded cells sedimented homogeneously in the microholes and after three days of culture the cells did form tumor-spheroids, needed for the chemotherapeutic assays. Homogeneous distribution of the cells with a coefficient of variation < 10% could be achieved, which is important to get reproducible results from the subsequent chemotherapeutic assays. Further it is shown, that the system has a high loading efficiency, meaning, that almost 100% of the loaded cells aggregate within the microholes. Therefore between 2'000 and 16'000 loaded cells could be distributed homogeneously in the array of microholes and form spheroids. 4'000 loaded cells led to eight spheroids with a diameter of 140µm and it was shown before, that 500 cells are needed to form a spheroid of this dimension.

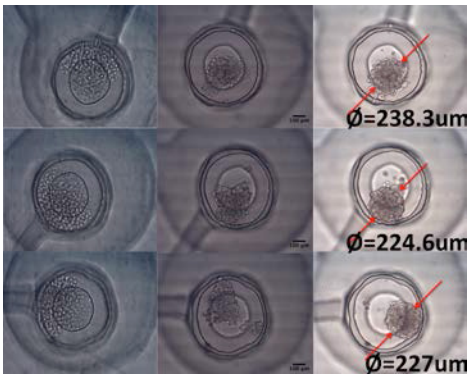

Fig. 2 Cell aggregation after loading, tighter aggregation after two and compact spheroids after three days of culture.

Discussion

The system designed in the scope of this master thesis provides an efficient solution to load cells in suspension and distribute them homogeneously in small microholes to form spheroids. It is shown, that a small amount of loaded cells is sufficient to obtain spheroids of homogeneous size. Thus, this device may be suitable for personalized medicine applications for which only a limited amount of cells are available.

References

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2D-3D Reconstruction-based Implant Migration Measurement

Benedikt Thelen

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Examiners: PD. Dr Guoyan Zheng and Prof. Dr. Moritz Tannast

Introduction

Total hip arthroplasty, is one of the surgeries with high socio-economic impact. Post-operative hip joint dislocation still presents as a major hazard to patients today. It is known that bad initial placement of the acetabular cup implant and early cup implant micro-migration are correlated with high rate of loosening and early revision. Migration is conventionally measured in clinical routine by two-dimensional (2D) methods which lead to high error rates and do not allow for accurate orientation migration measurements. The goal of this thesis is to investigate the feasibility of using 2D-3D reconstruction techniques to provide a non-invasive and accurate 3D measurement method for post-operative acetabular cup orientation migration.

Materials and Methods

For the testing and evaluation of the proposed measurement methodology a custom-made mockup setup was developed to simulate cup implant migration in a controlled experiment. The device allowed measuring cup migration via 2D-3D reconstruction, Roentgen Stereographic Analysis (RSA) and optical tracking. The latter two measurements provided two independent ground truths to verify our method.

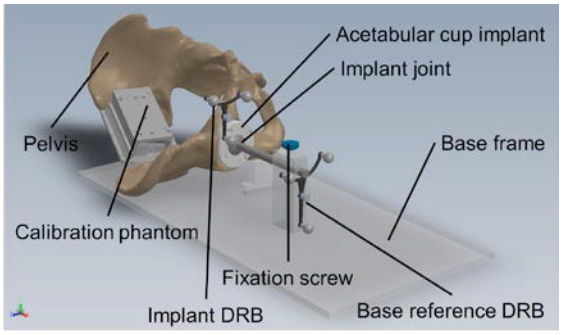

Fig. 1 Computer aided design drawing of the mockup device. This device consists of a cadaveric bone mounted rigidly on a base frame. Thereby the cup implant is allowed to rotate around a spherical joint relative to the pelvis.

A specially designed algorithm allowed determining the cup orientation in respect to the reconstructed pelvis from calibrated input images. The implant orientation was determined based on the projection of the implant rim and the known implant size.

Results

The measurements of the simulated migration by the 2D-3D reconstruction based method and both ground truths were statistically comparable. A comparison of the correlation between the measurements of the incremental angles showed that our proposed method correlated very well with the measurements of the gold standard RSA method. Lower correlation was found between the two ground truths as well as between the optical tracking and our method.

Discussion and conclusions

The high correlation between our measurement method and the RSA method showed, that the additional error introduced by the reconstruction was only very small (0.27±0.72° for anteversion, 0.63±0.76° for inclination). As we found larger deviations between our method and the optical tracking measurements (2.03±1.64° for anteversion, 0.18±1.00° for inclination) and between the two ground truths, we can conclude that the used image calibration system remained the main error source of our system.

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Acknowledgements

We would kindly like to thank the MTRA team of the Inselspital, Bern for their kind support during the acquisition of the X-ray radiographs. Furthermore the helpful input in design and construction from Urs Rohrer and Patrick Moser is gratefully acknowledged.

Reconstruction of Optical Metamorphopsia Produced by Pathological Retinal Layers

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Examiners: Prof. Dr. Philippe C. Cattin and Prof. Christoph Meier

Introduction

The eye, as one of the more complex sensory systems of the human body, is susceptible to many diseases, which influence heavily the visual perception mechanism. Especially the region of the retinal layers suffers from deformation (cysts, detachments, folds) caused by many retinal diseases such as age-related macular degeneration (AMD). These deformations distort the path of light interacting with the light sensitive layers of the retina and thus provoke a bad vision, leading even to legal blindness. Optical metamorphopsia is a typical symptom of patients beginning to suffer from AMD. An early detection improves the success of therapies of AMD. However, an estimation of the severity of optical metamorphopsia can, up until now, only be done in a qualitative manner by experienced ophthalmologists.

Optical coherence tomography (OCT) offers an approved technique to produce images of the retinal layers of a patient. By reconstructing the pathological layers of the retina it should be possible to derive a quantitative estimation of the distortion and to reproduce optical metamorphopsia.

Methods

An algorithm developed in this thesis segments standard OCT B-scan images to gain structural information of the pathological outer retinal layers, where the photoreceptor cells are attached to the retinal pigment epithelium (RPE).

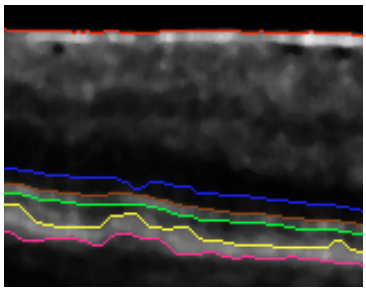

Figure 1: Segmented OCT B-scan image with 6 retinal layers. ILM (red), ELM (blue), IS (brown) and OS (green) of the photoreceptor cells, RPE (yellow) and Bruch's membrane (purple). Light is incident on the ILM.

Based on a series of segmented images, a 3D model of the pathological retina is reconstructed. A novel approach then uses light ray tracing to analyse the 3D retina model and to determine a description of the deformation produced by the pathological retinal layers.

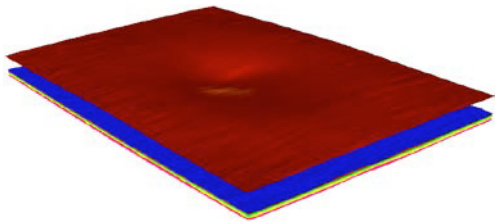

Figure 2: 3D rendering of the retina in the region of the macula. Such a model is analysed by light ray tracing. The coloured layers correspond to the layers given in Figure 1.

Such a description is applied in an image warping step to deform an input image to reproduce optical metamorphopsia.

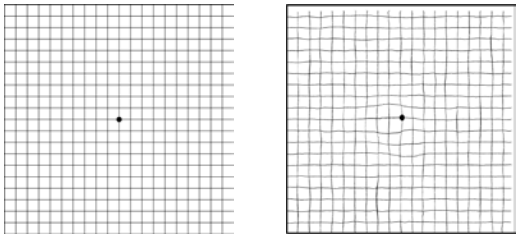

Figure 3: Normal representation of an Amsler grid (left). Deformed Amsler grid according to the distortion detected by the light ray tracing algorithm (right).

Results and Discussion

The provided data based on manually drawn Amsler tests of patients and the obtained warped images do not show significant similarities. This thesis cannot confirm whether the design of the retina model and its parameters are accurate. A larger test base is necessary to find representative settings for the model to reproduce optical metamorphopsia. However, the implementation shows that it is possible to build models of the retina based on segmented OCT B-scans and that light ray tracing is able to reconstruct a distortion description based on the pathological retinal layers. Therefore, the implementation presented in this thesis can be used for further scientific experiments in this field.

NaviPen – An Inertia-based Navigation System for Spinal Instrumentation

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Introduction

Spinal instrumentation describes a surgical procedure to implant metallic or non-metallic devices into the spine. Typically, these implants consist of plates, rods and screws to connect parts of the spine. The goal of such a surgery is to restore stability or correct deformations of the spine. One of the crucial steps of such an intervention is the placement of the screws into the spine's bone. Because of the fact that screws with diameters in the range of millimeters and the lengths of up to ten centimeters have to be applied, the direction of the implanted screw has to be very precise. A wrongly placed screw does not provide enough bone purchase or even worse, does harm the patient's neurovascular tissue.

Materials and Methods

State of the art techniques to place such a pedicle screw are based on the surgeon's experience, tactile feedback and multiple intraoperative fluoroscopic images. Alternatively, various tracking based navigation devices have been developed. Because of the price and the complexity of these devices, they are not widely applied.

Fig. 1: The surgeon applies a pedicle screw according to the software's guidance during a cadaver study.

Together with a neurosurgeon of the University Hospital of Basel, a new method for spinal instrumentation has been developed. The simple and cost effective technique is based on planned insertion angles for the screws and a simple navigation device. Together with dedicated software, this inertial measuring unit (IMU) based device is able to guide the surgeon to the correct tilt angles for the surgical tool during screw placement.

Results

Three cadaver studies have been performed to test the newly introduced device and to compare it against the traditional freehand technique (see Figure 1). With the developed method, 95% of the applied screws were placed clinically correct. During the same test, the experienced surgeon achieved a success rate of 90% with the freehand technique. As a quantitative measure, the angles of the screws' final position as seen in the postoperative CT were compared to the pre-operatively planned ones. The mean-error of the navigated screws was 2.8° for the axial angle and 3.2° for the sagittal angle. The freehand approach's error was 2.9° (axial) and 5.2° (sagittal). All the mentioned results were achieved without the use of any fluoroscopic image.

Discussion

The gained results showed that the proposed method, based on the developed device and software, could exceed the freehand results. Furthermore, the rate of 95% clinically correctly placed screws is equal to the rate achieved by expensive and more complex optical navigation systems.

The successful placement of the S2-ilium screws without the use of a single fluoroscopic image showed that the approach even works for these even more challenging screws.

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Myoblast Differentiation under Simulated Microgravity: Long Term Cell Culture on Random Positioning Machines

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Introduction

Muscle atrophy is of great medical concern, not only for astronauts in space but also for immobilized patients or elderly people on earth. Random Positioning Machines (RPM) are ground based devices frequently used to expose cells to simulated microgravity. The RPM consists of two gimbal mounted frames which rotate constantly to average the earth gravity vector over time. Many studies on myoblasts have been carried out to study muscle development but only a few data are available concerning myoblast differentiation under simulated microgravity. The goal of the thesis was to improve the means of cell cultivation on the RPM and to study myoblast differentiation under simulated microgravity.

Materials and Methods

A device was designed and implemented to perfuse adherent cell cultures with culture medium for prolonged periods of time on the RPM. Computations showed that a low flow rate (< 1 ml/h) does not negatively affect cell culture behavior. This was confirmed by an experiment where mouse myoblasts were exposed for 24 hours to the low medium perfusion. Finally mouse myoblasts were allowed to differentiate under simulated microgravity for six days and samples were taken every second day. The cells were stained with DAPI and Rhodamine-Phalloidin and subsequently analyzed by fluorescent microscopy.

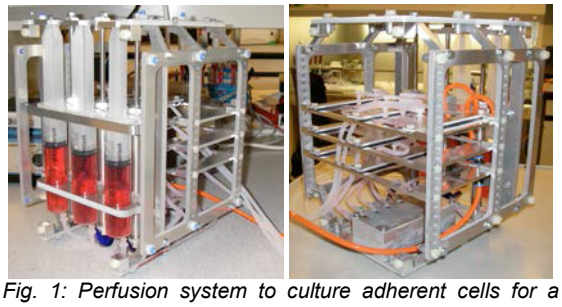

Fig. 1: Perfusion system to culture adherent cells for a prolonged period of time on Random Positioning Machines.

Myoblast differentiation was determined by factors such as cell density, the ratio of fused cells, the area coved by myotubes, the area covered by fibrous structures, the myotube width and by myotube orientation.

Results

Myoblast exposed to perfusion for one day showed no change in morphology or cell alignment. In comparison to a non-perfused control, proliferation was enhanced through the improved nutrition situation.

Myoblasts differentiating under simulated microgravity showed no enhanced or impeded differentiation. Proliferation was reduced in all three experiments and myotube width was unaffected.

Discussion

The finding on reduced proliferation on the RPM is in agreement with previous studies [1]. The finding on unchanged differentiation disagrees with a previous study carried out with rat myoblast differentiating on the RPM. Myoblasts were found to have differentiation significantly disturbed [2]. In two other studies mouse myoblasts were exposed to two-dimensional clinostat rotation. Clinostat also simulates microgravity, but rotate around one horizontal axis. At first differentiation appeared to be reduced [3], but was non-significantly reduced after the hardware was changed to cause less shear stress [4]. However, the results among all of the studies are not directly comparable due to differences in biological models, hardware and differentiation measuring method. Observations during this thesis suggest that shear stress caused through entrapped air bubbles disturb differentiation.

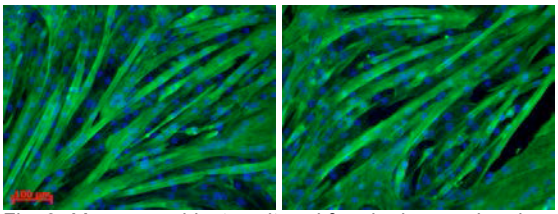

Fig. 2: Mouse myoblasts cultured for six days under simulated microgravity (right) showed no difference in differentiation compared to a static control group (left).

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Acknowledgements

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GPU-based processing of long-term esophageal ECG

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Introduction

The esophageal ECG (eECG) is a method to measure heart's electrical activity. Long-term eECG in particular is needed to diagnose different types of paroxysmal arrhythmias. It is done by introducing a catheter with up to five electrodes through the nose into the esophagus. As the electrodes have a close vicinity to the heart, there is a better insight into their electrical activity.

Like conventional signals, eECG recordings suffer from relevant disturbances that mainly arise from electrode and patient movements. So called baseline wander is primarily a low frequency disturbance. Filtering of this baseline wander becomes demanding, because it features a frequency spectrum that overlaps with the eECG spectrum range. However, in the digital domain, high-pass filters with very high order and steep slopes can be built. Their disadvantage is the complexity that leads to time and power consuming algorithms. The power consumption is the major concern why the filtering, is not performed on the esophageal recorder itself, rather is done during post-processing of the eECG signals on powerful machines.

Materials and Methods

FIR / IIR and wavelet-based baseline-wander filters were investigated to run on central processing unit (CPU) and graphics processing unit (GPU). The parallelization of the algorithms, programmed in CUDA C++ (Compute Unified Device Architecture) necessitated the adaption of particular processes. In case of the FIR filter the parallelizing was done by breaking up the convolution into a series of independent summations. Each summation processes on one of the more than a thousand parallel working cores of the GPU (Figure 1).

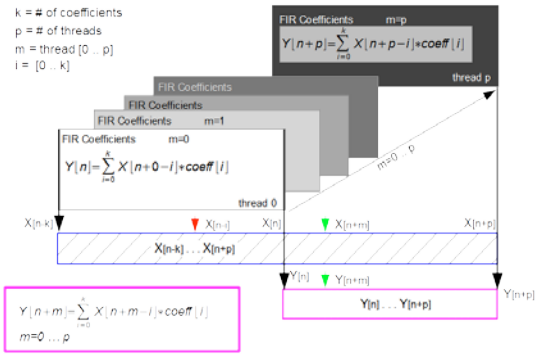

Figure 1 Parallelized FIR filter design dedicated to run on GPU. Each sample Y[n] is processed as one thread.

The optimal filtering parameters were evaluated with a synthetic eECG signal, which includes respiratory and cardiac motion perturbations. The parameters were chosen so that each method results in equal signal quality.

Results

The gain in filtering speed with GPU-based algorithms is considerable. The FIR and wavelet filters processed 148 and 232 mega samples per second (MS/s) when running on GPU and were thereby 50 and 45 times faster than on CPU, respectively (Figure 2). The IIR CPU-based algorithm achieved 49 MS/s at maximum, but turned out not to be suitable for parallelization

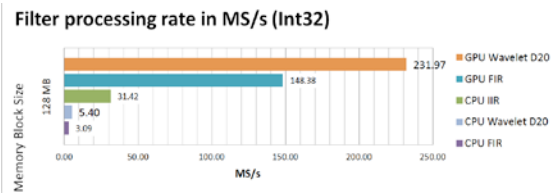

Fig. 2 Filter rate of the investigated algorithms. Processing on GPU is much faster than on CPU.

Discussion

The filtering speed of the wavelet-based baseline wander filter was extrapolated to calculate the process time of a 30-days eECG. Running on GPU only, it results in six seconds filtering time. This time is highly acceptable in clinical practice. To emphasize the speed-up with the GPU design, the multi-level signal transformation might serve as basis for eECG signal classification. Taking both features into account, this algorithm is the first choice in eECG signal processing.

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Acknowledgements

The Thesis is part of a project that aims at the development of an implantable long term recorder for esophageal ECG signals. The project is done in collaboration between the ARTORG, University of Bern, the microLab BFH Biel and the University Hospital in Bern. All the people behind this project are gratefully acknowledged.

The Dynamics of a Side-Ways Impact on the Hip

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Introduction

The pelvic region is the main part in human mobility. It allows walking and upright standing. After traumatic events, this mobility is endangered. Fractures in the pelvic region caused by side-ways falls, especially in the elderly population, can be a huge problem and often they are a cause of death. Another cause of fractures in the pelvic region is side impacts in traffic accidents. These two are the main causes of fracturing the hip.

The aim of this thesis is to set up a finite element model to simulate side-ways impacts. By understanding the gap between side-ways impacts and falls, the results from higher energy impact experiments can be used for the research on the lower energy side-ways fall.

Materials and Methods

The finite-element-model is based on CT-datasets from the Virtual Skeleton Database (VSD). The simulations were performed with the LS-DYNA solver from LSCT (Hallquist, 1998), which is a commercial, explicit solver for highly dynamic impacts.

Segmentation of the CT-data was done in Amira and for further modeling SolidWorks was used. In ANSYS Workbench, the individual parts were first assembled and then meshed together. The generated k-file – an ASCII format input file for the LS-DYNA solver – includes node and element information. Further preprocessing was done with LS-PrePost or via a text editor directly in the k-file. The heterogeneous, CT-based material properties for bone were mapped in Matlab by tri-linear interpolation to each element (Helgason et al., 2008) of the osseous model parts.

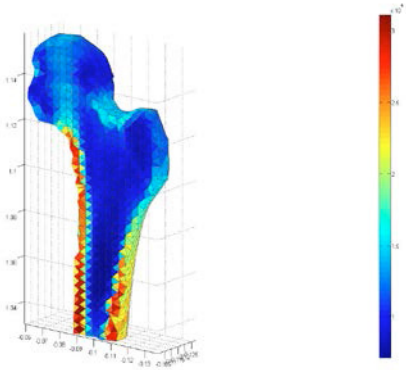

Fig. 1 Cross-section of the femur with mapped stiffness for heterogeneous material properties.

An impactor loaded the model, under two different load cases, in sitting and standing postures. After finishing the simulations, post processing was done with LS-PrePost and Matlab. Measured was the load on the greater trochanter, the femoral head and the pubic symphysis.

Results

The measured peak loads on the greater trochanter are higher, by trend, in a standing posture, than in a sitting posture. The opposite occurs at the pubic symphysis: in a sitting posture the results show higher peak forces than in a standing posture.
By comparing the measured values on the greater trochanter and the pubic symphysis, estimation on the load path during a lateral impact can be done. In a standing posture 7.9% ± 1.6% of the load passes through the anterior part of the pelvis, 13.2% ± 1.1% in the sitting posture respectively.

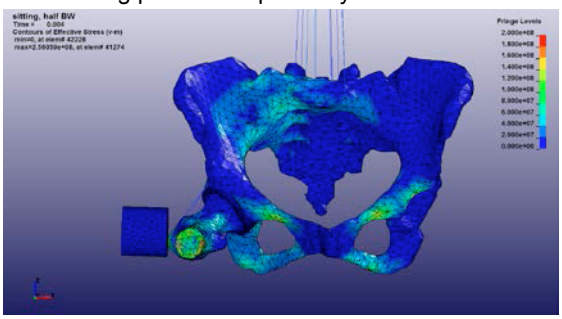

Fig. 2 Von Mises stress visualized in LS-PrePost.

Discussion

Simulations with the developed model show higher peak results than the values in literature, but they are in an expected range. The actual used bone material seems to be to stiff and has to be adapted in further work. The influence of soft tissue and impact velocity is well known from former research in literature and can also be implemented. Not finally known yet is the influence of the acetabulum and symphysis cartilage respectively, the very stiff ligament capsule around the hip joint. This could be a topic of additional studies.

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