# $8^{th}$ European Medical and Biological Engineering Conference (EMBEC 2020)

29 November – 3 December, Portorož, Slovenia

EMBEC 2020

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29 Nov - 3 Dec 2020

# ABSTRACT BOOK

Tomaž Jarm, Samo Mahnič-Kalamiza, Aleksandra Cvetkoska,
Damijan Miklavčič (Editors)

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# Preface

**8th European Medical and Biological Engineering Conference (EMBEC 2020)** was organized by ***Slovenian Society for Medical and Biological Engineering*** and by ***University of Ljubljana, Faculty of Electrical Engineering***. The conference was endorsed by the ***International Federation for Medical and Biological Engineering (IFMBE)*** and the ***European Alliance for Medical and Biological Engineering & Sciences (EAMBES)***. Originally, EMBEC 2020 was announced to be held in Portorož, Slovenia, between 14 and 18 June 2020. Due to the first wave of Covid-19 pandemic outbreak, the Conference was postponed to the period between 29 November and 3 December 2020. However, due to worsening of the global Covid-19 situation in the fall of 2020 and despite our efforts to host a hybrid EMBEC 2020 in such severe conditions, we were unfortunately unable to bring EMBEC 2020 to full fruition.

However, as the Organizers, and with the encouragement from the endorsing professional societies, the IFMBE and the EAMBES, and supported by Springer the Publishing Company, we remained committed to make sure that the footprints of EMBEC 2020 remain. After all, the work and effort invested by the authors of the received scientific contributions, by the scientific reviewers who peer-reviewed the contributions, and by the chairs and organizers of the special sessions for EMBEC 2020 should not have been done in vain. As a result, the Proceedings book of EMBEC 2020 containing the accepted full-length papers has been published by Springer, as has been the tradition for IFMBE-endorsed conferences for many years. The Proceedings Book is part of the IFMBE Proceedings Series.

This Abstract Book is another result of our dedication to keep EMBEC 2020 visible. It contains all reviewed and accepted abstract-only contributions and includes abstracts from full-length papers from the Proceedings. Even the EMBEC 2020 was heavily affected by the Covid-19 pandemic, it attracted a lot of attention. We are proud that we received no less than 370 contributions in total, representing 61 countries from all around the globe, of which 168 contributions were full-length scientific papers, the rest were short abstract submissions. In total, 130 papers representing 43 countries met the standards for publication in the Proceedings of EMBEC 2020. In addition to this, 208 abstract-only submissions were accepted for presentation at the Conference making a total of 338 abstracts that you can find in this Abstract book. Abstracts are listed in this book alphabetically by the title.

The local organizers would like to thank IFMBE and EAMBES for their support in organizing EMBEC 2020. Our thanks go to the members of the International Scientific Programme Committee and the International Advisory Committee for their contribution. And last, but certainly not least, we extend our thank you to the organizers of topical Special Sessions and other external reviewers.

We wish you to stay sound and healthy wherever you are and hope to meet you in person at some other time in the near future.

Damijan Miklavčič
*Conference Chair*
On behalf of the Organizing Committee

## Organisation

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# Contents

# ABSTRACTS

# 3D breast cancer models: hybrid electrospun scaffold in electrochemiotherapy evaluation

Bianca Bazzolo[1], Elisabetta Sieni[2], Monica Dettin[1], Annj Zamuner[1], Martina Roso[1], Fabio Pieretti[1], Maria Teresa Conconi[1]
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Electroporation has been already used successfully to improve the cellular uptake of anticancer drugs for the treatment of breast cancer. Nowadays, in order to develop novel chemotherapeutic molecules and to set up the electroporation conditions (i.e. voltages, number of pulses and their length), 3D in vitro models resembling the tumor microenvironment are needed. In this context, we propose a 3D in vitro model of breast cancer composed of HCC1954 cells cultured on electrospun polycaprolactone. The electrospun biocompatible polymer was functionalized with self-assembling peptides carrying IKVAV motifs which demonstrated to support tumor growth, metastasis, activation/secretion of proteases and angiogenesis. At various time points (1, 3, and 7 days from seedings), the cultures have been characterized in terms of cell morphology, cell growth, and matrix deposition. Furthermore, the best conditions for intracellular delivery of bleomycin through electroporation have been identified. Finally, the results obtained on 3D cultures have been compared to those of HCC1954 cells grown in 2D environment.

# 3D Printed Human Thorax Phantom With Biomimetic Radiation Attenuation

Gunpreet Oberoi
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Introduction: Conventional medical imaging phantoms are often limited by ideal geometry and radiographic skeletal homogeneity, which confines their usability for image quality assessment and radiation dosimetry. Despite the advancement in material science, the existing phantoms still show unrealistic radiation attenuation (RA) properties. To overcome these limitations, the flexibility in material manipulation and accurate anatomical replication by 3D printing serves as a promising tool.
Methods: The study was approved by the Ethics Committee of the Medical University of Vienna (EK1253/2012). Anonymized patient Computed Tomography (CT) data was collected as DICOM files, and processed (segmented and designed) in Materialise computer software forming a printable STL file. CT derived hollow skeletal components of the thorax (sternum, ribs, dorsal and ventral vertebra) were 3D printed in rigid Vero pure white (RGD837) polymer in dorsal and ventral segments, in 1:1 scale using PolyJetTM printer Connex3 Objet500. This was embedded in human soft-tissue equivalent 3D printed polymer Agilus30 Clear (FLX935). Next we prepared radiopaque polymer-amalgamates of three materials (epoxy, polypropylene and bone meal powder) which were scanned using CT and Hounsfield Unit (HU) measured using Analyze 12.0 tool kit to create 12 different ratios. We filled the 3D printed hollow skeletal component of thorax with 3 selected amalgamates which closely mimicked human thorax RA. We performed dimensional and RA comparison between the patient CT with the 3D printed thorax CT; reproducibility tests for RA of the prepared polymer-amalgamate; both, using Materialise software.
Results: Our results showed that physical dimensional comparison test between the patient and phantom segmentation displayed 97% of overlap in the range of 0.00 mm – 4.57 mm embracing the anatomical accuracy of the workflow and 3D printing technology. Structural densities in the range 42 to 705 HU could be generated by the prepared polymer-amalgamate, as evaluated by (CT). The HU values of the reconstructed phantom was comparable to the three skeletal structures investigated in a real patient's thorax CT.
Conclusion: Our study offers the possibility to build modular phantoms with biomimetic RA with the opportunity to add pathologies like tumors, fractures, etc. The main limitation of our workflow was operator-induced artifacts in the phantom production, e.g., air bubbles, during the polymer filling process which can be solved in future by constructing and filling the phantom in small segments.

# 3D printing of medical devices for low-resource settings: a case study on intrauterine balloon tamponades for post-partum haemorrhage

Davide Piaggio, Scott Hyland, Leandro Pecchia
*University of Warwick, United Kingdom*

The United Nations Sustainable Development Goal (SDG) number 3 – Good health and well-being –aims at reducing post-childbirth maternal death amongst others. In fact, target 3.1 aims at "reducing this phenomenon to less than 70 per 100,000 live births by 2030".
Although maternal mortality has been decreasing since the new millennium, in 2015, over 300'000 women worldwide died due to complications during pregnancy or childbirth. The existing gap among low- and high-resource settings is evidenced by the higher probability for mothers to die during childbirth in the former. In fact, it has been demonstrated that mothers are 20 times more likely to die during childbirth in low-resource settings than in the USA. One of the main causes of death in such circumstances is post-partum haemorrhaging, a condition affecting about 50% of women in Benin and accounting for 25% of maternal deaths in Sub-Saharan Africa (SSA).
In high-resource settings, this severe condition is treated with intrauterine balloon tamponades which are medical devices that stop the bleeding by applying pressure inside the uterus. Although such devices are listed as one of the priority medical devices by the World Health Organisation, they are rarely seen in low-resource settings as they are single-use and not affordable.
To combat this, a cheap technique known as a condom-catheter was adapted, resulting in the contextualized design of a system which allowed the assembly of a very basic balloon tamponed using a bottle, and specifically designed bottle caps, valve and clasp, flow stopper and silicon tubes. To ensure an adequate supply of valves and clasps, it is proposed that the valves and clasps are manufactured within hospitals using fused deposition modelling 3D printers, following a circular economy approach.
This talk will present the prototype of the device and the preliminary validation that we performed.

# A current-based forward solver for the shunt model of electrical impedance tomography

Erfang Ma
*Xi'an Jiaotong-Liverpool University, China*

We present a new numerical method for the solution of the forward problem of electrical impedance tomography (EIT) with the shunt model. Given a mesh over the EIT region, we discretize directly the conditions on the current density in equilibrium, and solve the resulting system of linear equations for the amount of current flowing through each side of every element. Afterwards, the distribution of current density and potential are reconstructed. Results of simulations on both 2D and 3D models indicate that the new method gives comparable results to those of the traditional finite element method with linear elements.

# A decision-making support algorithm for active implantable medical devices evaluation

Martina Andellini[1], Elena Bassanelli[1], Leandro Pecchia[2], Matteo Ritrovato[1]
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The management of active implantable medical devices (AIMDs) has been becoming a pivotal topic due to their significant economic value and to the high levels of safety and clinical effectiveness, which AIMDs have to guarantee. This work aims at developing a rigorous decision-making support algorithm to evaluate the AIMDs' performances and to finally select the most suitable and patient-specific AIMDs model.
The pilot study was conducted focusing on Implantable cardiac pacemakers (PMs) for pediatric patients. Firstly, a scientific literature review was carried out to define the evaluation criteria and the performance indicators able to distinguish between different PMs' models.
Following the health technology assessment (HTA) approach, a decisional hierarchy structure including all the safety, clinical, economic and organizational PMs-related aspects was built, aiming at classifying all the parameters identified within the related domains singled out by the EunetHTA Core Model.
A list of 21 PMs-specific technical features have been drawn up. A number of PM models from different manufacturers were described with respect to the indicators' list previously developed in order to build an appropriate database.
Together with the technology "decomposition" into its main technical features, we broke down the clinical question into the patient's physio-pathological characteristics, defining 40 indicators. Through a fuzzy logic approach, a number of rules were developed linking the 40 patient characteristics to one or more of the 21 PM technical features emulating the current physician's decision-making process.
At the end of the fuzzy logic process, each technical characteristic assumed a percentage value, which represent whether the specific PM's feature is useful to address the patient-specific clinical problem. Applying the fuzzy algorithm output (percentage scores associated to each technical characteristics) to the database previously built, in which all PMs were described with respect to the same technical features, it is possible to understand which are the limited number of models, that best fit the clinical question, resulting in those with the highest performances' score.
As the "perfect" PM, including all together the most appropriate technical characteristics, does not seem to exist on the market, the integration of the HTA process within the Multicriteria Decision Analysis represents a reliable solution.
The analytical decision-making algorithm, providing quantitative and repeatable results, can guide the selection and the introduction of innovative health technologies in clinical settings, optimizing and standardizing patient-specific pacemaker selection process increasing decision-makers awareness.

# A MATLAB app to assess the reliability of new methods compared to their benchmarks

Shaul Ajo[1], Davide Piaggio[1], Mahir Taher[1], Franco Marinozzi[2], Fabiano Bini[2], Leandro Pecchia[1]
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Emerging technologies for physiological signals and data collection enable the monitoring of patient health and well-being in real-life settings. This requires novel methods and tools to compare the validity of this kind of information with that acquired in controlled environments. In this paper, we describe a method and a tool for comparing the reliability of features extracted from wearable sensors, with those obtained using more costly and sophisticated technologies in lab environments. After introducing the key steps of the proposed statistical analysis method, this paper describes its implementation in a MATLAB app, developed to support researchers in testing the extent to which a set of features, captured with a wearable technology, can be considered a valid surrogate of a benchmark technique. An example of the application of the tool is provided in order to validate the method and illustrate the graphical user interface (GUI). The app development in MATLAB aims to improve its accessibility, foster its rapid adoption among the scientific community and its scalability into wider MATLAB tools.

# A Novel Convolutional Neural Network for Continuous Blood Pressure Estimation

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This article demonstrates the feasibility of convolutional neural network (CNN) and pulse transit time (PTT)-based approach in estimating the systolic blood pressure (SBP) and diastolic blood pressure (DBP). We employed electrocardiogram (ECG) and photoplethysmography (PPG) signals and calculated the PTT which is the time delay between the R-wave of ECG, and specific points of the PPG waveforms. The Blood pressure (BP) is inversely related to PTT. A total of 22 patients with available ECG, PPG and SBP data were selected from the Medical Information Mart for Intensive Care (MIMIC III) dataset to validate the proposed model. A window of five minutes of recoding was chosen for each patient. The duration of each cardiac cycle was around 0.6 seconds, centred at R-peaks and sampled at 125 Hz. A CNN-based model was developed with four convolutional layers. The results showed that the average of root mean square error (RMSE) of 5.42 mmHg and 7.81 mmHg were achieved for SBP and DBP, respectively; which are within an acceptable error margin that set by the Association for the Advancement of Medical Instrumentation (AAMI).

# A novel robot-world calibration in surgical robot system for zygomatic implant placement based on its motion characteristics and mechanical structure

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Zygomatic implant technology has been successfully applied to the repair of atrophic maxilla to avoid a large number of grafting surgery and shorten the recovery time. However, because of the long trajectories of zygomatic implant placement, the destruction of normal anatomical landmark and the narrow operating space, it is difficult to operate and ensure the accuracy. At present, the surgical robot system with real-time optical navigation system assistance is widely used in the field of zygomatic implant placement. The robot-world calibration is the crucial process of an optical-navigated surgical robot system, which is accompanied by complex mathematical calculation and a large number of time consumption. In this study, an automatic robot-world calibration method based on mechanical structure and motion characteristic of an UR (Universal Robots, Odense, Denmark) is proposed. The calibration reference frame fixed at the end-effector of the robot makes a circular and linear motion with the rotation and translation of the terminal joint. Further, the least square fitting algorithm is used to calculate the center of the circular motion and the direction of the linear motion. The terminal joint of the robot automatically carries out a set of specific motions according to the preset command, then the position and direction of the tool center point (TCP) of the robot are determined and the matrix of robot-world calibration is calculated. Through an animal experiment on the maxilla of a pig, the accuracy of the surgical robot system with this robot-world calibration has been evaluated. The deviations of the entry point, exit point and angle are respectively 1.44±1.01mm, 1.68±0.76mm and 1.01±1.06º. It demonstrates that the surgical robot system has a higher operation accuracy than that of the surgeon, and overcome the limitation of the line-of-sight problem of the optical tracking device to some extent.

# A novel validation framework to assess segmentation accuracy of inertial sensor data for rehabilitation exercises

Louise Brennan, Antonio Bevilacqua, Tahar Kechadi, Brian Caulfield
*University College Dublin, Ireland*

Digital biofeedback systems (DBS) which use inertial measurement units (IMUs) can support patients during home rehabilitation. Models which accurately segment IMU data for rehabilitation exercises are required to provide biofeedback but assessing accuracy in a clinical context is challenging due to technical and patient-related factors. In this paper, we propose a three-staged validation framework to overcome these challenges. We present the results of stage one and two segmentation accuracy assessment for our DBS for shoulder rehabilitation. The results demonstrate that most of the chosen exercises can be segmented to a high level of accuracy in an unseen, uninstructed dataset. Errors in segmenting and recommendations for improvement are presented, which must be addressed prior to the final stage of validation.

# A retrospective observational study of health facility ownership type and performance on HIV indicator data reporting in Kenya

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In low- and middle-income countries, private and public facilities tend to have highly variable characteristics, which might affect their performance in meeting reporting requirements mandated by ministries of health. There is conflicting evidence on which facility type performs better across various care dimensions, and only few studies exist to evaluate relative performance around nationally-mandated indicator reporting to Ministries of Health. In this study, we evaluated the relationship between facility ownership type and performance on HIV indicator data reporting, using the case of Kenya. We conducted Mann-Whitney U tests using HIV indicator data extracted from years 2011 to 2018 for all the counties in Kenya, from the District Health Information Software 2 (DHIS2). Results from the study reveal that public facilities have statistically significant better performance compared to private facilities, with an exception of year 2017 in reporting of indicators for HIV counselling and testing, and prevention of mother-to-child transmission programmatic areas.

# A self-applicable EEG recording approach to supplement home sleep apnea testing: a usability study

Laura Kalevo[1], Tomi Miettinen[2], Susanna Westeren-Punnonen[3], Juha Seppä[3], Johanna Sahlman[3], Timo Leppänen[1], Juha Töyräs[4], Erna Sif Arnardottir[5], Sami Myllymaa[1], Katja Myllymaa[3]
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Introduction: For practical reasons, portable sleep monitors without electroencephalography (EEG) recordings are increasingly used as an alternative to in-laboratory polysomnography (PSG) for the diagnosis of obstructive sleep apnea (OSA). Whereas portable monitoring devices offer indisputable advantages such as increased accessibility [1], the lack of EEG, electrooculography (EOG) and chin electromyography (EMG) recordings complicates accurate assessment of total sleep time and sleep the structure. This may lead to a significant underestimation of the severity of OSA. The utilization of EEG, EOG and EMG recording in portable home monitoring has remained limited due to the present cumbersome electrode systems being unpractical for patient self-application. Thus, there is a need for a wearable sensor that enables comprehensive sleep recordings as fully self-administrated. We have recently developed and validated a novel self-applicable facial electrode set (BruxHome), consisting of frontal EEG channels, EOG, and EMG in patients with suspected sleep bruxism at their home [2]. In this study, we investigate the usability of the BruxHome electrode set as a self-applicable EEG recording approach supplementing the conventional home monitoring device.
Materials and methods: Thirty-nine patients (23 males), aged 25-78 years, referred to the outpatient clinic of the Otorhinolaryngology at Kuopio University Hospital (Kuopio, Finland) because of clinical suspicion of OSA were recruited to this study. The patients conducted a sleep recording with a portable polysomnography device (Nox A1, Nox Medical, Reykjavik, Iceland) supplemented with BruxHome at their home. The usability of the electrode set was evaluated by patient questionnaires. The response scales were from 1 (easy) to 10 (difficult) or yes/no.
Results: According to the preliminary results, 35 patients considered that the facial electrode set fitted properly on their face whereas three patients had difficulties wearing it and one did not answer to this question. In 32 cases, all electrodes remained firmly attached over the night, but four patients reported that at least one electrode was detached and three did not answer. 27 patients graded the ease of use of the electrode set from 1 to 4, ten patients from 5 to 10, and 2 patients did not answer to this question.
Conclusion: These initial results suggest that the new facial electrode set (BruxHome) is simple enough for patient self-application. Thus, BruxHome could provide an easy and inexpensive solution enabling EEG to be recorded as a part of conventional home sleep recording.
References:
1. Collop et al. JCSM. Dec;7(22): 737
2. Miettinen et al. IEEE J Biomed Health Inform. 2018 Jul;22(4):1124-1132

# A sensitivity analysis of heart rate variability algorithms

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Heart rate variability analysis (HRV) is a non-invasive technique for the study of autonomic nervous system activity. HRV algorithms have a large number of configuration parameters, and it is not always clear how variations in some of these parameters influence the final result. This makes it difficult to choose appropriate parameter values, and hampers reproducibility of HRV studies [1].

We have carried out a sensitivity analysis of HRV algorithms to gain a better understanding of how changes in their parameters influence their results. For this end the R package RHRV was used; with about 500 monthly downloads this may be the most used HRV tool [2]. For the sensitivity analysis of the time domain algorithms and frequency domain algorithms (both based on the Short-time Fourier transform and Wavelet transform), the MIT-BIH Normal Sinus Rhythm Database from Physionet was used. For the sensitivity analysis of ventricular beat filtering algorithms, the MIT-BIH Arrhythmia Database was used. The analysis was initially carried out using the parameters set by default in RHRV. Then, each parameter was systematically varied, reapplying the algorithms over the entire database for each variation of each parameter. The results obtained for each recording were stored in csv files for subsequent analysis.

Shapiro-Wilks test ruled out the normality of the results in all cases. Friedman nonparametric test was used to assess the significance of the differences in the results. When statistically significant differences were found, the specific parameter variations that presented significant differences were found with the Post-Hoc Conover test. This permits identifying from what amount of variation of a parameter the changes are significant.

Using this methodology, we have been able to identify the parameters for which even small variations produce statistically significant differences in the results of some HRV algorithm. For example, variations as small as 2% in the length of the time window used produced statistically significant differences in the time-domain index SDNN, although variations in the time window did not produce significant differences in the spectral power of the VLF, LF, and HF frequency bands.

[1] Jarrin, Denise C, et al. ”Measurement fidelity of heart rate variability signal processing: The devil is in the details.” International Journal of Psychophysiology 86.1 (2012).
[2] Martínez, CA García, et al. Heart rate variability analysis with the R package RHRV. Springer International Publishing, 2017.

# A Step recovery diode based sub-nanosecond device to study the morphological features of the cervical cells

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A sub-nanosecond pulse generator with a high amplitude was developed to study the morphological features of the cervical cells. The prototype developed uses the concept of step recovery diode which produces a pulse that is symmetric and the shape of the pulse is Gaussian in nature. The ringing present in otherwise pulse generators has been reduced to a very low level. The amplitude developed by this generator is 70 V and the duration is from 300 picoseconds to 1.5 nanoseconds. This output has been generated across the 50-ohm load. The device is coupled with electroporation cuvette with a 1 mm and 0.5 mm gap to generate the required electric field. The pulse generator is used to create a reversible electroporation environment that can be used to determine the morphological features of the cells. The cell model was created in COMSOL 5.0 to test the above concept. The cervical cell electrical properties had been used to study the effects of the sub-nanosecond pulse on the cells. The high field strength causes apoptosis in the cell or generally known as programmed cell death which is the main cause to introduce this device as it generates electric field enough to electroporate the cells. This electroporation develops a trans-membrane voltage 500 mV which is the threshold voltage for having nano-pores produced in the cell. The pores produced can accept dyes that can enter easily into the cells which reseal after a short interval of time and can highlight the shape of the cell when observed under the microscope. This device offers a very easy method to operate as it has an inbuilt triggering system and uses 30 V Dc supply which is easily available. The device can also be applied to diagnose the various stages of tumor development and with great accuracy in early detection can be achieved by the use of this device.

# A study of baseline in psychophysiological experiments

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Psychophysiology studies human autonomic nervous system's responses related to hers/his mental activity and behavior. Psychophysiology usually compares physiology during stimulus presentation (or task solving) with physiology of the person's baseline state. This paper investigates instructions to the participants for them to achieve an optimal relaxed baseline state during psychophysiological studies. It is focused on physiology of human skin - electrodermal activity (EDA). Four different conditions for achieving the optimal baseline were tested: i) relaxing with no special instructions, ii) watching a fixed dot on the screen, iii) watching a video of a calming fish-tank, and iv) playing a mentally non-demanding computer game. The results indicate that comput-er game was not an appropriate condition for reaching an optimal baseline. The EDA in other three conditions did not differ significantly. Our findings suggest that the content of the instructions for reaching the perfect baseline may not be very relevant.

# A Study of Sofa-Type Capacitive Coupling Electrocardiograph System to Measure Stress Relief for Sleeping or Resting with Oxygen Taking

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Non-contact electrode type electrocardiograph system was researched in various fields, but few products are commercially available. In this study, we proposed a sofa-type capacitive coupling electrocardiograph which has possibilities to be commercialized. The base system is a commercially available oval shape sofa that provides oxygen. We developed a capacitive coupling electrocardiograph and embedded it into the base system. The system gives feedback by measuring the ECG signal on stress relief during resting with taking oxygen provided by the sofa. In the capacitive coupling electrocardiograph, it is inevitable to develop a suitable active electrode for the target system, so we developed that comprised of a surface electrode, electronics, and metal case. The surface electrode was made of PCB with two layers of copper plate: the top layer is for coupling function (coated with AU), and the bottom layer plays a role as a shield. The fabricated active electrode module is embedded into the sofa. The purpose of the developed electrocardiograph is to measure HRV of sofa users. The measured HRV was compared with that from a reference system by various different coupling distances (cloth thickness) to guarantee the quality of measured signals. The comparison result shows that RRI correlation was mostly over 0.99, SDNN variation rate was mostly under 1%, and LF/HF variation rate was less than 1% in the tested thicknesses.

# A Tool for Automatic Estimation of Patient Position in Spinal CT Data

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Most of the recently available research and challenge data lack the meta-data containing any information about the patient position. This paper presents a tool for automatic rotation of CT data into a standardized (Head First Supine) patient position. The proposed method is based on the prediction of rotation angle with a convolutional neural network, and it achieved nearly perfect results with an accuracy of 99.55 %. We provide implementations with easy to use the example for both, Matlab and Python (PyTorch), which can be used, for example, for automatic rotation correction of VerSe2020 challenge data.

# A wearable gait training device for the stroke patient's rehabilitation

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Abstract : This paper present a simple way to assess the stroke patient's gait pattern for the stroke patients rehabilitation. A wearable device with gyroscope and accelerometer are placed at both side of foot to provide the information of gaits. The precise optical motion system which is often used for biomechanical research, however, it can just perform in the laboratory. Therefore, the wearable device can provide a lower cost and simple way to obtain the gait analysis. Gait assessment is critical in rehabilitation process for patients with motor deficit in lower limbs. We have developed a wearable system based on Android to get real-time gait monitor. Acceleration and angular velocity of foot motion were measured and processed by the algorithm developed in our laboratory. The gait pattern information displayed in cell phone can provide the stroke patient for biofeedback rehabilitation.
Method: The accelerometer and gyroscope (inertial unit) are used as wearable sensor and installed them to lateral side of the left and right shoe respectively. Data were transmitted via Bluetooth with low energy protocol from inertial sensors to smartphone for further processing. This wireless technology reduces power consumption and increases durability of the device about four hours. Signals from sensor were processed and visualized with algorithm embedded in Android App. The gait information such as: toe off, heel contact, stance phase and swing phase were extracted and visualized on user interface. To eliminate interference of gravity on sensors, the angle between sensor and orientation of gravity were measured, then gravity component was subtracted from accelerometer. Stride length was measured by Integration during swing phase (starts from toe off, and ends by heel contact) to minimize motion artifact.
The device was test when subject was asked to walk straight in various velocity: slow (0.3 m/s), medium (0.6 m/s) and fast (1.2 m/s). The step length was limited to 0.6 m. The gait cycle between normal and abnormal subjects. A simple gait analysis system with features of real-time, portable and convenient operation is implemented. More clinical assessment will be presented in the conference.
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# A web platform for 3D electric field modeling for electroporation based therapies

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Electroporation therapies are based on the increased permeability to ions and macromolecules of cells under the application of high electric field pulses. This effect is used to introduce anti-cancer drugs in a therapy known as electrochemotherapy, or to force homeostasis loss and cause cell death (irreversible electroporation). It is generally accepted that, for a given tissue and pulsing protocol, an electric field magnitude threshold exists that must be overreached for treatment efficacy. However, it is difficult to preoperatively model the electric field distribution because it is highly dependent on the tissue electric conductivity, on how many electrodes are inserted, their geometry and arrangement, and the voltage applied. To illustrate such dependencies, we have created EView (https://eview.upf.edu), a web platform for 3D simulation of the electric field in homogeneous tissues for arbitrary electrode geometries and overlays it on 3D medical images.

With this web platform, the user can set the electrode configuration easily using up to six electrodes. The electric field is then simulated on a dedicated server by means of the finite element method. It is modelled assuming a homogeneous tissue with non-linear dependence on the electric field (sigmoid function), by using one of the predefined tissues (liver and pancreas) or by manually defining the sigmoid. A simulation is computed for every electrode pair and the result is displayed as electric field isosurfaces from 50 to 2000 V/cm in 50 V/cm steps. If more than one pair is simulated, the isosurfaces are obtained by computing the union between simulations. Additionally, a medical image can be loaded to place the electrodes according to anatomical landmarks and observe the simulated electric field as an overlay.

With EView, the electric field distribution can be obtained in minutes: setting the electrode configuration can take just a few seconds, and the time to send the data to the server, compute the simulation and display the results on the web, takes from 2 minutes (with two electrodes) up to 40 minutes (with six electrodes and fifteen pairs). The implemented model has been validated against COMSOL Multiphysics,a widely used FEM solver in the electroporation field, and they provide the same results (Dice = 98.3 ± 0.4 %).

EView is a free platform that provides expert and non-expert electroporation users a way to rapidly model the electric field distribution for arbitrary electrode configurations.

# A Web-Based Service Portal to Steer Numerical Simulations on High-Performance Computers

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Benefiting and accessing high-performance computing resources can be quite difficult. Unlike domain scientists with a background in computational science, non-experts coming from, e.g., various medical fields, have almost no chance to run numerical simulations on large-scale systems. To provide easy access and a user-friendly interface to supercomputers, a web-based service portal, which under the hood takes care of authentication, authorization, job submission, and interaction with a simulation framework is presented. The service is exemplary developed around a simulation framework capable of efficiently running computational fluid dynamics simulations on high-performance computers. The framework uses a lattice-Boltzmann method to simulate and analyze respiratory flows. The implementation of such a web-portal allows to steer the simulation and represents a new diagnostic tool in the field of ear, nose, and throat treatment.

# An Alternative Way to Measure Tidal Volumes

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In this study an alternative way to measure the tidal volume is introduced and evaluated. While the gold standard is spirometry or body plethysmography, the introduced measurement system used three respiration induced changes in cir-cumferences of the upper body to determine tidal volume. Thus, no face mask or mouthpiece is required, and the respiratory measurement is more comfortable for the subjects. R2 >0.95 and a mean error < 208 ml showed that the system can be used as an alternative and comfortable way to gain tidal volumes and would be suitable for surveillance reasons or for longer tidal volume measurements.

# An Efficient Microcontroller for Visual Cortical Prosthesis

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The medical implant devices (MID) are popular today for solving the human's disorders. Amongst those MIDs, visual cortical prosthesis (VCP) is an example of the treatments that deals with restoring sight for blind people. The visual cortex stimulator (VCS) is an implant part that requires an efficient power supply and fast data transmission. In addition, data processing unit has very specific requirements e.g., low power consumption, small size and an efficient processing. In this paper, the most powerful microcontrollers available in the market are highlighted. Their features and performances are investigated so that we can choose an efficient microcontroller that meets the health and safety and all other VCP requirements. The selected microcontroller (ARM-Cortex M4) with all necessary hardware were mounted on a single round shape printed circuit board (PCB) with dimeter 30 mm and thickness 2.68 mm. In addition, data link speed of 170 Kbps was achieved using low power Bluetooth. Moreover, image decompression time was only 19.55 ms with overall system power consumption of 80 mW.

# An Example Case of Pancreatic Ductal Carcinoma against Which On-Site EUS-FNA was Effective

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Summary:We experienced a case in which on-site pancreatic endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) was effective in making a diagnosis of pancreatic ductal carcinoma. According to the cytological findings based on the on-site Diff-Quik staining, we failed to provide a definite diagnosis because the tumor was just suspicious of being pancreatic cancer although the cells were atypical. We washed the residual samples of the blood and mucus components adhered to the glass slides with PBS and made measurements for tumor markers after the EUS-FNA examination, and DupanII, Ca-19-9, and SpanA hit abnormally high values, which was useful for diagnosis. On-site examination by a cytotechnologist inferentially lessens the burden on the patient and is effective in giving a definitive diagnosis.

Case:Patient: Woman in her 50s,Chief complaint: Pain in the area from the epigastric region to the back. Past medical history: Cystic ovarian tumor History of present illness: About 4.6 cm of tumor was confirmed on the pancreas head through abdominal ultrasound and computed tomographic (CT) scanning (Figure 1). We suspected that the patient had pancreatic cancer, endocrine tumor, or acinic cell carcinoma. We conducted EUS-FNA for making a definitive diagnosis.

Discussion:Accounting for about 70% of pancreatic tumor, pancreatic ductal carcinoma tends to show strong cellular atypia, which makes it possible to give cytological diagnosis. Definitive cytological diagnosis of pancreatic tumors through EUS-FNA is often made based on the Diff-Quik, Pap, and cell block-HE staining; however, it is not always possible to provide a firm diagnosis in some cases where the amount of cells taken is limited or the amount of atypical cells taken is not adequate.

If we take a great amount of cells on site and diagnose the tumor as a malignant one at the stage of the Diff-Quik staining, we will be able to make a definitive diagnosis in the Pap and cell block-HE staining as well. As in this case where the amount of the cells taken was limited, examination of the tumor markers of the residual samples of the blood and mucus components adhered to glass slides .

Conclusion:When a cytotechnologist goes to an endoscopic room in order to treat samples and judge atypical cells on site, cytological diagnoses will be made successfully with fine needle aspiration performed at minimum frequencies.

# Analysis and Measurement of Cardiac Output based on Pulmonary Artery Thermodilution in Laboratory Conditions

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This paper describes the concept of laboratory process based on measuring cardiac output using pulmonary artery thermodilution (trans-right-heart thermodilution) method. The blood circulation is in the process simulated by simple water flow in the measuring chain driven by water pump. Measuring is performed by Swan-Ganz catheter used in medical practice connected to simple electronic circuit using Wheatstone bridge to obtain temperature value from thermistor. Analog values come to NI Engineering Laboratory Virtual Instrumentation Suite (NI ELVIS) connected to PC. There is also a programme designed in Labview enviroment to calculate cardiac volume, which is an important indicator of the cardiovascular system state.

# Anisotropic iteratively re-weighted TV regularized reconstruction for linear tomosynthesis

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Linear tomosynthesis is a limited angle, cone-beam X-ray based imaging modality. In practice, typically 40-60 low dose projection images are acquired over 20°-80°. As the consequence of the limited total scan angle, the reconstruction problem is highly under determined. Therefore, the resolution of the reconstruction is highly anisotropic, it is poor in perpendicular direction to the plane of the detec-tor. This paper proposes an anisotropic weighted TV-L0 regularized (maximum a posterior estimation based) reconstruction method to linear tomosynthesis modality. The numerical optimization problem of the reconstruction is solved by majorization - minimization optimization. This paper compares the proposed method with isotropic TV-L0 regularized one and other well-known approaches by re-constructions calculated from simulated projections.

# Anisotropy of mechanical properties of pig lung pleura

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It is known that the postoperative recurrence rate of primary spontaneous pneumothorax is high. In most cases, recurrences occur near the thoracotomy resection line. Mechanical properties of the lungs and pleura are needed to clarify how resection lines affect recurrence using finite element analysis. While there are many reports on their mechanical properties, few reports explain inhomogeneity or anisotropy. Tensile tests on pig pleura were carried out along two main directions, parallel and perpendicular to the rib bone. As a result, the pleura has greater resistance along with directions parallel to the rib bone than perpendicular.

# Antenna Model for Localization of Pulmonary Nodules during Thoracoscopic Surgery

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Worldwide, deaths related to lung cancer have the largest incidence among cancer-related diseases. When diagnosed, a lung nodule is usually removed through minimally invasive surgery. However, during the surgery the lung collapses and an in-operando localization of the tumor mass is necessary. Several methodologies exist but all show relative drawbacks.

Here we suggest microwave imaging as an alternative method for lung cancer localization which can be applied to thoracoscopic surgery. Microwave imaging is based on the use of an antenna which illuminates the lung tissue and recovers the backscattering signal associated with inhomogeneities inside the tissue. These signals are then used to reconstruct an image of the organ.

The antenna plays the most critical role in the localization and it bears heavy constrains on its dimensions as to be used during thoracoscopic surgery.

In this contribution, we investigate several parameters affecting the design and utilization of a bowtie antenna through numerical simulations. The challenges for an efficient antenna are sufficient bandwidth, directionality, and sensitivity also when working in close proximity with biological tissues that possess high dielectric permittivity and conductivity.

Our results show that the distance of the antenna from the lung is the main parameter affecting its sensitivity regarding a deep lung nodule.

# Anti-tumor effectiveness of calcium electroporation in subcutaneous murine tumor models is dose dependent

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Calcium electroporation is a local tumor ablative treatment, where supraphysiological concentration of calcium is used in combination with elec-troporation to eradicate tumors. It was demonstrated in preclinical in vitro and in vivo studies that calcium electroporation has similar effectiveness as elec-trochemotherapy with bleomycin in differrent subcutaneous tumors. In this study two murine tumor models were used to evaluate how different tumors respond to increasing concentrations of calcium solution alone or in combination with electrporation. For this purpose, two histologically, physiologically and immunologically different tumors B16F10 mouse melanoma and 4T1 mouse breast carcinoma tumor models were selected. We showed that both tumor models respond to calcium electroporation in a dose dependent manner. How-ever, 4T1 tumor model responded better with tumor cures even without addition of electroporation, when 250 mM calcium solution was used. These results demonstrated variable antitumor effectiveness of calcium electroporation which is dependent on tumor properties.

# Application of Artificial Neural Networks for Analysis of Ice Recrystallization Process for Cryopreservation

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Cryomicroscopy is one of the main techniques to visualize freezing and thawing events taking place during cryopreservation of cells, native and artificial tissues with the ultimate goal to provide cell- and tissue-specific cryogenic preservation. However, there is currently no unified software tool for the automated analysis of ice recrystallization kinetics for a variety of cryoprotective agents used in the cryobiological practice. In this regard, we focused on the particular aspect of image analysis in the course of ice recrystallization, i.e. the possibility of using a neural network for the segmentation of ice crystals during isothermal annealing. In the work, the U-Net deep neural network was used for segmentation of ice crystals on cryomicroscopic images. Using 100 images as training set, the resulting accuracy of ice crystal segmentation was about 74% percent on the test sample (30 images). The obtained results show the possibility of segmentation of ice crystals in cryomicroscopic images taking into account the overlapping of intensity levels of an object and background.Further improvement of the model through the use of an additional training data as well as augmentation techniques is required to more efficiently validate this approach.

# Application of electro-mechanical model for investigation of human heart behaviour

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Having the accurate electro-mechanical model is of great importance for better understanding of various heart diseases such as heart failure, cardiac arrhythmia, and cardiomyopathy. In order to make computational models feasible for applications, we summarize our smeared methodology for modelling physical fields, so called composite smeared finite element (CSFE) for electrophysiology simulations. Electric signals are traveling to the heart through the Purkinje fiber network located in thin layer of heart wall called the subendocardium. Additional uniform 3D layer of FE element is generated and added to 3D heart domain, to appropriately take into account this Purkinje network in our CSFE model. Further, for calculation of calcium current and concentration within the cell, we coupled CSFE and OHara-Rudy (oRD) membrane model, a human ventricular action potential (AP) model formulated using undiseased human ventricular data. Electrophysiology module is than coupled with muscle mechanics with widely used Hunter's relation for heart muscle that connects calcium concentration and active stress along fibers. Methodology is tested with respect to real 3D heart model, with using linear elastic and recently developed orthotropic material model based on Holzapfel experiments. This approach has potential to be used in coupled solid-fluid simulation of whole heart in order to give accurate prediction of heart beat for different heart diseases.

# Application of Modeling Techniques in the Process of Health Technology Assessment

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Complex processes and systems are often evaluated in conditions without enough data, where can´t be use an experimentation with a real system. In this case, it is appropriate to use modeling techniques, including simulations. The aim of this paper is to present results of selected master theses carried out by students of Faculty of Biomedical Engineering (FBMI) that used modelling techniques. Paper contains three student's master theses, which applied technique of Decision Tree and Markov Models. In the paper we present: Cost-effectiveness Analysis Fluorouracil's Administration in Patients with Gastric Cancer; Cost-utility analysis of the medical device Cacipliq® and Cost-effectiveness analysis of introducing men vaccination against human papillomavirus in the Czech Republic. Many works then have a practical impact with results that are usable in practice. Students also have the opportunity to participate in the doctoral study program of Biomedical Engineering, where they have the opportunity to further develop their knowledge in clinical engineering.

# Application of smeared modeling concept and Holzapfel material model for investigation of human heart properties

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Application of biomechanical and computational simulations in the field of cardiac tissue modeling, gives us a powerful tool to understand heart function and right course for developing novel therapies to understand disease process better. The authors recently introduced a smeared modeling concept for physical fields in biological media which is here extended to mechanics of these composite media. The CSFEM has a supporting (basic) medium in which are embedded other deformable constituents. Interaction relations are set at the boundaries between constituents and supporting medium, to couple velocities or displacements. The interaction forces are modeled by introducing connectivity elements at the boundary nodes which occupy the same spatial positions. Nodal parameters used in the smeared model are: volumetric fractions, boundary surfaces fractions, material characteristics of each medium etc. In order to test mechanical properties of heart tissue wall we use recently formulated orthotropic material model based on Holzapfel experimental investigation of passive material properties of myocardium. The Cauchy stress/stretch and shear stress/amount of shear relation curves are used in FE computational model (averaged and reconstructed from diagrams), which are estimated experimentally under different loading conditions: biaxial extension and triaxial shear. Accuracy of the CSFEM model is assessed by its comparison to detailed 2D models which consist of fluid domain, solid environment and number of different types of cell domains. Applicability of Holzapfel material model is tested on real 3D heart models. Presented modeling approach offers a simple tool for modeling of complex tissue deformation as in case of tissue with tumors, and can potentially be used in coupling solid-fluid simulation of whole heart.

# Application of SOFA Framework for Physics-Based Simulation of Deformable Human Anatomy of Nasal Cavity

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Surgical medicine is one of the most radical approaches for the treatment of numerous types of diseases. Recently broad application has taken the direction of computational surgery that aims to improve the quality of treatment through the use of computer tools. The use of computational surgery in rhinoplasty is important due to the fact that the results of the intervention directly affect the geometry of the nasal cavity and, as a consequence, the aerodynamic parameters of the nose. In turn, these parameters determine the functional characteristics of the patient's nasal cavity. In this paper, we have focused on modeling the deformation of anatomical structures using SOFA framework software library considering tetrahedron finite element modeling (FEM), hexahedron FEM, triangle FEM and mesh spring force fields. The simulation results indicate the high functionality of the SOFA framework for modeling the deformation of the airway in rhinosurgical interventions. These results could further be applied for modeling the deformation of the anatomical structure taking into account the change in the topology of a 3D model to simulate such surgical procedures as a cut.

# Application optimized shielding strategies for OPM based MEG devices

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Intrinsic properties of optically pumped magnetometers (OPM) are very different from those of superconducting quantum interference (SQUID) devices. This leads to different requirements for magnetically shielded rooms if arrays of several sensors are utilized for magnetoencephalography (MEG). Two important properties, dynamic range and bandwidth, are almost opposite for the two types of sensors. Current commercial OPMs have a dynamic range of about 5 nT and a bandwidth of 150 Hz, whereas for SQUIDs the same properties can be as large as 200 nT and 1 MHz.

Due to the radio frequency (RF) sensitivity of SQUIDs the „classic“ Ak3b shielded room (present commercial name Vacoshield Advanced, Vakuumschmelze) has two layers of mu-metall and additionally a RF shield made of copper or aluminium. This can in future be omitted for OPMs as they are insensitive to RF magnetic fields. The small dynamic range of current commercial OPMs is a severe limitation if an existing Ak3b is used for OPM based MEG, because in such a room the slow field fluctuation in the range of 0.1 Hz can reach +- 10 nT. These fluctuations saturate the OPMs or drive them into their non-linear regime. The slow fluctuations are not a design fault, but an intrinsic property of mu-metall based magnetic shielding which becomes much less effective below 1 Hz in comparison to higher frequencies.

A very efficient but complicated approach is the design of compensation coils based on MRI shimming coils (Boto et al., 2018), which are placed inside the room. Another solution is the inclusion of a 3rd mu-metall layer, which improves shielding sufficiently for OPM operation (Reermann et al., 2019). A third solution are xyz-Helmholtz coils along the outside edges of the room and to use fluxgates on the outside surfaces of the room as correction signal for the compensation. Using this third approach we will demonstrate, that it is possible to operate an OPM-MEG covering the head similarly to SQUID-MEG in the Ak3b. This active shielding enables OPM operation without sensor saturation and avoiding the non-linear regime of the sensors. The dynamic range of the compensating electronics is sufficiently large to allow 30 min and more continuous OPM operation.

Boto E et al. (2018) Nature, 555:657-661.

Reermann J et al. (2019) IEEE Sens J, 15:4237-4249.

# Artificial intelligence for medical imaging. How does it work? Which impacts could be anticipated for imaging departments and operating theater?

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This presentation is an outreach about artificial intelligence (AI) for medical imaging and the impact we could anticipate for the next years in our hospitals. This work is not the outcome of a research study but the vision of the clinical engineers that we are. Our missions, in public or private health establishments are to purchase, lead the deployment and assume the maintenance of medical systems, softwares included. To follow the technology's evolution and help French biomedical engineers to integrate innovation, AFIB (French association of biomedical engineers) frequently lead missions of technology monitoring, e.g. at the RSNA (Radiological Society of North America) annual meeting in Chicago or to the Arab Health congress.
AI is a huge topic which should strongly impact our organizations and will require important investments. In this context of fast innovation we also have to think the future of our buildings, in particular, the imaging departments and operating rooms.
This presentation will introduce, in the medical imaging context, the new vocabulary we are facing: machine learning, deep learning and convolutional neuronal networks (CNN). Then, we will explain how these new AI-based-algorithms are created, how CNN works, and have a focus on the importance of data based used for their learning and so, on their performance evaluation. We will also list the major aspects improved by AI like images reconstruction, x-ray dose reduction, segmentation and diagnostic applications.
We will share our purchaser vision about the market situation and the items to consider before buying an AI-based-diagnostic (automated) solution, like the workflow integration or return on investment evaluation.
To conclude we will try to anticipate few major impacts for our hospitals, for the imaging departments of course, but also for in operating rooms. Indeed, AI will bring great progress in segmentation and image fusion capacity. Added to augmented reality and robotics, images will take an increasingly important place in the theaters and will deeply modify their conception.

# Artificial Intelligence in Nanotechnology: Recent trends, challenges and future perspectives

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Nanoscience and nanotechnology are two overlapping areas of human activi-ty, that take into consideration characteristics and utilization of nanoscale materials, and thus have applications in the majority of scientific fields. Na-noscience and nanotechnology can be used in conjunction with Artificial In-telligence since they are present in various fields ranging from medical diag-nostics to robotics. Advancements in the precision of medicine were highly influenced by nanomaterials. This paper is a review of artificial intelligence in nanotechnology and was done through a literature review of 10 papers. According to the available literature on different platforms, it can be con-cluded that the concern for artificial intelligence in nanotechnology has been highly increased in the past decade. The paper presents how this combination of sophisticated techniques can be used for different medical purposes, and with different methodologies of both, artificial intelligence and machine learning.

# Assessment and Classification of Muscle Contusion by Ultrasound Quantitative Parameters and Image Texture

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Muscle contusion is a common lesion applicable to almost all individuals. A non-invasive means, such as ultrasound imaging, to better detect and assess the region and status of muscle contusion is essential for further treatment planning. Yet, the accuracy of diagnosis with typical ultrasound B-mode image is still largely dependent on operator's experience and system settings. In the present study, in vivo muscle contusion model were arranged by applying a certain impact onto the rat's leg in which a 30 MHz ultrasound transducer was subsequently implemented to acquire a series of signals and images from a tissue volume of 6(D)x15(L)x10(W) mm. The experiments were carried out from 22 rats and that data were daily collected for three weeks covering such healing stages of muscle contusion as the health, destruction, repair, and remodeling. To further eliminate the system factors, ultrasound quantitative parameters, including integrated backscatter (IB) and Nakagami m-parameter, and image texture parameters estimated from gray-level co-occurrence matrix (GLCM) were calculated. Results showed that ultrasound quantitative and image texture parameters are capable of differentiating healthy tissues from those of contused muscles of different healing stages. Specifically, the largest IB and Nakagami m-parameter were obtained from the destruction stage at the second day of contusion healing. The support vector machine using ultrasound quantitative and GLCM parameters was further applied to classify stages of muscle contusion healing. The 96% and 80% classification accuracy corresponding to the destruction and repair stages, respectively, were achieved. This study demonstrated that ultrasound parameters and image textures analysis are feasible to be further applied for clinical diagnosis of contused tissues.

# Assessment of Associations between Arterial Mechanical Properties and Biochemical Blood Markers for Early Detection of Atherosclerosis

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Extensive research has been carried out to find associations between arterial stiffness markers and blood levels of low-density lipoprotein cholesterol (LDL-Chol), triglycerides (TG), total cholesterol (TC) and high-density lipopro-tein cholesterol (HDL-Chol) relating to assessment of cardiovascular diseases' (CVD) risk factors and early detection of atherosclerosis. However, data on levels of atherogenic lipoproteins as apolipoprotein B (apoB), low-density lipopro-tein(a) (Lp(a)) and high-density apolipoprotein A (apoA) related to arterial bio-mechanical properties are scarce.

The aim of this study was to investigate whether stratification of the popula-tion according to serum levels of atherogenic lipoproteins (apoB, Lp(a), TG, TC, LDL-Chol) and high-density lipoproteins (HDL-Chol, apoA) are related to arte-rial biomechanical properties for early and non-invasive cardiovascular risk di-agnosis.

The investigation was conducted on 44 healthy subjects with familial hyper-cholesterolemia in their anamnesis. A SphygmoCor device for the aortic pulse wave velocity (PWVao) and augmentation index estimation, and an ultrasound device for carotid intima-media thickness, the radial artery, and the femoral artery wall thickness and lumen diameter measurements, were utilized.

An association between the serum apoB values and the radial artery wall thickness ($p = 0.03$) and the radial artery wall thickness to lumen diameter ratio was found ($p = 0.05$), indicating that the apoB level may be related to the arterial remodeling process. Also, a dependence between TG levels and age-related PWVao ($p = 0.02$) was discovered, which needs further investigation.

# Assessment of least square boosting to estimate apnea-hypopnea index from at-home oximetry recordings

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Polysomnography (PSG) is the standard diagnostic test for sleep apnoea-hypopnoea syndrome (SAHS), but it has been proven technically complex, costly, and time-consuming. Favoured by the high prevalence of SAHS, it helps increase waiting lists and delays access to treatment of the affected population. In this context, the diagnostic assessment of automatic machine-learning techniques applied to a reduced set of the signals involved in PSG has become a common investigation field. We hypothesise that the information obtained from portable nocturnal oximetry along with the generalisation ability of the ensemble-learning methods could be useful to simplify SAHS diagnosis. Particularly, our aim is the analysis of 322 overnight single-channel oxygen saturation signals (SpO2) recorded at patients' homes. First, each SpO2 recording is characterised by the extraction of 32 features from different analytical approaches (clinical, statistical, spectral, and non-linear). Then, the fast correlation-based filter is used along with a bootstrap procedure to select the most relevant but non-redundant among them. The optimum set of selected features from a training set (N=200) is used to obtain a least squares boosting model (LSBoost) with ability to estimate the apnoea-hypopnea index (AHI), which is the clinical measure used to establish SAHS and its severity. Then, the model is validated on a previously unseen test set (N=122). Our results show that 4 SpO2 features were considered relevant and non-redundant: 3% oxygen desaturation index (clinical), kurtosis of the SpO2 time series (statistical), Wootter's distance of the spectrum (spectral), and the scale with the maximum value of the multiscale entropy (non-linear). Using these features, the LSBoost training process ended up in an ensemble of 100 decision trees. The automatically estimated AHI showed an intra-class correlation coefficient of 0.918 with actual AHI, as well as 0.658 Cohen's kappa when using it to classify SAHS into the common 4 severity degrees (no SAHS, mild, moderate, and severe). Moreover, the binary assessment of its performance on each of the 3 AHI thresholds that defines these severity degrees (5 e/h, 15 e/h, and 30 e/h) resulted in the next respective accuracies: 94.3% (99.1% sensitivity, Se, 40.0% specificity, Sp), 86.9% (84.8% Se, 93.3% Sp), and 92.6% (84.6% Se, 98.6% Sp). Thus, our results suggest that LSBoost could be used to automatically estimate AHI from at-home SpO2 to simplify SAHS diagnosis. Funding: MINECO and FEDER (DPI2017-84280-R) and CIBER-BBN

# Asymmetric uptake of calcium ions into cultured cardiac cells after electroporation

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Electroporation of cardiac cells has drawn attention in recent years due to the possibility to treat heart fibrillations. Ablation of arrhythmogenic tissue creating a permanent transmural lesion was currently explored using different pulsing protocols with pulse durations from a few microseconds to a few milliseconds (1). However, the electroporation extent on a cellular level and transport of molecules and ions such as calcium ions into cardiac cells after applying electric pulses of different durations is not yet fully explored. Moreover, the polar direction of marker dyes and ions uptake into different cells (from anode- or cathode-facing pole of the cell) depends on different factors and is still not completely understood (2, 3).
Therefore, the changes in intracellular concentration of calcium ions following exposure of cells to electric pulses of microsecond and nanosecond range was compared experimentally in vitro on H9c2, an attached cell line with elongated cells (rat cardio myoblasts, ventricular). Cell calcium was monitored under a fluorescence microscope using a fluorescent calcium indicator Fura-2, in conditions with or without external calcium. Monitoring was performed during the first few seconds after pulse application with an image acquisition in the millisecond time range. The uptake of calcium ions was different for microsecond than for nanosecond pulse electroporation in terms of direction and source of calcium ions (internal, external).

References:

1. Sugrue A, et al. Irreversible electroporation for catheter-based cardiac ablation: a systematic review of the preclinical experience. J Interv Card Electrophysiol. 2019. 55(3):251-265
2. Tekle E, et al. Selective and asymmetric molecular transport across electroporated cell membranes. Proc Natl Acad Sci U S A. 1994. 22;91(24):11512-6.
3. Semenov I, et al. Diffuse, non-polar electropermeabilization and reduced propidium uptake distinguish the effect of nanosecond electric pulses. Biochim Biophys Acta. 2015. 1848(10 Pt A):2118-25.

# Atlas Optimization for Deep Brain Stimulation

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Electrical stimulation of the deep parts of the brain is the standard answer for patients subject to drug-refractory movement disor- ders. Collective analysis of data collected during surgeries are crucial in order to provide more systematic planning assistance and understand- ing the physiological mechanisms of action. To that end, the process of normalizing anatomies captured with Magnetic Resonance imaging across patients is a key component. In this work, we present the op- timization of a workflow designed to create group-specific anatomical templates: a group template is refined iteratively using the results of successive non-linear image registrations. In order to improve the results in the basal-ganglia area, the process is refined in this specific volume of interest. All non-linear registrations were executed using the Advanced Normalization Tools (ANTs). The quality of the normalization was mea- sured using the manual delineation of anatomical structures produced during the planning of the surgery and their spacial overlap after trans- formation in the template space by means of Dice coefficient and mean surface distance. The parameters of the workflow evaluated were: the use of multiple modalities sequentially or together during each registration to the template, the number of iterations in the template creation and the fine settings of the non-linear registration tool. Using the T1 and white matter attenuated inverse recovery modalities together produced the best results, especially in the center of the brain. The optimal num- bers of iterations of the template creation were higher than those advised in the literature and our previous works. Finally, the setting of the non-linear registration tool that improved results the most was the activation of the registration with the native voxel sizes of images, as opposed to down-sampled version of the images. The use of the delineation of the anatomical structures as a mean to measure the quality of the anatomi- cal template of a group of patient allowed to optimize the normalization process and obtain the best possible anatomical normalization of this specific group of patient. The most crucial points were the combination of multiple modalities in order to maximize the quality of information available during image registration and the activation of the registration with native voxel size. The anatomical template of the group will be used to summarize and analyze peri-operative measurements during test stimulation. The aim is that the conclusions obtained from this analysis will be useful for assistance during the planning of new surgeries.

# Augmented reality biofeedback for muscle activation monitoring: proof of concept

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Augmented reality is an emerging technology allowing to add computer-generated perceptual information superimposed to a real-world object. Biofeedback based on electromyography converts the muscle activation levels into visual or auditory information. This information can be used to facilitate or inhibit muscle contraction and is considered a suitable treatment for a wide range of musculoskeletal disorders. However, current feedback techniques are simplistic and not intuitive for the patient which limits clinical effectiveness. This work describes the design and development of an Augmented Reality system which allows the visualization of a graphical information about muscle activity superimposed on the EMG detection system over the investigated muscle. The system integrates sensors for muscle activity detection (both bipolar and high-density sEMG), wearable acquisition systems for the conditioning and wireless transmission of surface EMG signals, and a processing/visualization system to provide information on muscle activation to the user through augmented reality. A proof of concept of the developed system has been conducted for the following application fields: rehabilitation, sport, and ergonomics. The system is expected to: i) provide a novel tool to assess muscle activity in different scenarios and 2) increase the effectiveness of EMG biofeedback.

# Automatic detection of naming latency from aphasia patients – using an extended threshold-based method

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Word finding difficulties represent the major symptom in aphasia which can be trained and diagnosed using naming exercises. Existing evaluation tests in German for aphasia are based on subjective assessments. No quantitative evaluation tools exist so far able to objectively identify changes in speech performance in aphasia patients with time. The naming latency, i.e. the time it takes until a patient says the word after showing him an image of an object f. ex. could be a candidate. The aim of the present study was to develop an automatic naming latency detection algorithm and to evaluate its potential as such a quantitative parameter.
Eight aphasia patients were included during an observational study (BASEC-ID: 2019-00083). Audio data were collected from four consecutive evaluations through 20 images of the naming test of the German Aachener Aphasie Test (AAT). In total 272 recordings were available.
Manual determination of the naming latency was performed as a gold standard.
An extended threshold method based on three parameters was implemented to automatically determine the naming latency. The first parameter describes how long the envelope of the speech wave must be over the threshold. The second one tells how long the envelope may fall below the threshold during a word. The third parameter is the value of the threshold itself. To define those three parameters, the Nelder-Mead algorithm (fminsearch function from Matlab®) was selected as an optimization method. With these three optimized parameters, the speech latency of all available patients was measured and statistically compared to the manually determined ones using a two one-sided t-test and the Pearson correlation.
The optimization showed the highest performance with a threshold value of 19.8% of the signal amplitude, a minimal word-length of 105ms and a time under threshold of maximal 417ms. The comparison of the automatically measured naming latency based on these three parameter values with the manually determined ones, showed a variance of -229ms and +323ms with the two one-sided t-test with a 95% confidence interval and a Pearson correlation coefficient of 0.98 with a p-value $< 0.01$ (2.1*10-192).
The result shows a high correlation between the automatic measured naming latencies using an extended threshold-based method and the manually measured ones. It has the potential to be implemented for automated progress evaluation in aphasia patients during naming exercises performed at home or during naming tests for diagnosis.

# Automatic Detection of Real and Imaginary Parts of Electrical Impedance with Single Synchronous Demodulation Channel

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Measurement of a voltage response caused by a current excitation signal sent to a biological system under study, i.e. measurement of electrical bioimpedance, is typically using analog or digital lock-in detection. Such a detector consists multiplying unit together with following low pass filter. Result of such a multiplication is typically acquired in-phase with excitation signal, and in quadrature with it. Later the actual bioimpedance vector can be calculated with its magnitude and phase. It can be viewed as performing correlation between excitation and response signals in two positions: with zero shift and 90 degrees shift. It requires two identical channels, exact identity of which is hard to achieve. Method for automatic single channel detection is proposed, analyzed and tested in the lab for acquisition of the electrical bioimpedance signal at the radial artery. Proposed method is useful when wearable low power acquisition of the electrical bioimpedance is required. It simplifies circuitry significantly, by thereby increasing reliability and lowering power consumption.

# Automatic MR spinal cord segmentation by hybrid residual atten-tion-aware convolutional neural networks and learning rate optimi-zation on real world data

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MR is the most sensitive clinical tool in the diagnosis and monitoring of multiple sclerosis (MS) alterations. Spinal cord (SC) evaluation has gained interest in this clinical scenario in the last 10 years but unlike in brain, there is a lack of algorithms assisting SC segmentation. Our goal was to investigate and develop an automatic MR cervical SC segmentation method that would enable seamless imaging biomarkers extraction related to SC atrophy and lesion infiltration. This algorithm was developed using a dataset based on real-world MR data of 121 MS patients. 96 cases were used as training data and the remaining 25 cases were retained as the testing data. MR sequences used consisted of 3D T1 gradient echo MR axial images, acquired in a 3T system (SignaHDUSA),(TE/TR/FA:1.7-2.7ms/5.6-8.2ms/12º). Manual labeling ground-truth is performed under radiologist supervision. The architecture of the 2D convolutional neural network consisted of a hybrid residual attention aware segmentation method trained to extract the region of interest. The training was designed with a focal loss function based on the Tversky-index to address the issue of label imbalance in medical image segmentation and an automatic optimal learning rate finder. Our model provided an automated and accurate method achieving a DICE coefficient of 0.87. An automatic method for SC segmentation from MR was successfully implemented. It will have direct implications for accelerating the process for MS diagnosis, follow-up and extraction of imaging biomarkers.

# Average Walking Speed Estimation with an Inertial Sensor in 10-m Walk Test: A Validation Test with Healthy Subjects

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Information obtained from an inertial sensor attached on the foot would be useful in gait rehabilitation, healthcare and so on, because it provide various evaluation parameters such as stride length, inclination angle and gait event timings. The purpose of this study was to develop an estimation method of average walking speed with the inertial sensor attached on the foot. In this paper, average walking speed was estimated by estimated stride length and time of movement state of each stride during walking. The proposed estimation method of average waking speed was evaluated in comparing to measured walking speed with a stopwatch in 10 m walking test with healthy subjects. Mean difference of walking speeds between measured and estimated walking speeds was -0.60±4.04% (-0.007±0.048 m/s), and mean absolute value of the difference was 3.05±2.71% (0.035±0.033 m/s). Correlation coefficient between them was 0.986. Most of average walking speed were estimated with good accuracy, which were almost be-tween ±10% and between ±0.1 m/s. These results suggested that the average walking speed estimation with an inertial sensor would be useful. In order to improve estimation accuracy for a specific subject and fast speed walking, in which stationary state between strides is very short time, is expected.

## Bacteriostatic supports with gold nanoparticles for osteoblast cells sustaining

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Introduction: Antibiotic resistance is a worldwide problem regardless economical factors. These rank among one of the most significant causes of non-healing wound which implies longer hospital stays and even increased mortality. Therefore new solutions need to be investigated including novel materials for biomedical applications. Metallic nanoparticles can serve as effective bacteriostatic element of this materials. We have been developed the nanocomposite membranes based on polyethyleneimine with gold nanoparticles (AuNPs) incorporated within in combination with chosen additives for human osteoblasts immobilization as an element for bandages application. The constructed membrane contact angle and transport properties were evaluated. The membrane cytotoxicity was assessed. Moreover the cellular uptake of the nanoparticles by evaluated cells was assessed.
Methods: The layer or bilayer membranes based on polyethyleneimine or hydroxyapatite were constructed. The contact angle of the membrane substrates for water was measured using a surface energy analyzer. ImageJ was used to analyze the drop photos. The coniungation of the AuNPs with fluorescein isothiocyanate (FITC) was performed and confirmed spectrophotometrically. The cellular uptake of Au-FITC was assessed. For that purpose the cells were cultured in the medium supplemented with Au-FITC at different concentrations. As a negative control the cells were cultured in culture medium without Au-FITC addition. Then the cells morphology was examined by fluorescence microscopy. Moreover, cell viability was assessed using propidium iodide in a flow cytometer.
Results and Discussion: All investigated membranes showed hydrophilic character. The immobilized cells revealed presence of fluorescent Au-FITC during microscopic observation. Results of the flow cytometry analysis allowed to assess the optimal Au-FITC concentration unlimiting the osteoblasts function. This study demonstrates that polyethyleneimine-based membranes with incorporated gold nanoparticles can be recommended for biomedical application, although the concentration of the nanoparticles needs to be considered.
Acknowledgements: This project was partially supported by ESF, POWR.03.02.00-00-I028/17-00

# Beat-to-Beat Detection Accuracy Using the Ultra Low Power Senbiosys PPG Sensor

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Heart-rate variability (HRV) is a strong indicator of a healthy cardiovascular system. It is the physiological phenomenon defined by the variation of the duration between consecutive heartbeats. Consequently, for a proper and a reliable HRV analysis, it is essential to have an accurate estimation of the inter-beat intervals (IBI). In addition to accurate IBI detection, unobtrusive and low power consuming devices are important for long term HRV monitoring. In this study, we aim at evaluating the beat-to-beat detection accuracy of the ultra low power Senbiosys Photoplethysmography(PPG) sensor, the SB200. Eight male subjects ($37.25 \pm 10.67$ years of age) participated in the study. The recordings include a finger PPG from the SB200, another finger PPG from the Shimmer3 optical development kit, and a reference ECG from the Shimmer3 ECG development kit. The study shows that the SB200 detects 99.27% of the beats with IBI values of mean absolute error (MAE) 6.58ms compared to the R-to-R interval (RRI) values derived from the ECG and an average current consumption of less than $190\mu A$. Moreover, reducing the LED power consumption of the SB200 by 1/2 and 1/4 does not affect the detection rate, maintaining its value at 99.25% and 99.22%, respectively. However, it does reduce the IBI estimation accuracy resulting in an MAE of 7.37ms and 8.43ms, respectively.

# Bio-Medical Equipment Technicians: Crucial workforce to improve quality of health services in rural remote hospitals in Nepal

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Continuous developments in science and technology are increasing the availability of thousands of medical devices – all of which should be of good quality and used appropriately to address global health challenges. It is obvious that biomedical devices are becoming ever more indispensable in health service delivery and among the key workforce responsible for their design, development, regulation, evaluation, and training in their use: biomedical technician (BMET) is crucial. As a pivotal member of the health workforce, biomedical technicians are an essential component of the quality health service delivery mechanism supporting the attainment of the Sustainable Development Goals.

The study was based on a cross-sectional descriptive design. Indicators measuring the quality of health services were assessed in Mechi Zonal Hospital (MZH) and Sagarmatha Zonal Hospital (SZH). Indicators were calculated based on the data about hospital utilization and performance of 2018 available in the Medical record section of both hospitals. MZH had employed the BMET during 2018 but SZH had no BMET in 2018. Focus Group Discussion with health workers in both hospitals was conducted to validate the hospital records. A client exit interview was conducted to assess the level of client satisfaction in both hospitals.

In MZH there was round the clock availability and utilization of Radio diagnostics equipment, Laboratory equipment. Operation Theater was functional throughout the year. The bed Occupancy rate in MZH was 97% but in SZH it was only 63%.In SZH, OT was functional only 54% of the days in 2018. CT scan machine was just installed but not functional. Computerized X-Ray in SZH was functional only in 72% of the days. The level of client satisfaction was 87% in MZH but was just 43% in SZH. MZH performed all (256) the Caesarean Sections but SZH performed only 36% of 210 Caesarean Sections in 2018. In annual performance ranking of Government Hospitals, MZH was placed in 1st rank while SZH was placed in 19th rank out of 32 referral hospitals nationwide in 2018.

Biomedical technicians are the crucial member of human resources for the health team with a pivotal role. Trained and qualified BMET professionals are required within health-care systems in order to design, evaluate, regulate, acquire, maintain, manage and train on safe medical technologies. Applying knowledge of engineering and technology to health-care systems to ensure availability, affordability, accessibility, acceptability, and utilization of the safer, higher quality, effective, appropriate and socially acceptable biomedical technology to populations for preventive, promotive, curative, rehabilitative and palliative care across all levels of health service delivery.

# Biocompatible cryopreservation of multipotent mesenchymal stromal cells for clinical use

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Therapeutic potential of multipotent mesenchymal stromal cells (MSCs) has been demonstrated in numerous reports and clinical trials. Usually, freshly harvested cultured cells have been used for applications in regenerative medicine and tissue engineering. However, long term storage of the cells is often desired, either due to preparation of multiple advanced therapy medicinal product (ATMP) doses from a single source or due a necessity for an off-the-shelf stem cell-based ATMP e.g. for acute indications.
Cryopreservation allows such storage with a swift availability of the cells and, importantly, allows performing of all required quality tests. Most of the available cryopreservation media contain cryoprotectants (i.e. dimethyl sulfoxide - DMSO) at toxic concentrations, usually requiring their removal by washing and resuspension of the cells in a final solution. Such steps, however, prevent the direct application of the ATMP to the patient, may discount previous manufacturing process in accordance with Good Manufacturing Practice (GMP) and they require qualified equipment and validation enforced by regulatory authorities.
Generally, concentrations of up to 5% and 2% of DMSO are accepted for systemic and local clinical applications, respectively. In this study, we introduce a method of cryopreservation of MSC that is non-toxic, fulfills GMP requirements and is suitable for direct application to patients. The protocol has a short pretreatment step followed by fast freezing. Our method does not require any special equipment for thawing and the product can therefore be thawed at the clinical site and the cells can directly be applied systemically or locally. Importantly, the cells maintain their viability (80-90%) and phenotype in this solution at least for 24 hours after thawing, providing convenience for transportation at 2-8°C within this time period.
In summary, our cryopreservation protocol provides a convenient stem cell-based ATMP handling and a biocompatible clinical grade long-term storage method.

# Biological predictive factors for the response of tumors to electrochemotherapy: preclinical studies

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Electrochemotherapy is effective in treatment of cutaneous and deep seated tumors. However, recently variability in the repose rate of tumors was observed, that needs to be explored and understood. The early studies have sought for the correlation between the intrinsic sensitivity of the tumor cells to electrochemotherapy and the response of tumors to electrochemotherapy. It was shown that SA-1 (fibrosarcoma) tumors were more responsive than EAT (Ehrlich ascites carcinoma) tumors, which was in correlation with the tumor cell sensitivity to electrochemotherapy with bleomycin. However, also other factors may affect the response rate of cells and tumors to electrochemotherapy with bleomycin or cisplatin. Previously irradiated tumors may be resistant due to the two reasons, either the intrinsic resistance of tumor cells that was acquired during the tumor irradiation or the tumor bed effect, i.e., hampered vascularization of the tumor bed. Our study demonstrated that tumors with induced intrinsic radioresistance (obtained by fractionated irradiation of tumor cells) had a lower response rate to electrochemotherapy with cisplatin. The modification of tumor cells by mutations or viral infection could also affect the response rate of the tumors. We found that BRAF tumor mutation does not affect the response of tumor cells to electrochemotherapy, providing preclinical evidence that tumors refractory to targeted therapy can be successfully treated with electrochemotherapy. Furthermore, also the HPV infection of tumor cells in head and neck squamous cell carcinoma can modulate the tumor response. It was found that HPV-positive tumors respond better to electrochemotherapy with cisplatin than to electrochemotherapy with bleomycin. Also, tumor vascularization may affect the response of tumors to electrochemotherapy as it is important for drug distribution and drug pharmacokinetics. In our preclinical study the TS/A carcinoma tumors were more responsive to electrochemotherapy with bleomycin than B16F10 melanoma. This could be attributed to the difference in bleomycin pharmacokinetics, which was attributed to the differences in tumor vascularization, as carcinoma tumors had numerous well-distributed small blood vessels, while melanomas were less vascularized, exhibiting larger vessels. Furthermore, the immunogenicity of the tumors might contribute to the responsiveness of the tumors. All these studies demonstrate that there are predictive factors that may help to tailor electrochemotherapy to specific tumor characteristics, and consequently improve treatment effectiveness of specific tumors.

# Biomechanical characteristics of non-stationary respiration regimens as possible indicators of fatigue in monotonic hypokinetic load

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The target of the study was revealing of a potential relationship between the fa-tigue accompanying a hypokinetic monotonic load and breathing. The secondary target was to describe it with the respiration parameters. After that, there was a question whether some of the parameters used can be applicable not only to the fatigue indication but also to its prediction.
Five volunteers participated in the experiment, who underwent measurements with simultaneous monitoring of the brain electric activity, respiration and chang-es in volumes of the thorax. For the whole time period of the experiment, their ac-tivities were recorded by a video camera. In the first part of the experiment, the probants carried out a monotonic task (Tracking Task), in which they were sup-posed to pursue as precisely as possible a small target on the monitor moving with random velocities in random directions. In the second part of the experiment, the probants only relaxed watching a movie. The two parts of the experiment were measured in two variants – active and tired (after 24-hrs sleep deprivation) probants. The data acquired were subsequently compared.
The results achieved demonstrated that the presence, and to a considerable extent also intensity, of the fatigue, can be reliably indicated and evaluated through the mediation of monitoring the occurrence of respiration volume and frequency non-stationarities manifested in otherwise steady-state breathing regimens in the per-sons monitored. Based on the results achieved, it is also possible to state that the respiration cycle monitoring can also be used for the prediction of the fatigue.

# Biomedical and Clinical Engineering in Europe: An Insight Into the Current Situation

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The global medical device market is projected to expand at a compound annual growth rate (CAGR) of 5.4 percent between 2019 and 2025. In recent years, Europe has been leading this growth by accounting for about 40 percent of the market. This is reflected in the number of patents filed with the European Patent Office (EPO) for medical technologies (MTs) - around 13,000 in 2017, doubling that of pharma- and biotechnologies. It can therefore be inferred that the medical device market will become one of the main drivers of the European economy in the next decade.

Increasing concerns about non-recognition of biomedical/clinical engineers, and their massive contributions to the delivery of safe, reliable and effective MTs and patient outcomes led to a 3-year examination of published evidence by the international federation for medical and biomedical engineering (IFMBE)/clinical engineering division (CED). This process yielded success stories highlighting great improvements in quality of human life, care management decision support and operational efficiency. Also in 2014, the World Health Organization (WHO) stated the importance of trained and qualified biomedical engineering (BE) professionals in promoting the safe and efficient use of medical devices around the world. Based on this, in 2015, the European Economic and Social committee (EESC) concluded that BE is not a subset of modern medicine, but rather, that modern medicine is the product of BE.

Considering that the time required for a medical device to hit the market is becoming progressively shorter (with a typical lifecycle of about 18-24 months before an improved product becomes available), the world might face a “tsunami” of medical devices over the next 10 years - a situation which may further revolutionise the way health initiatives are delivered. Stronger regulation for medical devices, as well as MT professionals are thus required. Recently, Europe has been steadily focusing on new medical device regulations to improve medical device surveillance, and devise a novel European nomenclature for medical devices. Nonetheless, no common regulation currently exists to guide experts in the field who would be most qualified for guaranteeing the safe and efficient use of medical technologies.

In this talk, we present the results of a survey involving over 100 biomedical and clinical engineers from around Europe, which yielded 8 priority claims for the consideration of the European Parliament with regards to MT professionals, and we map the different requirements necessary to work as a clinical engineer across Europe.

# Biomedical application of Fe-Mn Oxide Nanoparticles

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The paper presents the thermal characterization of Fe-Mn oxide nanoparticles with high SAR value, when used in magnetic field hyperthermia conditions. The synthesis shows good reproducibility. Finally, the paper presents a possible use of the presented nanoparticles included in PLGA nanocarriers for biomedical ap-plication.

# Biomedical Engineering Education in Europe: A 30 Years Review

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The aim of this work is to perform a survey of the Biomedical Engineering (BME) educational programs offered in Europe today, compare them with the situation ten and twenty years ago and identify potential trends and approaches. The results demonstrate the exploding growth of the field with the number of graduate and postgraduate study programs offered, to approximately double every 10 years. According to our findings today across Europe 182 Universities offer 344 BME educational pro-grams, of which 115 are Undergraduate offering BSc degrees, and 229 postgraduate programs, 175 of them offering an MSc degree and 54 PhD degrees. The Clinical Engineering (CE) programs are still less than ten, but their number is increasing. In conclusion BME education is getting a leading role in engineering studies, almost everywhere in Europe. However, harmonisation of studies is necessary for the advancement of the BME/CE profession. This should come out from a wide acceptance, of a consensus-based agreement on a generic core curriculum, that will facilitate a worldwide opening of the BME job market, through mutual recognition of the competencies acquired.

## Biomedical Engineering; Biorobotics and Social Innovation

Maria Chiara Carrozza
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Research, science and social innovation are strictly interdependent, and in this framework, my vision for the future is that progress of humanity is the ultimate mis-sion of science.

Today, it is universally accepted in science that challenges of the society will re-quire a strong interdisciplinary effort for scientists: it is not possible to address global problems as clean energy production, urbanization, migration, antibiotics resistance or climate change without a holistic approach. Social challenges require comprehensive methods and knowledge, which must include human sciences, ethical issues and sus-tainability.

The integration of robotics with artificial intelligence, deep learning and high-speed connection will revolutionize the society because devices will be connected to inter-net, and will become physically powerful, intelligent and adaptive. Large amount of data will be available with small latency and cloud robotics will share information, data, intelligence activities and brains. Robots were originally designed for manufac-turing plants, and nowadays mass production is not possible without robots but now they are more and more applied in Medicine and they are revolutionizing surgery, endoscopy, rehabilitation medicine and prosthetics.

The next step will be for Robots to enter in our everyday life: in the streets with self-driving cars, in education robotics, or 'at our place' in doing cleaning, entertain-ment or service activities at home. Robotics is becoming social.

In order to achieve these goals, biomedical engineers must address several issues, related to human-robot interaction, to safety, to sentience and adaptability. The prob-lem of safe, secure and effective interaction between human being and robot is one of the open issues for future biomedical engineering scientists. The human-robot integra-tion is based on different levels of physical, cognitive and biomechanical synergy between robots, bionic technology and artificial intelligence, and can be classified according to the invasiveness of hardware into the human body, from Wearable ro-botics to Implantable or Endo Robotics.

Many interesting scientific and technical questions are open for Biomedical engi-neering in this area.

# Bridging multiphysics simulation and cell culture to validate the potential of electroporation in liver cancer

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Among all minimally invasive cancer therapies, electroporation-based therapies are promising new methods, mainly due to their non-thermal effect and tumor specific approach. This study aimed to define the distribution between irreversible and reversible electroporated cells at different electric field strengths through simulation and cell suspension experiments.
In order to predict the results that should be acquired from the cell culture, different simulations were done in COMSOL-Multiphysics simulation software with different voltages to see how the electric field was spreading across the cells. In order to define the fraction between irreversible and reversible electroporated cells, the following fixed parameters (70 pulses / 100 µs pulse length / 100 µs interval) and variable parameters (0 V / 200 V / 400 V / 600 V / 800 V) were applied on the model.
In order to validate this model, in vitro cell suspension experiments with a human hepatocellular carcinoma cell line (Hep G2) were conducted. 500 µL Hep G2 cells (1*106 cells/mL diluted in HEPES buffer) was added to the 0.2cm gap in the electroporation setup. In order to define the threshold for irreversible electroporation, the same parameters were applied on the cells as during the simulations. For each experimental condition, the cell viability was determined by a dye exclusion assay with Trypan Blue after 0, 5, 10 and 15 minutes.
To conclude, this study found an increasing fraction of irreversible electroporated cells over reversible electroporated cells at increasing field strengths through both simulation and cell suspension experiments.

# Can a cuffless blood pressure monitor replace cuff-based sphygmomanometers in clinical practice?

Toshiyo Tamura
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Small mobile devices with an embedded cuffless blood pressure (BP) monitor have been developed. Although these devices do not use cuffs and are easy to handle and inexpensive, they are difficult to evaluate. No study has evaluated the healthcare applications of such devices in nursing homes or clinics. Therefore, it is difficult to determine their advantages and effectiveness in that context. Only a few devices have been approved by the US Food and Drug Administration and the Conformité Européenne(CE). We evaluated a cuffless sphygmomanometer based on standards for current non-invasive sphygmomanometers.
A small, cuffless BP monitor (Checkme, Viatom, China) with the CE mark was studied. The BP is estimated through beat-to-beat determination of the pulse transit time (PTT), calculated as the interval between the R-wave on the electrocardiogram and the arrival of the corresponding pulse wave (determined from the finger photoplethysmography signal) at a peripheral site. Systolic and diastolic blood pressure (SBP and DBP, respectively) are estimated based on the relationship between the BP level and PTT. We tested the accuracy and long-term stability of the Checkme device. The study protocol was approved by the ethics committee of our institution. All participants provided informed consent before entering the study. To evaluate accuracy, 30 normal subjects of both sexes, aged 25 years or more and with SBP and DBP levels of 80–75 and 57–117 mmHg, respectively, were enrolled. Two observers measured the SBP and DBP with a mercury sphygmomanometer. The beat-to-beat PTT was measured simultaneously and averaged at 30-s intervals, and BP was estimated using a formula. The two values were then compared. A stability test was performed in four subjects based on measurements obtained over 1 month under ISODIS81060-3. After calibration, we compared the SBP, DBP, and PTT five times for the first 5 hours, again at the end of the first day, and twice per day thereafter.
The SBP and DBP readings were accurate to within $0.17 \pm 4.11$ and $-1.27 \pm 4.65$ mmHg, respectively. There were strong correlations between the Checkme and the auscultatory SBP ($r = 0.979$) and DBP ($r = 0.958$) values. The long-term stability was acceptable for both the SBP ($4.02 \pm 8.80$ mmHg) and DBP ($1.36 \pm 6.19$ mmHg) readings.
The Checkme sphygmomanometer meets all of the validation criteria of standard ISO81060-2 for both SBP and DBP measurement, and its long-term stability is acceptable according to ISODIS81060-3.

# Can cerium oxide nanoparticles improve cryopreservation?

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This research is to hypothesize if cerium oxide nanoparticles (CeO2NPs) can be useful in cryobiological practice. To check the hypothesis two solutions of DMSO with and without CeO2NPs were compared.

The features of aqueous solutions crystallization are the subject of many cryobiological studies since the uncontrolled ice crystals formation is often the main cause of damage during cryopreservation of cells and tissues. The effect of CeO2NPs on phase and glass transitions in aqueous DMSO solutions was studied using the method of low-temperature differential scanning calorimetry.

The results of the study indicate that adding the CeO2NPs to the aqueous solution of DMSO leads to significant changes in low-temperature phase transitions. CeO2NPs increase the tendency of solutions to supercooling, and the transition of a part of the liquid into a glass-like state, which demonstrates that nanoparticles influence the water structure. The crystallization temperature of the water-DMSO eutectic composition at the heating stage was 5.5 ° C higher, the eutectic and ice melting temperature did not undergo significant changes.

The research results showed that the confirmation of the hypothesis necessitates further comprehensive research.

# Can Functional Infrared Thermal Imaging Estimate Mental Workload In Drivers As Evaluated By Sample Entropy of the fNIRS signal?

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Mental workload (MW) represents the brain resources an individual devotes to a task. The evaluation of MW is fundamental for Advanced driver-assistance sys-tems (ADAS). To assess MW, non-invasive techniques are preferable to avoid interference with the driver. Infrared Thermal Imaging (fIRI) is highly suited giv-en its contactless nature. The research reported aimed at developing a contactless physiological method to measure MW employing fIRI features obtained from human facial skin temperature modulations. The novelty of this study is that MW was evaluated employing functional Near Infrared Spectroscopy (fNIRS), a non-invasive optical technique that measures the hemodynamic oscillations related to cortical activations. Particularly, the Sample Entropy of the fNIRS signal was as-sumed as indicative of MW. A two-level (i.e. High MW vs. Low MW) Support Vector Machine (SVM) classifier with linear kernel was employed to predict the level of MW from fIRI features. A leave-one-subject-out cross-validation was implemented to test the generalization performances of the method. The classifier showed a cross-validated sensitivity of 75% and specificity of 71%. This study represents the first attempt to estimate MW evaluated by fNIRS from fIRI fea-tures.

# Cell Segmentation in Quantitative Phase Images with Improved Iterative Thresholding Method

Tomas Vicar, Jiri Chmelik, Radim Kolar
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Quantitative Phase Imaging (QPI) is a label-free microscopic technique, which provides images with high contrast, moreover, it provides quantitative cell mass measurements for each pixel. Segmentation of particular cells is an important step in the analysis of QPI image data. This paper presents a method for automatic cell segmentation in QPI images. The proposed method improves iterative thresholding, which is a very promising method, however, it is not able to segment densely clustered cells. Our improved iterative thresholding includes two additional steps – Laplacian of Gaussian image enhancement and distance transform-based splitting. The method was compared with original iterative thresholding and another method on two cell lines, where the proposed method successfully deals with a densely clustered type of cells and achieves significantly better results on both datasets.

# Changing gait dynamics using self-induced torques on a lower leg: a pilot study

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Dynamic gait exercises can be effective in therapeutic gait training by targeting a specific group of leg muscles while walking. Assisting patients during dynamic exercises is a tiring and cumbersome procedure for therapists. State-of-the-art wearable devices are often complicated to use which makes them less efficient for simpler tasks and exercises. Control moment gyroscopes (CMGs) can provide opportunities to design minimalistic wearable devices for training and assisting balance. CMGs impart torque as a result of change in the angular momentum of the flywheel controlled by gimbal rotation. To exploit CMGs technology, we designed a device for the lower extremity without gimbal control. High-speed spinning flywheels fixed to the leg generate torque as a result of the angular velocity of the shank during swing phase. As the person wearing the device controls their walking speed -which is proportional to the angular velocity of the shank- the person also controls the self-induced gyroscopic torques. The objective of the current study was to explore the feasibility of self-induced torques for the modulation of gait dynamics. Configuration of the device was set to impart torques either in the transverse plane (internal or external rotation of the leg) or frontal plane (abduction or adduction). We collected kinematic data of the lower body using a motion capture system by placing passive markers along with surface electromyography (sEMG) sensors on the thigh muscles responsible for the abduction, adduction, and rotation of the hip joint. Subjects walked at preferred speed with no device, device inactive (deadweight), and device active. The primary outcome measures were hip joint angles during swing phase. An SPM1D paired t-test analysis was performed to compare device active and inactive conditions for each configuration. Preliminary results obtained by this pilot study showed significant difference ($n=1$, $p< 0.001$) for external and internal rotation, and abduction, while no significant difference for adduction was observed. Due to the low sample size, the results were not conclusive but they motivate further study of the effectiveness of such a device for gait modulation and its effect on muscle activation.

# Characteristic Waveforms for Testing of Medical Aerosol Inhalers

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Respiratory diseases are characterised by high prevalence among the European population. Medical aerosol inhalers are the most commonly used means of drug delivery into the human respiratory system. This paper focuses on characteristic waveforms that can be utilised during aerosol deposition studies to simulate conditions of rapid human inhalation. Additionally, an inhalatory waveform based on clinically recorded spirometry data is introduced. Experimental measurements are performed and simulation results mutually compared using the electro-mechanical lung simulator xPULM™. The inhalatory waveforms are repeatably simulated with high fidelity in regards to the waveform shape and characteristic parameters opening the possibility to utilise xPULM in medical aerosol inhalers testing.

# Characterization of hand tendon by using high frequency ultrasound imaging

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Hand injuries are the damage commonly seen in emergency department, usually resulted from exercise and working. Because treatment of hand injury is usually the immobilization by splints and long-term rest, evaluation of finger injured area is important to understand the effectiveness of therapy. The purpose of our study is to obtain the relation between the shear wave speed of the human digital extensor tendon and the stress of the tendon during finger extension and flexion with different strength of these movements. Porcine tendon tensile test was view as a verification of our method and a comparison to human test result. Shear wave from external vibrator and high frequency ultrasound transducer were applied to five healthy human subject and five porcine tendons for shear wave generation and record. Results showed the linear relationship between the shear wave speed and stress of the tendon in animal test and the stress from load-cell reading in human test and animal experiment. The human result of finger flexion has the more concentrated data distribution and more likely to the animal result than finger extension. These results can be a reference to the patients for rehabilitation.

# Classification of upper airways images for endotracheal intubation verification using convolution neural networks

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Endotracheal intubation (ETT) is an essential procedure performed in many elective operations as well as in many medical emergencies. Unfortunately, the anatomy of the patient does not always allow easy insertion of the ETT. Failing to insert the ETT or incorrect tube positioning may result in a failure to ventilate the patient, hypoxia and many other complications such as Pneumonitis.
The correct position of the ETT is between 2-5cm above the bifurcation of the trahcea into the left and right bronchus, namely the "carina", which may therefore be considered as the definitive anatomical landmark for confirming endotracheal intubation. Confirmation of correct tube positioning is a challenging task that requires high skills and the use of secondary objective devices. Numerous methods have been proposed for this purpose, but to date, none have been proven to be full-proof.
We propose a system to confirm correct tube positioning based on automatic identification of the relevant anatomical landmarks by a computer-aided diagnosis scheme. The system consists of a designated video-stylet whose tip of the stylet comprises a miniature complementary metal oxide silicon (CMOS) sensor. The inner part of the stylet contains wires to transfer the image and a narrow lumen to spray water or air in order to clear blood and secretions away from the camera sensor. The image sensor is connected to a processor with an integrated image acquisition component. During intubation, this rigid stylet is inserted into a standard ETT with its camera at the tip. Video signals are continuously acquired and processed by the confirmation algorithm implemented on the processor. In order to classify the images, a scheme based on convolutional neural networks has been developed. We used an architecture that was pre-trained on the ImageNet dataset and applied transfer learning in order to fit it to the problem at hand.
In order to evaluate system performance, we assembled a dataset of 500 images recorded from the upper airways of 10 patients where the images were taken at different angles and directions. All the images were visually inspected by a medical expert and classified into one of the following categories: upper-trachea, carina and esophagus. The system achieved an overall test set accuracy of 95.6%.

# Clinical research needs biomedical engineering for innovative development

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Introduction: The Biomedical Engineering, Research and Development (BME-R&D) department work assignments include conducting clinical research in close collaboration with the University Hospital medical representatives. The department participates with its technical knowledge in research on physiological signals and images, and in development of devices, sensors and methods that makes healthcare more effective. The outcome is often an innovation to be valued for the health care market.
Methods: The BME-R&D department works with three core processes: research, development and education. The research generates new and better measurement and analysis methods for clinical research and health care, often in national and international collaborations. The strong areas of research at the department are, for example, digitization through sensor development, biomechanics, biomedical imaging and signal analysis. The development projects usually include the development of electronics, mechanics and software for measuring, digitizing and analysing physiological signals. The purpose is to support both clinical research and clinical activities. The R&D projects are taken from the needs of the healthcare system. The BME-R&D department also participates in university education in Biomedical Engineering.
Results: Clinical research is conducted in neurology with e.g. MRI projects towards stroke and hydrocephalus as well as development of methods for gait and motion analysis. In the cardiovascular area, research is conducted with ultrasound, MRI and flow technique to characterize plaque formation, and through analysis of heart rate variability. Sensor development for better methods of detecting prostate cancer and a measurement technology for understanding glaucoma are other areas. The department has also developed an e-health system for listening to heart sounds remotely with a digital stethoscope and a quality register for medical images in the cancer field. Several projects are run within the Västerbotten Region's profiled (expertise) areas, e.g. measurement of how premature babies are affected by noise and vibration during transport and the development of a portable motion analysis system for measuring and visualizing body movement. The educational work also generates high-grade thesis work within current research and development projects.
Discussion and conclusion: The hospital have chosen to have a Biomedical Engineering R&D department located in the centre of the clinical environment and with high scientific competence. As such, BME-R&D contributes both to the local clinics as well as to the frontline of international research. It can be noted that the design of a BME-R&D department.

# Clinician Engineers - the future of healthcare

Neel Sharma
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Traditionally doctors diagnosed and managed patients based on undertaking a history and physical examination. However this approach is limited by the accuracy of the history obtained and clinical skill. A diagnosis based on what was most likely was reached and management commenced accordingly. Presently doctors diagnose and manage patients by choosing the most appropriate engineering solution, CT scans for pain, endoscopy for GI bleeding, dialysis machines for kidney injury, ventilators for respiratory compromise - the list is endless. However clinicians are simply adopters of such engineering platforms without any engineering know how. By gaining engineering expertise clinicians can help to recognise limitations with current platforms and develop new solutions accordingly. This talk will highlight the development of the first international platform aimed at bridging the gap between medicine and engineering - the clinician engineer hub. And how this platform will aim to produce the next generation of clinicians, namely clinician engineers.

# Cluster analysis on biological data using algorithms

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One of the major problems of modern research biology is the exploitation of the vast biological data that has accumulated to draw useful conclusions. The solution to the problem is to develop methods that can detect recurring patterns, discover links between biological entities, and create models that help predict and make useful decisions. The above are perfectly served by the science of data mining.

The requirements that a clustering algorithm must meet are: Scalability, Manage different type attributes, Locate groups, Define the input parameters, Ability to deal with noise, Unaffected by the order of data entry, High dimensionality.

Specifically in clustering and in general data mining it is necessary to have a detailed and in-depth understanding of the nature of the problem, the quality of the data and the parameters and algorithms to be used. Also due to the volume of real data problems the computational requirements of clustering algorithms need to be revised so that they can be incorporated into real data mining problems such to analyze a large number of biological and non-biological data as gene clustering.

The algorithms used for gene clustering were searched for the optimal management of the three resulting data types (numerical, categorical and mixed data type). In more detail, for our figures we need an algorithm that will make a clear separation of the genes whose measurements are quantitatively matched. Ideal for this is the k-means algorithm. For our categorical data we need an algorithm that will divide our data into data sets that are very similar to the centers of the algorithm, focused solely on this purpose is k-modes. Finally, combining the above requirements applies to the mixed data type o k-proto, which makes a very good approach to separating the data based on their inequalities in both numerical and categorical values.

In this abstract an attempt was made to combine multiple sources of information (multiple variables) to give a different dimension to the clustering algorithms used. The use of multiple variables aims to find possible patterns and links between all the data and is likely to reveal 'hidden' similarities between genes.

Our future work plan is to develop and implement an application that has been developed for the users.

# Combining electrochemotherapy with targeted therapy olaparib in vitro

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Electrochemotherapy is a local tumor ablation technique with different effectiveness in different histological types of tumors. In the treatment of breast cancer metastases, the effectiveness of electrochemotherapy is among the lowest. There-fore, combined therapies are needed. The aim of our study was to combine electrochemotherapy with PARP inhibitor olaparib, which would inhibit the repair of bleomycin/cisplatin caused DNA damage and would most likely potentiate the effectiveness of electrochemotherapy. First we demonstrated the effectiveness of electrochemotherapy with bleomycin and cisplatin alone in human breast cancer cell line MCF7 in vitro. Further, we con-firmed that effectiveness of elec-trochemotherapy could be potentiated by combining it with olaparib, but only when bleomycin was used as a cytotoxic drug.

# Comparison between conventional SQUID based and novel OPM based measuring systems in MEG

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Magnetoencephalography (MEG) is a neuroimaging technique for measuring magnetic signals in vicinity of the head. With various source localization algorithms we can estimate the excited areas inside cortex which produce the magnetic signal. Standard MEG devices use SQUID gradiometers which, despite their very good signal-to-noise ratio (SNR) have numerous drawbacks. As an alternative to these, commercial magnetometers on alkaline metal vapor (OPM) have recently developed to such a degree, that they have comparable sensitivity as the SQUID sensors. In this work we present measurements of the brain auditory evoked fields (AEF) with a system of 15 OPM sensors, that can detect both radial and tangential components of the magnetic field. These results are compared to the results obtained with the SQUID system. However, the quantitative comparison of two MEG systems is not trivial. We present a method for comparing two MEG system, which operates on the principle of minimum norm estimate (MNE) source localization algorithm. We show, that performance of the MEG system consisting of a small number of OPM sensors is slightly worse, but still comparable to results of the complete standard squid system with 125 gradiometers.

# Comparison of Standard and Microneedle Array Electrode Impedance of Skin Electrode Interface for EEG signals: A Review

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This paper presents a literature review of dry electrodes based on microneedle technology to measure biological signal and its advantage in regard with wet standard electrodes. Surface electrodes require skin preparation and conductive gel to maintain low interface impedance, which limit biomedical applications in long-term monitoring of the electroencephalogram (EEG) signals. The skin electrode interface plays a very important role in the acquisition of high-quality biological signals due to its low impedance requirement in order to reduce the transduction resistance among ionic and electrical currents. Wet electrodes are currently using, which require abrasive/conductive gels to improve the conductivity of the skin. Advances in dry electrodes, which do not require gels, have simplified this process and contributed to maintain a good electrical contact with the skin surface.

The objective of this paper is twofold: i) to provide an overview of electrodes using currently based in microneedle array and ii) to compare it with traditional wet-based electrodes used to acquire of EEG signals for medical applications.

# Comparison of Wearable UHF RFID Antenna Designs and Materials

Adnan Mehmood, Han He, Xiaochen Chen, Johanna Virkki
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Passive RFID (radio frequency identification) technology, especially in the UHF (ultra-high frequency) range, is one of the key technologies turning our everyday clothing into intelligent communicative textiles. Passive RFID uses remotely addressable tags, composed only of an antenna and a small RFID IC (integrated circuit) component, having a unique ID. A passive RFID tag gets all its energy from an RFID reader and then responses with its ID by backscattering.
Integrating sensing possibilities into passive RFID tags has been widely studied. Further, by tracking tag IDs and changes in the backscattered signals, wearable passive UHF RFID tags can themselves be used as sensing elements. Passive UHF RFID-based solutions have been used for example as body moisture, temperature, and movement sensors. As the technology is simple and cost-effective, these sensors have countless applications in the healthcare and welfare sectors. RFID antennas and antenna-electronics interconnections can be easily and cost-effectively integrated into clothing for example by embroidery with conductive thread, printing with conductive inks, or by cutting from electro-textiles.
However, closeness of the lossy human body is an extremely challenging environment for RFID antennas. Thus, versatile antenna designs have been presented to overcome the challenges. We are presenting an on-body comparison of two common types of wearable antennas (dipole and split ring resonator) as well as our new wrist antenna with antenna bands. Further, we fabricate all three antenna designs from traditional copper tape material as well as from commercial electro-textile material, and present a comparison between the two materials.
Based on the achieved results, our new wrist antenna shows optimized on-body performance. The wireless performance is excellent on both wrist, where it was designed for, as well as on other parts of the body, where it shows similar or better performance (i.e. longer read ranges) than the other two antennas. Further, electro-textile, which has the advantages of feel and look of traditional textile, shows comparable results to copper tape.

# Complexity Analysis of a Biosignal Time Series Similarity Indexing Approach

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This work deals with similarity measuring and indexing in biosignal time se-ries. In particular, it focuses in an approach proposed by the authors in pre-vious works, which consists in a transformed-based method, performed by means of a set of Haar wavelet basis functions that is reduced to an optimal subset through the Karhunen Loève transform (WKLT). This allows a bi-osignal to be efficiently described by the combination of a compact set of ba-ses which coefficients are used in the similarity process. For similarity index-ing, the method uses an iterative formulation that leads to a significant re-duction of the computational complexity, namely in the required number of operations.
Therefore, the goal of the present work is to demonstrate the efficiency of the referred approach, through a complexity analysis study. For this purpose, biosignals collected in intensive care units (MIMIC-II dataset) are employed in a set of experiments that compare the proposed approach with others, and which results confirm expectations.

# Compliance of a cardiovascular system is non-linear – influence on the relation between blood pressure and an impedance cardiography in the reservoir-wave model

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The reservoir-wave model postulate that the blood pressure curve can be separat-ed into two components: reservoir pressure and wave pressure. The linear rela-tion between reservoir pressure with aortic volume and wave pressure with blood flow velocity where assume, which means that aortic characteristic impedance and arterial compliance should be constant in the whole cardiac cycle.

Impedance cardiography measure change in thorax impedance, signal reflects a change of arterial blood volume and can be used to estimate reservoir pressure.

The aim of this study was to examine the relation between blood pressure and impedance cardiography signal($\Delta$Z). We tested if it is possible to assume linear characteristic impedance and linear compliance for signals measured in humans.

We compared the theoretical pressure-volume loop compute using the model with the loop obtained from measured blood pressure and $\Delta$Z. We found that the slope of the "real" loop is disturbed. The slope becomes linear only in late diasto-le. Motion artifacts and extra waves distorted $\Delta$Z curves and occurrence of a backward pressure wave can corrupt the similarity between the two curves.

We also check the slope between estimated wave pressure and blood flow ve-locity recorded by Doppler ultrasonography. Obtain characteristic impedance is a nonlinear function of blood flow velocity, it can be described by a power function (y=xn).

We consider that compliance should be treated as a function of blood pressure, assumption of constant value of cardiovascular parameters is a simplification, which makes it difficult to fit $\Delta$Z to blood pressure.

# Composite Polymers for Bone Tissue Engineering: Why and how to stimulate vascularization and innervation of the bone tissue?

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The effective reconstruction of large bone segments remains a major unsolved problem in the clinical field, evident in cases of severe trauma, cancer treatment and reconstructive surgery. Tissue engineered approaches have mainly focused on the stimulation of osteoconductive properties of the bone substitutes, as main parameter for bone repair. These have been shown insufficient to achieve efficient bone repair, especially when the vasculature and the nerve fibres of the host bed tissue, are damaged tumor resection and radiotherapy.
The importance of vascularization in bone repair has developed a robust body of literature and been considered to play a pivotal role in new bone formation. However, besides our knowledge on coupling between osteogenesis and angiogenesis1, and conscious of the complexity of the bone tissue, we are widening to new and innovative horizons towards other key players in bone regeneration, especially nerve fibers.
In such context, we have first developed different co-cultures models, both in 2-D (2D) and three (3D) dimensional structures, to dissect the biological mechanism of how sensory neurons can support osteogenesis and angiogenesis. Based on these fundamental data, our objectives are to initiate new strategies for bone tissue engineering using composite polymers. in this context, two examples of polymer-based scaffolds will be given to support such strategy. For both, cellular responses of mesenchymal stem cells, endothelial cells and / or sensory neurons were investigated before in vivo analysis of the nature of the tissue after implantation in different preclinical models for validation of the efficiency of these scaffolds.

# Computational analysis of intracellular Ca2+ elevations related to morphology changes in astrocytes

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In the past, neurons have been studied as the main brain cells. However, numerous recent evidence shows that astrocytes, the major type of glial cells, are involved in synaptic events, and are crucial for the normal brain function. Moreover, they seem to be part of many neuropathologies. For example, in Alzheimer's disease, the astrocyte's morphology changes. Astrocytes use intracellular calcium (Ca2+) elevations to encode information and generate main functional chores of the cell. Several mechanisms can trigger the increase of the intracellular Ca2+ levels in astrocytes. This signaling cascade begins with the production of inositol trisphosphate (IP3) that induces the rise of the intracellular Ca2+ concentration. There is a lack of understanding of the detailed spatiotemporal Ca2+ dynamics in astrocytes and how the cell morphology affects them. Computational modeling can aid us to better understand astrocytic Ca2+ dynamics. In this work, we will study how morphological changes in the astrocytes affect their intracellular Ca2+ dynamics using mathematical modeling.

This study proposes a 2D single-cell astrocyte model, simulated with the finite elements method in COMSOL Multiphysics. It extends the previous work by Khalid et al. (IFMBE Proceed, 2018) that was based on the model by De Pitta et al. (J Biol Phys, 2009). The model describes spatiotemporal, IP3-induced Ca2+ release from the internal stores following a glutamate stimulus. Furthermore, it includes diffusion of both Ca2+ and IP3. We investigated how the geometry of the astrocytic processes affect Ca2+ dynamics in them. Also, the influence of different Ca2+ buffering models was examined. We studied separately how different spatial parameters, such as width and length affect the Ca2+ event and if there is any correlation between them. MATLAB and Minitab software were used for analyzing the data.

The results showed that the width and length of the processes affect the Ca2+ dynamics differently: With narrow processes, frequency and propagation distance of the Ca2+ event is higher compared to wider ones while having the same glutamate stimulus. Also, when the process's width grows, Ca2+ event emergence depends on the whole area. Furthermore, the magnitude of Ca2+ events was reduced by varying amounts by the different buffering models, depending on their parameters and complexity.

This work forms a base for the analysis of the Ca2+ in astrocytes. It also clarifies the impact of morphological changes, like the thickening of astrocyte processes in different pathologies, on astrocytic Ca2+ signaling.

# Conductivity determination of lung and mediastinal mass lesions

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Introduction: MR-Electric Properties Tomography (EPT) estimates tissue conductivity in vivo [1]. Brain [2], breast [3], and hepatic [4] tumor conductivity studies suggested potential clinical usefulness. Applicability of EPT in lung and mediastinal lesions is yet unknown, as hampered by low proton content in adjacent lung tissue, abrupt magnetic susceptibility changes at tissue interfaces, and cardiothoracic motion.
This study evaluated the feasibility of EPT for lung and mediastinal mass lesions.
Methods: Institutional Review Board approved this prospective study, including 21 patients (written informed consent obtained) with lung or mediastinal mass lesions without prior treatment, using a 3T scanner (Philips Healthcare) and 2D-steady state free precession sequences (10 dynamic sagittal scans, single breathhold). Scans with successful breathholding entered 2D phase-based EPT [4]. Each lesion's conductivity and its relationship with histological findings, lesion size, and location was evaluated (two-sample t-tests, Pearson's product-moment correlation analyses).
Results: From 22 lesions total (15 adenocarcinomas, 1 adenosquamous carcinoma, 3 squamous cell carcinoma, 1 schwannoma, 1 bronchial cyst, 1 leiomyoma), EPT reconstruction was impossible in 4 adenocarcinomas and 1 squamous cell carcinoma (too small lesion size / strong cardiothoracic motion) yielding 17 lesions for evaluation.
Malignant tumors showed larger maximum (P=0.026), standard deviation (P=0.025) and contrast (P=0.014) than benign lesions.
Lesion size was 4-1951/23-73 mm2 in malignant/benign lesions. Malignant tumors tended to larger size (P=0.067). Larger lesions had larger intralesional contrast and entropy, surviving even after controlling for histologic findings.
Discussion: Higher maximum conductivity of malignant than benign lesions is thought to be due to higher sodium ion concentration and/or mobility within these tumors. Larger intralesional standard deviation and contrast of conductivity in malignant lesions are thought to indicate intratumor heterogeneity, being a characteristic of malignant tumors and probably due to genomic/biologic variations within tumors gained by cell evolution under diverse microenvironments linked to different etiologies [5].
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References:
[1] Katscher U etal. Comp Math Meth Med. 2013;546562
[2] Tha KK etal. Eur Radiol. 2018;28:348
[3] Kim SY etal. Eur Radiol 2016;26:2317
[4] Tha KK etal. Proc ISMRM 2018;26:5085
[5] Liu J etal. Exp Mol Med 2018;50:e416

# Conductivity tensor imaging (CTI): a new electrodeless method

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The electrical conductivity is a passive material property primarily determined by concentrations of charge carriers and their mobility. The macroscopic conductivity of a biological tissue at low frequency may exhibit anisotropy related with its structural directionality. When expressed as a tensor and properly quantified, the conductivity tensor can provide diagnostic information of numerous diseases. Conductivity imaging usually requires probing the imaging object by externally injecting conduction current or inducing eddy current. Conductivity tensor imaging (CTI) is a novel electrodeless method to reconstruct conductivity tensor images of the human body using an MRI scanner without current injection. B1 mapping is adopted to recover a high-frequency isotropic conductivity image which is determined by contents in both extracellular and intracellular spaces. Multi-b-value diffusion weighted imaging is then utilized to extract the effects of the extracellular space and incorporate its directional structural property. Clinical applications of CTI may include imaging of tumor, ischemia, inflammation, cirrhosis and other diseases. CTI can provide patient-specific models for EEG source imaging, transcranial dc/ac stimulation, deep brain stimulation and electroporation. Introducing the CTI framework, details of its implementation and validation will be described. Conductivity tensor images of phantoms, animals and human subjects will be presented and discussed. Potential clinical applications will be suggested with examples.

# Consolidation of educational resources from research projects in biomedical engineering and medical physics

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Excellence in education is always sought beyond the traditional curricula and teaching materials. Professional development is a continuous process of learning, often through participation in dedicated seminars and specialized training courses. This is also valid for the biomedical engineers and medical physicists, who are specialists working in a rapidly developing interdisciplinary field. In some cases, due to lack of time and financial resources to follow specific courses, specialists in these areas are deprived of the possibility to enhance their knowledge and skills in the given field. This work presents an approach for transferring accumulated resources from research projects in the field of biomedical engineering and medical physics to accessible teaching resources, based on which a continuous learning is implemented.
Over the past decade, the research team has participated in several EU projects, both as a coordinator and partner. Amongst others, all these projects have had a strong goal to enhance the scientific capacity of the host research team in the specific field of breast phantoms modelling, simulation, and imaging as well as development of relevant anthropomorphic phantoms used for breast cancer research. During the implementation of the research projects, novel educational materials used for the training events have been created from the partners participating in the projects. These materials have been consequently systemized and stored at the host team space. To achieve a long-term sustainability of the projects' outcomes and boost the host scientific capacity beyond the projects' lifetime, the research team initiated continuous education and training of the group members participating in the research activities. Next, in order to achieve better management and exploitation of all educational materials, the team proceeded a step further and implemented an in-house repository.
Following analysis of the learning objectives and the expected results, the team considered Moodle Learning Management System as a favorable repository carrier, which is in operation at the Medical University of Varna. All learners enrolled have unlimited free access to the uploaded educational materials at the e-learning platform.
In conclusion, the accomplishment of Systematization, Consolidation, and Digitalization approach in the creation of educational and training resources has had a significant benefit for increasing the added value of the learning process as well as establishing networks for sharing e-materials.

# Contribution of algebraic iterative reconstruction algorithm for joint space segmentation based on cone beam computed tomography images

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Measurements derived from the joint space segmentation are clinically pertinent to study knee osteoarthritis. Cone beam computed tomography (CT) is an emerging low dose imaging method with the potential to be used in a weight bearing position. With a cone beam CT prototype, we have tested 2 methods of reconstruction: iterative reconstruction (SART) and FDK reconstruction with different intensities and projections number. We used the segmentation of the joint space as a metric to assess the quality of reconstructions. For this aim, we calculated Jaccard and Hausdorff indexes, and thickness measurements (2D and 3D). We have found that the results were more consistent with the SART reconstruction than FDK reconstruction with more stable results whatever the intensities and the projections number.

# Control System and User Interface of Cooling Module for Braces

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The use of a controlled cooling therapy may help in pain management and pain treatment, for example, of carpal tunnel syndrome. The article deals with possibilities and design of the control system and user interface for Peltier-based cooling module for braces. The experimental brace fixing the hand in the carpal region was designed to verify the control system of cooling forearm orthosis. This brace was fitted with 3 thermoelectric modules. The users can select their own cooling intervals, cooling intensity, or the set periods of required cooling with respect to the presumed battery lifespan. The verification of the system was performed on patients with carpal tunnel syndrome during 60-minute measurement. The proposed system has proven to be useful in the field of rehabilitation, but also reveals some limitations of using fans as tools for heat transfer.

# Correlation between the NEDOCS and EDWIN indices to measure overcrowding in an emergency department

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In this study, the National Emergency Department Overcrowding Scale (NEDOCS) and the Emergency Department Work Index (EDWIN) were analyzed for their use in predicting overcrowding. This analysis report was conducted in an Emergency Department (ED) and included 1,678 clinical cases. Both indices show good discrimination for predicting ED overcrowding, which establishes construct validity for these scales as measures of overcrowding. The results showed that the ED is overcrowded in the morning, particularly in the middle of the week, compared to the weekend. The indices were correlated with one another and showed high discrimination for predicting ED crowding. Our analysis improves our understanding of overcrowding due to the accurate pre-diction of emergency department status.

# Cortical Auditory Evoked Responses to Continuous Speech Stimuli with Extended Pauses

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The stimulus reconstruction approach, or the decoding model, is one of the most used method to investigate the evoked responses to continuous speech. It attempts to reconstruct the speech envelope using the recorded electroencephalogram (EEG). Stronger correlation between the reconstructed and actual speech envelope implies stronger envelope entrainment in the auditory cortex. Envelope reconstruction is found to be affected by factors such as intensity, signal-to-noise ratio, and attention. The assumption underlying most methods is of a linear relationship between speech envelope and the EEG. However, it is also known that evoked responses are stronger following sound onset than for ongoing stimuli.

The current work aims at investigating if stronger onsets in recorded speech lead to increased cortical auditory evoked responses. The specific objectives are to test if an increase in the duration of pauses between words in the continuous speech stimulus increases the correlation between the speech envelop and its reconstruction from the EEG, and if removing the pauses during the analysis (gapped signals) can further increase correlation. Stronger correlations could allow shorter recordings to be used in detecting evoked responses to speech stimuli.

In this study, we modified the speech stimulus by inserting small (0.25 seconds) and large (0.5 seconds) silent pauses between each word. Participants listened to stimuli under three conditions; normal speech, speech containing small pauses, and speech containing large pauses. EEG and speech envelopes were filtered and decoded in delta (0.5 – 4 Hz), theta (4 – 8 Hz) frequency band, and broad band from 0.5 to 15 Hz.

Our results demonstrate that the speech envelope reconstruction improves when the participants listen to continuous speech stimulus with extended pauses between words ($p<0.05$ for theta, delta, and broad band). We found that the correlation between the reconstructed and the actual speech envelope is lowest when participants were presented with normal speech, higher when presented with speech containing small pauses, and highest when presented with speech containing large pauses. Removing regions of stimulus gaps from the analysis did not significantly improve the reconstruction.

Our findings supports the hypothesis proposed by previous studies that the evoked responses to speech envelope is largely influenced by the acoustic onset. The extended pauses in speech appear to provide more time for the auditory cortex to recover and generate stronger onset responses after each word. Therefore stronger cortical activity correlated to the speech envelope can be decoded.

# Cortical Auditory Evoked Responses to Continuous Speech with Extended Pauses

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Cortical auditory evoked responses to continuous speech can be examined using the stimulus reconstruction approach, or the decoding model. This is an inverse problem, where the model attempts to reconstruct the speech envelope using recorded electroencephalogram (EEG). Stronger correlation between the reconstructed and actual speech envelope implies stronger responses. However, since evoked responses are stronger following sound onset than for ongoing stimuli (Wang et al., 2005), and also increase when interstimulus-intervals in periodic stimuli (e.g. tone pips) are longer (Davis et al., 1966), it may be expected that onsets in continuous speech might be a major contributor to speech evoked responses.
Motivated by these studies, the objectives of the current work are to test if an increase in the duration of pauses between words in the continuous speech stimulus increases the correlation between the reconstructed and actual envelope. We will also test if removing the pauses during the analysis (gapped signals) can further increase correlation. Stronger correlations could allow the time required for data collection with speech evoked responses to be reduced.
In this study, we modified the speech stimulus by inserting small (0.25 seconds) and large (0.5 seconds) silent pauses between each word. Participants listened to stimuli under three conditions; normal speech, speech containing small pauses, and speech containing large pauses. EEG and speech envelopes were filtered and decoded in delta (0.5 – 4 Hz), theta (4 – 8 Hz) frequency band, and broadband (0.5 - 15 Hz).
Our results demonstrate that speech envelope reconstruction improves (correlation increases from 0.0639 to 0.1192 in delta-band (p 0.001), and 0.0314 to 0.05 in theta-band (p 0.012)) when participants listened to speech stimuli with extended pauses. Correlation between the reconstructed and actual speech envelope is lowest when participants listened to normal speech, and highest when listened to speech added with large silent pauses. Removing stimulus gapped segments from the analysis did not significantly improve the reconstruction.
Our findings support the hypothesis proposed by previous studies that evoked responses to continuous speech is strongly influenced by the acoustic onset (Howard and Poeppel, 2010). The extended pauses in speech appear to provide more time for the auditory cortex to recover and generate stronger onset responses after each word (Davis et al., 1966). Therefore stronger cortical activity correlated to the speech envelope can be decoded from the EEG, resulting in a better envelope reconstruction.

# Counteracting balance loss in transfemoral amputees by using an active pelvis orthosis: a case series

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This case series study was designed to provide an overview of the efficacy of an active pelvis orthosis (APO) against the fall risk after multi-directional slippages in transfemoral amputees (TFA). To achieve this goal, we investigated the dynamic stability after antero-posterior (AP) and diagonal (D) slippages, as assessed by the Margin of Stability (MoS) in both the frontal and the sagittal planes.

Results revealed that the detection algorithm can actually signal a lack of balance in about 400 ms, for both AP and D slippages, for three over five amputees. However, it was also noticed that its performance decreased with the severity of the amputee's clinical status. Specifically, for most impaired amputees walking patterns are inherently less smooth thus the detection algorithm failed to detect abrupt modifications of gait patterns due to external perturbations.

Results also demonstrated that the proposed assistive strategy can effectively promote balance recovery in the sagittal plane while subjects managed AP-slippages. On the other hand, the analysis of the stability in the frontal plane showed that the balance control does not systematically improve due to the APO assistance. Therefore, despite the APO could partially restrain the hip movement of the users in the frontal plane, balance control is mostly mediated by subjects' abd/adduction muscle groups leading them to adopt a context- and subject-dependent counteractive strategy to manage the lack of balance.

Concluding, the outcomes of this preliminary study are promising and suggest to further investigate subject-specific tuning of the control algorithm underlying the APO-mediated assistance.

# Creating salt induced 3D electrospun artificial matrices for biomedical purposes

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Huge amount of polymers are used for a wide range of medical or pharmaceutical purposes. The technology, and new materials we have now are always being developed for better or for new purposes. The bases of such materials are coming from polymers which can be found in nature. We expect from these polymers to be biocompatible and biodegradable, so not to cause immune reaction and after degradation build into the living system. Poly(aspartic acid) can be a good choice for medical application, which can be created from Poly(succinimide) by alkaline hydrolyzation.
Nanotechnology is one of the most intensively developed discipline. With its help, we can create artificial matrices which have fiber diameters like in the living organism. Among other technologies, the method of electrospinning is appropriate for creating such fibers. We can modify fiber parameters by adding different nanoparticles or salts. Changing the electrospinning parameters we affect the properties of these systems to fine-tune it for our needs. With different setups and modifications, 3D structures have been experienced but for the causes there is no universal explanation yet. To create a high porosity fibrous mesh for culturing different cells in a suitable three-dimensional way, we need to step forward from conventional electrospinning.
Our aim was to create artificial 3D fluffy fiber structures from Poly(succinimide) with the help of electrospinning. Therefore, the effect of different inorganic salts were investigated (CaCl2, MgCl2, LiCl). The scaffolds were analyzed with the help of Scanning Electron Microscopy and Raman spectroscopy. To understand the effect of salt on the resulting meshes characterization of the ion-ion and ion-solvent interactions were carried out using vibration spectroscopy and density functional theory calculation. These interactions correlate to what we experienced with the electrospinning process. In the future, our results could contribute to creating designed structures which main and most important area of usage could be biomedical applications.
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# Cryopreservation of mesenchymal stem/stromal cells in combination with trehalose and reversible electroporation

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Mesenchymal stem/stromal cells (MSC) have emerged as a potent cell-based therapy for a wide array of diseases due to their immunomodulatory properties and the capacity to differentiate into various cell types. Long-term storage and fast availability of MSC products for therapeutic applications is provided only by cryopreservation. The common clinical-grade cryopreservation media contain 10% of dimethyl sulfoxide (DMSO) which is toxic towards cells at positive temperatures. Even more, direct administration of cryopreserved cells can cause serious adverse reactions in patients.
Trehalose has appeared as a promising alternative to DMSO cryopreservation protocols. However, a relatively simple and efficient approach for loading this impermeable sugar into mammalian cells was missing.
In our study we used reversible electroporation for loading trehalose into adipose-derived MSC (ASC) and umbilical cord-derived MSC (UC-MSC). After optimization of electroporation parameters, both types of MSC were cryopreserved and cells' viability was assessed after thawing. When comparing to standard cryopreservation protocol (10% DMSO in fetal bovine serum), similar MSCs' viabilities were obtained combining trehalose and electroporation. Surprisingly, comparable results were obtained also in protocols using high trehalose concentration without electroporation. To evaluate the impact of electroporation and cryopreservation in the presence of trehalose on MSCs' functionality, cell proliferation, differentiation and activation in the inflammatory environment were analysed. Successful cell growth as well as efficient adipogenic and osteogenic differentiation were achieved. Furthermore, efficient up-regulation of genes involved in immunomodulation was confirmed by real-time qPCR method. All together, cryopreservation in the presence of trehalose provides functionally intact and highly viable MSCs after thawing.

# Cyberlegs plus plus powered robotic ortho-prosthesis: wearable sensors apparatus

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Introduction: The general goal of the CYBERLEGs Plus Plus project (CL++) is to validate the technical and economic viability of the powered robotic ortho-prosthesis developed within the framework of the FP7-ICT-CYBERLEGs project. The CYBERLEGs ortho-prosthesis is a modular, multi-degree of freedom cognitive robotic system constituted of an active artificial leg for the functional replacement of the amputated limb, and a wearable active orthosis for assisting the movement of hips, and knee and ankle joints of the contralateral limb. Important element is also Wearable Sensory Apparatus. CL++ includes new Active Transfemoral Prosthesis, new Active Pelvis Orthosis, new Active Knee Orthosis, new Wearable Sensory Apparatus, new Bidirectional Interface, new Intention Detection algorithms and new Fall Risk Mitigation.
Aims: The objectives of CYBERLEGs Plus Plus Wearable Sensors Apparatus (WSA) are (i) to elevate WSA hardware (HW), WSA firmware (FW), and the algorithms to identify his/her intended movement, (ii) to make new Inertial measuring units (IMU) and shoes instrumented with pressure-sensitive insoles, (iii) to develop an algorithm (SW) to use the orthotic modules, and other locomotion-related tasks i.e., stairs ascending/descending).
Methods: The set of IMUs implements a new 9-DOF single chip device (3D accelerometer, 3D gyroscope, 3D magnetometer) and fast 32-bit Microprocessor Cortex-M4F (with floating point unit for on board calculation). The Insole Control Units and IMUs are also equipped with new RF module based on MAC layer of IEEE 802.15.4-2011 (Ultra-wide Band) standard interface for offering more robust real-time transfer of sensors data.
Results: New IMU are able to transfer 3D accelaration, 3D gyro and 3D magnetometer data, as well as insole data over wideband wireless links. hardware and software were tested in various environments, including all tests neede for CE certification. The system is currently used in clnical tests.
Conclusion: This project focuses on the demonstration in an operational environment from both the technical and economic viability viewpoint of a modular robotics technology for healthcare, with the ultimate goal of fostering its market exploitation. The project involves players from academia, end users, as well as robotics and healthcare industry. Therefore, CYBERLEGs Plus Plus fits the specific challenge of the scope c (namely Technology Transfer – Robotics use cases) of the call H2020-ICT-24-2015.

# Cytosolic DNA sensor and cytokine expression in normal murine cells in vitro and in vivo following gene electrotransfer

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used in more than 150 clinical trials for gene delivery. It is mainly used in three different fields: DNA vaccination, protein replacement therapy and cancer gene therapy. Plasmid DNA carrying a therapeutic cDNA or gene is delivered into the target cells' cytosol. This plasmid represents foreign DNA and thus cells respond by activation of cytosolic nucleic acid-specific pattern recognition receptors (PRRs – DNA sensors). PRRs are an ancient form of immunity found in both immune and non-immune mammalian cells. We have already demonstrated that (a) delivery of plasmid DNA devoid of therapeutic genes has a pronounced antitumor effect, that (b) tumor cells express DNA sensors, which can be upregulated and activated by gene electrotransfer, that (c) leads to expression of inflammatory cytokines, that could modulate the efficacy of cancer gene therapies. Furthermore, in mouse myoblasts, we described the early steps of binding of DNA to cytosolic DNA sensors and demonstrated that inhibition of p204, which is the mouse ortholog of Ifi16, inhibits DNA sensors' signaling. Since skin is also one of the targeted tissues for gene electrotransfer, the aim of the current study was to determine the DNA sensors' baseline expression and upregulation and inflammatory cytokine expression after electrotransfer of plasmid DNA devoid of a therapeutic gene in murine fibroblasts and keratinocytes as well murine skin. Plasmid gWiz Blank was delivered into murine Kera-308 keratinocytes and L929 fibroblasts using electroporation. Two different pulse protocols were compared: EP1, 600 V/cm, 5 ms, 8 pulses, 1 Hz and EP2, 1300 V/cm, 100 µs, 6 pulses, 4 Hz. In vitro, RNA was isolated after 4h analyzed by qPCR. For in vivo experiments the same pulse protocols were used for gene electrotransfer of gWiz Blank into murine skin. One and 6h after transfection, skin was excised and embedded in OCT medium, frozen in liquid nitrogen and stored at –80 °C. Thin cryosections were stained for inflammatory cytokines and different cell markers to determine which cells in the mouse skin are responsible for the inflammatory reaction to gene electrotransfer. Several DNA sensors were expressed in keratinocytes and fibroblasts. After pDNA electrotransfer, DDX60 and ZBP1/DAI were upregulated in both cell lines. In keratinocytes, the additional DNA sensors p202, p204 and AIM2 were upregulated. Downstream signaling resulting in cytokines IFN$\beta$ and TNF$\alpha$ production was also demonstrated in both cell lines. In vivo results will also be presented.

# Damage-associated molecular pattern molecules release from CHO cells in vitro due to electroporation

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Exposure of cell to high-voltage electric pulses results in a transient membrane damage (dynamical and structural reorganization of the plasma membrane), i.e. electroporation which is followed by cell recovery in an active cellular process which involves cellular machinery. Therefore, pore formation by itself is an injury. Since many pathways of cell injury and cell death overlap, the main reason for cell death after electroporation in still unspecified. Most of the studies describe apoptosis as the main cell death pathway. Now, a novel pathway of cell death is being investigated, so called immunogenic cell death; i.e. type of death that involves innate immune system. In response to stress, cell or tissue damage, endogenous molecules are being released from cells or are exposed on cell's surface. These endogenous molecules are referred to as damage-associated molecular pattern molecules (DAMPs) and induce inflammatory responses in vivo by activating the innate immune system. Release of DAMPs was also observed and reported in relation to cell electroporation and activation of immune response.
CHO cells in suspension were exposed to 8 pulses of 100 µs duration between stainless steel electrodes (d = 2 mm). DAMPs were detected at different time points after pulse treatment, depending on the properties of targeted molecule. After centrifugation, samples were analyzed for the presence of DAMPs, i.e. ATP, nucleic acids, calreticulin and uric acid. The release of DAMPs was statistically correlated with cell permeabilization and cell survival, e.g. reversible and irreversible electroporation.
Generally, once DAMPs were detected, their amount increased with the increasing pulse amplitude. Our results showed that release of DAMPs has a stronger correlation to cell survival/irreversible electroporation than to membrane permeabilization/reversible electroporation.

# Dealing with open issues and unmet needs in healthcare through ontology matching and federated learning

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Open issues and unmet needs in healthcare include the enhancement of the statistical power of the clinical outcomes along with the development of prediction models for effective disease management, the detection of prominent factors for disease progression and the identification of targeted therapies. In this work, we deploy a computational pipeline that uses data curation and ontology matching to curate and align heterogeneous data structures to enhance the statistical power of the outcomes. Then, we use federated learning to develop disease prediction models across harmonized cohort data that are stored in private cloud databases. A preliminary case study was conducted for the first time on three European cohorts on primary Sjögren's Syndrome (pSS) yielding harmonized data with 90% average overlap along with a federated lymphomagenesis progres-sion model with accuracy 0.848, sensitivity 0.833 and specificity 0.849.

# Decellularized Hyaline Cartilage Graft (dLhCG) for Cartilage Repair

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In this study, we have developed a continuous methodology to directly set up a scaffold-free macro-scaled three-dimensional living hyaline cartilage graft (LhCG) with the aid of a biomaterial-based interim scaffolding system.[1,2,3] The practical performance of decellularized LhCG (dLhCG) is evaluated in the knees of large animal models with full-thickness chondral defects beyond critical sizes for 6 months. Hyaline cartilage based neo-tissue fulfills the desired in situ reconstruction. LhCG is also employed as an engineered biomimetic/pathological tissue platform for anti-arthritis drug evaluation in vitro.[4,5] Arthritic disease models are created with LhCG by replicating the inflammatory environment of an arthritic joint via co-culturing LhCG with lipopolysaccharide (LPS)-activated macrophages, after which the accuracy of this model for in vitro drug-testing was validated using a popularly applied nonsteroidal anti-inflammatory drug (NSAID). The results suggest that this new arthritic model is able to adequately mimic the native arthritic cartilage and is suitable to be used as an in vitro model for predicting native cartilage response to drug treatment.

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References:
1. Gong, Y.H., et.al, Tissue Engineering Part A, 16 (2010), 12: 3611-3622.
2. Su, K., et al., Advanced Functional Materials, 22 (2012), 5: 972.
3. Peck, Y., et al., Scientific Reports, 5 (2015), 16225. doi: 10.1038/srep16225.
4. Peck, Y., et al., Molecular Pharmaceutics, 11 (2014), 7: 1997.
5. Peck, Y., et al., Journal of Tissue Engineering and Regenerative Medicine, 12 (2018), 1: e237-e249.

# Decision support system based on Artificial Neural Network for prediction of antibiotic sensitivity of causative agents of urinary tract infection in certain geographical regions

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Urinary tract infection (UTI) is very common and caused by various bacteria. The treatment of UTIs should be handled carefully. With the rise of neural networks, a possibility occurred to predict the outcome of consuming antibioticis for treating UTIs. This paper presents the development of expert system based on neural network for prediction of antibiotic sensitivity of two bacteria: Escherichia coli and Klebsiella pneumoniae. For the development of expert system based on neural network, total of 3226 samples were used: 486 samples of Klebsiella pneumoniae and 2740 samples for Escherichia coli. All samples were collected in one geographical area from hospitals and primary healthcare units. Feedforward neural network based on Bayesian regularization backpropagation training algorithm resulted in accuracy of 72.16% for prediction of antibiotic sensitivity of K. pneumoniae bacteria and 99.81% for prediction of antibiotic sensitivity of E. coli bacteria. The results of this study are promising since the usage of such expert systems in healthcare environment contributes to rational usage of antibiotics for treatment of infections and therefore contribute in fighting the antimicrobial resistance which is one of the rising challenges of healthcare nowadays.

# Decomposition of Compound Muscle Action Potentials by Convolution Kernel Compensation Method: Improved Segmentation of Motor Unit Firings

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We analyze the performance of recently introduced technique for decomposition of compound muscle action potentials (CMAPs), recorded by high-density surface electromyograms (HDEMG). This technique utilizes Convolution Kernel Compensation (CKC) method to estimate motor unit (MU) fil-ters from HDEMG recordings of voluntary isometric muscle contractions. Afterwards, it applies these filters to the HDEMG recordings of elicited con-tractions and identifies MU spike trains. We then propose a novel method for segmentation of MU firings out of the identified spike trains and demonstrate on a synthetic HDEMG signals that at high MU synchronization levels this novel segmentation method significantly outperforms the spike segmentation introduced by CKC method. Namely, at 80 % MU firing synchronization the area under receiver operating characteristic curve (AUC) increases from $0.96 \pm 0.03$ to $0.99 \pm 0.01$ when newly proposed segmentation is used instead of the previously introduced CKC-based segmentation. Thus, newly proposed segmentation supports significantly more accurate discrimination of true positive and false positive MU firings. At low MU synchronization levels ($< 60$ %) the newly proposed MU firing segmentation yields results that are comparable with the previously introduced CKC-based segmentation.

# Decomposition of high density electromyogram reveals changes in motor unit action potential amplitude after intramuscular Botulinum toxin

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High-density surface electromyography(HDsEMG) decomposition has allowed us to study individual motor unit (MU) responses in great detail during voluntary or reflex muscle contraction. Being noninvasive in nature, the technique has been widely used for many different applications in both healthy and stroke impaired populations. Here for the first time, we demonstrate the use of a HDsEMG based MU decomposition technique to study the morphological changes in the recruited MU population after botulinum toxin (BT) injection in the biceps brachii muscle for spasticity management in chronic hemiparetic stroke survivors. Three stroke survivors were examined before and after intramuscular (biceps brachii) BT injections. The HDsEMG grid enabled simultaneous recordings over the entire muscle. We have recorded both force and the surface electromyogram (sEMG) during voluntary isometric contraction tasks. The HDsEMG was decomposed using the convolution kernel compensation (CKC) method. We report a 60% increase of the peak to peak amplitude of the motor unit action potential (MUAP) signals after the BT injection compared to pre-injection values. The overall generated muscle force and sEMG values decreased during this period compared to their pre-injection level. We discuss potential mechanisms that would result in the emergence of larger MUAPs in the weeks immediately following intramuscular BT.

# Deep Brain Stimulation: Opportunities and Challenges

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Deep brain stimulation (DBS) is an established technique used for movement disorders such as Parkinson's disease (PD), essential tremor (ET) and dystonia. Over the years DBS has also been evaluated for a range of other symptoms such as various psychiatric indications, pain and epilepsy. A DBS lead is implanted with stereotactic neurosurgical technique in the deeper part of the brain, in a specific brain target tailored for the patient's symptoms. As an example, in ET the ventral intermedius nucleus (VIM) of the thalamus and zona incerta (ZI) are common brain targets. Prior to surgery, stereotactic MRI and sometime diffusion MRI is done in order to plan the intervention and lead placement. Postoperatively, imaging is performed to exclude bleedings and to confirm the lead position. In the recent years' the four-contact conventional DBS lead has been accompanied with directional leads for steering of the electric field (EF). Furthermore, the systems are now available both in voltage and current control modes. These novelties increase the opportunities to tailor the EF to a specific brain region in order to optimize the therapy. However, they also make the programming more challenging as the number of parameters as well as the total data information for each individual patient increase. In the research project "DBS: data analysis for clinical support" these challenges are approached. The project aims at bringing together brain images, patient-specific EF simulations, tractography and brain atlas information and combine these with intraoperative physiological data and patient evaluation records in a comprehensive analysis for increased understanding of DBS mechanism of action, and for optimization of DBS therapy. Examples of ongoing activities are patient-specific EF simulations for different lead configurations and brain targets, and tractography of crossing thin white matter fibers in the deeper part of the brain. Furthermore, work is ongoing to create improvement maps and side disorder maps by combining EF simulations and intraoperative accelerometer recordings of movement in relation to test stimulations. The talk will give a review of opportunities and challenges in DBS, and an overview of the latest results of our DBS studies.

# Deep learning enables accurate automatic sleep staging based on EEG measured with an ambulatory electrode set

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Introduction: We have previously developed an ambulatory electrode set (AES), also known as BruxHome, for recording of electroencephalography (EEG). The AES is suitable for self-application in home polysomnographies (PSG) [2]. The electrodes in AES are screen-printed on a flexible PET film which attaches easily to skin with self-adhesive hydrogel and medical foam. The EEG acquired with AES has previously been proven to be suitable for manual sleep staging and the success rate and technical quality of the AES signals have been shown to be comparable to conventional home PSGs [2]. The aim of the study was to utilize a previously developed neural network [1] for sleep staging based on EEG signals acquired with AES. We hypothesized that the AES signal quality is sufficient for automated neural network scoring algorithm.
Methods: The neural network architecture comprises a combination of a convolutional and recurrent neural network and has previously reached an accuracy of 82.9% ($\kappa = 0.77$) with a single standard EEG channel (F4) [1]. The used dataset comprises 72 PSG recordings supplemented with AES, which were conducted for subjects with self-reported sleep bruxism. The recordings were manually scored with all available PSG channels according to prevailing AASM guidelines. The neural network model was trained and tested with a single Fp2-T9 channel, as the Fp2 electrode in AES is close to the standard F4 electrode. The performance of the neural network was evaluated using 10-fold cross-validation with manual scoring as a reference.
Results: The accuracy of the neural network was 71.8% ($\kappa = 0.60$) for five sleep stages (wake, N1, N2, N3, REM), 76.0% ($\kappa = 0.63$) for four stages (wake, light sleep, deep sleep, REM), and 84.5% ($\kappa = 0.64$) for three stages (wake, NREM, REM).
Conclusion: The utilized neural network was able to accurately determine sleep stages based on a single EEG channel (Fp2-T9) measured with AES. The accuracy is comparable to inter-scorer reliability between international sleep centers [3]. The signal quality was proven to be sufficient for accurate automatic scoring. Automatic scoring of EEG measured with AES could reduce the costs and improve the availability of home PSG studies.

References:
[1] Korkalainen et al., IEEE J. Biomed. Heal. informatics, no. 5133, 2019.
[2] Miettinen et al., IEEE J. Biomed. Heal. Informatics, 22(4):1124–1132, 2018.
[3] Magalang et al., Sleep, 36(4): 591–596, 2013.

# Deep Learning for Cardiologist-level Myocardial Infarction Detection in Electrocardiograms

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Myocardial infarction is the leading cause of death worldwide. In this paper, we design domain-inspired neural network models to detect myocardial infarction. First, we study the contribution of various leads. This systematic analysis, first of its kind in the literature, indicates that out of 15 ECG leads, data from the v6, vz, and ii leads are critical to correctly identify myocardial infarction. Second, we use this finding and adapt the ConvNetQuake neural network model—originally designed to identify earthquakes—to attain state-of-the-art classification results for myocardial infarction, achieving 99.43% classification accuracy on a record-wise split, and 97.83% classification accuracy on a patient-wise split. These two results represent cardiologist-level performance level for myocardial infarction detection after feeding only 10 seconds of raw ECG data into our model. Third, we show that our multi-ECG-channel neural network achieves cardiologist-level performance without the need of any kind of manual feature extraction or data pre-processing.

# Deep Learning Models for Brain Age Prediction

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Estimation of chronological age from T1-weighted brain MR images using machine learning algorithms shows great potential as a biomarker of healthy brain aging. Numerous studies showed its use for early detection of neurological diseases, such as Alzheimer's dementia. As a result of ongoing neurogeneradion the predicted age is generally much higher than the chronological age, indicating accelerated ageing. With the use of deep learning models, multiple studies made evermore accurate predictions of brain age. Previously published methods were applied to different datasets, or datasets differed in terms of subject count, age span, ethnicity, etc., or the authors used different image preprocessing pipelines, and different training protocols and settings, thus their results cannot be directly compared. In this paper we therefore re-implement and comparatively evaluate three deep learning models for brain age prediction on common publicly available of T1-weighted MR images (N=2543). Our MRI image preprocessing included intensity non-uniformity correction and affine registration to MNI152 space. Through our experiments we obtained results consistent with reports in the literature, with best mean absolute error between predicted and chronological age of 3.69 years. The observed difference between predicted and chronological age may be used to detect accelerated aging, as a result of neurological or other diseases and/or inappropriate lifestyle. This may open an early window of opportunity for moderating the accelerated ageing through pharmacological or non-pharmacological interventions.

# Design of Nonlinear Bi-emotional Classifiers Based on Multiple Bio-signals

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Bio-signals have been applied in many researches associated with emotional state identification of human. Although previous researches can be represented to identify emotional states, there is no guarantee that their results are global with respect to the definition of emotion and the accuracy. To circumvent these problems, we performed that emotion is defined as only two emotional states, and evaluated the various recognition machines using bio-signals. Galvanic Skin Response (GSR), Electrocardiogram (ECG) and Skin Temperature (SKT) were selected as representative bio-signals effectively among many bio-signals of Autonomic Nerve System (ANS). Twenty-five subjects participated in the emotion experiment. Some video clips which can induce negative emotion or positive emotion from the supine subject were used where the GSR, ECG and SKT were measured when they are watching the video clips. The measured data from those three parameters- GSR, ECG and SKT-were segmented from 10 to 30 second. We analyzed and extracted the features of each segment. The results showed that there was a significant difference between the positive and negative emotions using SVM-RBF kernel with 30 second segmentation. In this study, we can find suitable segmented time interval and the recognition algorithm for distinguish Bi-Emotional State using evaluate two general identifiers, Neural Network and Support Vector Machine.

# Detecting Sleep Spindles using Entropy

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Sleep spindles are bursts of brain activity during sleep. They occur during the NREM2 stage of sleep and appear as fluctuations in electric recordings, looking like yarn spindles. This increase of activity can be detected by complexity measures, the most popular of which are the entropy based estimations. In this paper, we use entropy to measure the brain activity during sleep spindle and non-spindle periods and discriminate them employing the machine learning technology. Two are the main outcomes of this work: a) we show that it is possible to achieve remarkable classification performance when detecting sleep spindles with entropy based measures and machine learning techniques, presenting classification accuracy of more than 95% and (b) we report that bubble entropy, a recently introduced definition of entropy, presented the lowest p-value of all examined features.

# Detection of acute inflammation of urinary bladder and acute nephritis of renal pelvis origin using artificial neural network

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Many different urinary tract conditions are characterized by overlapping symptoms, such as strong urge to urinate, burning sensation, abnormal urine output, and fewer, which make the diagnosis and treatment difficult and time-consuming. In order to skip traditional time-consuming diagnostic methods, the direct treatment of patients with confirmed symptoms may be administered. An expert system that uses artificial intelligence methods can be used in order to solve problems of a specialized domain. In this paper, Artificial Neural Network for the classification of acute inflammation of uri-nary bladder and acute nephritis of renal pelvis origin is presented. Dataset of 120 samples has been used to determine whether a patient is suffering from both diseases, only from one disease or is healthy. A feedforward neu-ral network was trained and yielded an accuracy of 95.83%. The sensitivity of the developed system is 94.44%, while specificity is 100%. This system allows the clinician to enter different symptoms observed or reported by a patient and understand the connection between them in order to more accu-rately provide diagnosis and prevent possible misdiagnosis.

# Detection of electroporation threshold using bioluminescence

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The cell membrane permeabilization can be quantified using many direct or indirect evaluation methods, however, fluorescent markers such as propidium iodide (PI) are commonly applied in electroporation works. In this work a methodology based on bioluminescence for detection and analysis of electroporation phenomenon is presented. Myeloma SP2/0 cells (transfected using Luciferase-pcDNA3 plasmid) were used as a cell model. The study focused the short (0.1 - 5 $\mu$s) and longer 100 $\mu$s pulses in the 1 - 2.5 kV/cm electric field range. It was shown that the bioluminescence response is dependent on the cell permeabilization state and can be effectively used to detect even weak permeabilization. During saturated permeabilization, the bioluminescence signal accurately predicts the loss in viability. Lastly, the SP2/0 tumors have been developed in BALB/C mice and the methodology has been tested in vivo using electrochemotherapy with bleomycin. This work was supported by grant Nr. S-MIP-19-22 from Research Council of Lithuania. The study was also partly supported by PL NCN Grant SONATA BIS 6 (2016/22/E/NZ5/00671; PI: J. Kulbacka).

# Detection of Temporomandibular Joint Disfunction in Juvenile Idiopathic Arthritis Through Infrared Ther-mal Imaging and a Machine Learning procedure

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Juvenile idiopathic arthritis (JIA) represents the most common rheumatologic disease in childhood, often characterized by temporomandibular joint (TMJ) dis-function (TMD). The gold standard to diagnose this pathology relies on magnetic resonance imaging. Alternatively, electromyographic (EMG) recordings could provide an early and immediate detection of TMD. Particularly, temporalis mus-cle is known to exhibit a greater EMG activity more frequently than the masseter in pathological subjects. Since muscular activity may influence the superficial cir-culation and, consequently, the skin temperature, the capabilities of functional thermal infrared imaging (fIRI) to detect TMD were also investigated. In this study, the feasibility of a multivariate data-driven approach based on General Lin-ear Model to estimate the EMG ratio between masseter and temporalis (sEMG-M/T) from fIRI features was investigated. A leave-one-subject-out cross-validation was implemented to test the generalization capability of the model (r=0.55; p=1.72 10-6). Moreover, the output of the model was used to classify TMD and healthy controls. Since the two classes were unbalanced, a bootstrap procedure was applied. The performances of the classifier were investigated through Receiver Operating Characteristic analysis, which exhibited an area un-der the curve of 0.71. The results suggested that fIRI could be a relative cheap and simple to use tool for TMD assessment.

# Detection of Vascular Access Obstruction Based on the Multiscale Entropy of Phonoangiographic Signals

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The number of patients with kidney diseases is increasing in Taiwan. At the same time, patients need to receive the hemodialysis treatment is also elevated. In either an arteriovenous fistula or an artificial fistula, stenosis or obstruction may take place after a period of usage. The purpose of the study was to investigate whether there was any difference in the nonlinear property of the phonoangiographic (PAG) signals produced in a fistula in the presence or the absence of a stenotic lesion. The study included 119 hemodialysis patients who were undergoing angioplasty surgery due to the existence of stenosis The PAG signals of about 10 seconds generated in the fistula was registered by a self-designed measuring device before and after surgery. Three measuring sites were selected, including the position A (at the fistula-artery healing end), the position C (at the fistula-vein healing end), and the position B (at the midpoint of the fistula). When the scale factor was chosen to be 4, the mean value of multiscale entropy (MSE) corresponding to the phono-angiogram signals recorded at the position A of the vascular access is significantly greater after surgery than before surgery ($0.38 \pm 0.25$ vs $0.33 \pm 0.23$, $p<0.05$). However, there was no significant difference in MSE values for the positions B and C. According to the present results, the MSE method can be employed to assess the irregularity of phono-angiogram signals in a fistula. Furthermore, the extent of the irregularity may be available for distinguishing the stenotic fistula from the unobstructed ones.

# Developing an Online Training Module for ENT Students

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A particular problem area that ENT head and neck operations (ENT: Ear-Nose-Throat) have to deal with is the air flow in the nasal cavities and paranasal sinuses. The extension of morphological diagnostics by a detailed functional analysis, i.e. the visualization of the nasal airflow and the physical analysis of its energetic properties, is a burning problem. The simulation of air flow by means of CFD (Computational Fluid Dynamics) is nowadays gaining in importance for diagnostics and the visualization and simulation of air flows from the nostrils to the nasopharynx primarily enables a precise and high-quality 3D reconstruction of the nasal cavities. However, the successive validation and interpretation of CFD simulation results is a challenge for non-CFD specialists.

Main activities for rhinosinusitis diagnostics ought to include the visualization of nasal cavities (using 3D modelling), the execution of CFD-simulation, and the interpretation of airflow simulation results. The introduction of these new technologies requires special education and training for both students and medical experts to learn how to use different tools and methods in the preparation of an operation. The ”flipped classroom”, a kind of blended learning, is a preferred method to support knowledge transfer not only to students and staff but also among all kinds of different members within organizations. The presentation will introduce to tools and methods for implementing a cooperative medical training course based on the flipped classroom method to train new technologies to ENT medical experts.

# Development and Future Challenges of Nature-inspired bio-hybrid robotics

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Soft robotics is an emerging discipline that employs soft flexible materials such as fluids, gels and elastomers in order to enhance the use of robotics into healthcare applications. Compared to their rigid counterparts, soft robotic systems have flexible and rheological properties that are closely related to biological systems, thus allowing the development of adaptive and flexible interactions with complex dynamic environments. With new technologies in bioengineering arising, the integration of living cells into soft robotic systems offers the possibility of accomplishing multiple and complex functions such as sensing and actuating upon external stimuli. These emerging bio-hybrid systems are showing promsing outcomes and open new avenues in the field of soft robotics for their application in healthcare and other fields.

As our understanding of cell biology, as well as of tissue homeostasis and pathology improves, the interest in biomimetic and bioinspired materials is growing. Here, this class of biomaterials is defined as a material that recapitulates key features of natural materials and/or biological structures. They can be of natural origin, as in the case of naturally derived sugars, be based on natural occurring monomer units, as in the case of nucleic acid (NA)-based molecules, or fully synthetic. Due to their similarities with biologically relevant structures, either at the chemical, physical, or morphological level, biomimetic and bioinspired materials are expected to outperform many of the currently available materials. At the chemical level one can take advantage of the similarity of biological constituents to attain chemical specificity, reduce cytotoxicity, or tune biodegradability. Microfluidics, bioelectronics, and engineered nanostructures, with close interactions with biology at the cellular or tissue levels, have already yielded a spectrum of new applications. Many new designs emerge, including of organ-on-a-chip systems, biodegradable implants, electroceutical devices, minimally invasive neuro-prosthetic tools, and soft robotics. In this review, we highlight a few recent advances of the fabrication and application of smart bio-hybrid systems, with a particular emphasis on the three dimensional (3D) bio-integrated devices that mimic the 3D feature of tissue scaffolds. We also discuss the progress in the construction of cell-enabled soft robotics, where a tight coupling of the synthetic and biological parts is crucial for efficient function.

# Development of a Dynamic, Static Balance Evaluation and AI-based Exercise Prescription System for the Elderly

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The ability of balance is the key to perform various tasks in daily life. It is also an important factor to maintain the motor function. Balance disorders would lead to falls, injuries and complications, such as anxiety and depression, affecting the quality of daily life. Especially in the elderly group, the sense of balance or the completeness of exercise ability is more important. The decrement of sense of balance or exercise ability often indicate physical illness and the high risk of falling. Therefore, for elderly group, doctors often design an exercise prescription to improve balance and athletic ability.
With increasing of senior population, the government's health care expenditures will also be increased. Chronic diseases such as disability or dementia or falling of the elderly are the most serious issues in aging society. Therefore, it is quite important to make effective exercising prescriptions to prevent the elderlies from suffering disability or dementia.
This study proposes a system using 9-axis inertial measurement units for automatically assessing the ability of balance and providing effective exercising prescriptions. The subjects' abilities of static and dynamic balance can be accurately evaluated by extracting several motor features while performing the simple tasks. In addition to the motor features, the physiological features of the subjects will also be included to build the automatic system via deep learning techniques. The prescription provided by the automatic system will be compared with the prescriptions given by the physicians. The system is expected to increase the accuracy of evaluating the ability of balance and assist the physicians to make prescriptions more efficiently.

# Development of a module for archiving the results of electrical impedance tomography measurements

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One of the important tasks in the development of an electrical impedance tomography module is the archiving of measurement results. This paper deals with the tasks facing the module for measurements archiving. These include ensuring the storage of information about the measurement parameters, recording the measurement procedure and storing the data obtained from the measuring device. The analysis of possible file storage formats is given. Storage of data in a DBMS, in JSON format and text files is considered. A comparison of these methods in terms of the amount of occupied disk space, the time of data archiving and the possibility of data scaling in the event of a change in the measurement protocol and procedure is considered. An algorithm for archiving data obtained during measurements of electrical impedance tomography has been developed. Two approaches for storing data are presented. In the case of the first approach, only the measurement data are saved, on the basis of which the conductivity field is reconstructed again. In the case of using the second approach, not only measurement data are archived, but also the reconstruction results of the conductivity field. This approach reduces the time spent viewing archived measurement results. The experiments carried out have shown that this approach is ineffective, since when using it, the volume of stored data increases significantly, while the reconstruction time decreases insignificantly. Software has been developed that implements the module for archiving the results of electrical impedance tomography. This software implements archiving of measurement data in JSON format. A module for reconstructing the conductivity field based on archived measurement results is presented. The work is carried out with the financial support of the Ministry of Science and Higher Education of the Russian Federation, project SP-21.2019.4.

# Development of a nanocomposites based anthropometric phantom to evaluate thermal effect induced by radiofrequency electromedical systems

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The significant progress made by science allows for more precise, less invasive and harmful diagnostic and therapeutic techniques. Particular interest is on the use of radiofrequency electromagnetic fields and on their capability to hit the human body in order to realize, for example, surgical ablation or aesthetic treatments. Now a legitimate question arises: whether these tools and, in particular, the aesthetic treatments with electromagnetic fields, can be harmful to patients during the medical examination or treatment. Modeling, understanding and studying the human body, however, both from an anatomical and functional point of view is somewhat complex.
Compared to traditional test methods based on animals or corpses, a third way has already been growing for many years: phantoms. These phantoms can be built by simulating certain properties of the human body (anthropometric phantom) or even mimicking their geometric characteristics (antropomorhic phantom).
In this work we will propose the use of nanocomposites materials to mimicking the electromagnetic and thermal responses of biological tissues interested by electromagnetic fields typically used in electromedical treatment applications. In particular a multilayer section of biological tissues (specifically, skin and abdominal muscle) is considered to be treated through the application of an electromagnetic signal in the radiofrequency range. The design and the realization of a circular slab to use as anthropometric phantom of this multilayer section in an ongoing laboratory experimental setup will be presented.
The proposed phantom is designed by considering the literature available geometrical, electrical and thermal properties of all layers of the tissue (epidermis, dermis and hypodermis) and of the muscle (in particular, abdominal). Fused deposition modeling (FDM) technique is used to print each layer according to the corresponding thickness by exploiting the Additive Manufacturing procedure. Already avalilable multifunctional nanocomposite materials, based on a polymer matrix (poly lactic acid – PLA) loaded with Multiwalled Carbon Nanotubes (MWCNT) and Graphene Nanoplatelets (GNP), are chosen according to their electromagnetic and termal properties. The CAD project was developed to create a circular multilayer slab on which the thermal response of the material subjected to 1-10 MHz electromagnetic field will be measured. Therefore, this project will reflect the presence of holes, at different depths, through which thermocouples will be inserted to measure the temperature of the layers during exposure to the electromedical field. Moreover, the geometry of the phantom is optimized by considering the total area of the threatment under test for the given electromedical system.

# Development of an instrumented chair to identify the phases of the sit-to-stand movement

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Instrumented versions of functional geriatric screening tests have been developed to improve clinical precision. Several different instrumented versions of the sit-to-Stand (iSTS) test have been developed using a range of sensors such as accelerometers and cameras. In previous work, an instrumented chair equipped with load cells was used to detect phases of the STS. However, the chair was unable to detect phases when the person was not in contact with the chair. A new version of the chair was designed with the addition of an ultrasound sensor to enable detection of all phases of the STS. The performance of the new iSTS chair was compared with the previous version, an RGB camera approach, and a data-fusion approach using the load-cell equipped chair and the RGB camera. Ten adult subjects were test-ed performing the 5STS at two self-selected speeds. The accuracy of the load cell equipped chair was 70%, while the RGB camera achieved 76?curacy. The ultrasound version of the chair and the fusion of the RGB and load-cell technique both achieved significantly better accuracy at 86% and 89%, respectively. The new version of the instrumented chair obtained a high degree of accuracy in detecting the different phases of the STS and is suitable to detect STS phases without requiring additional sensors. Future work will test older subjects and aim to develop new parameters based on the phases of the STS as indicators of physical performance.

# Different Amino Acid Coating of the Magnetic Nanoparticles Characterised by the MRI Relaxivity

Oliver Strbak[1], Iryna Antal[2], Iryna Khmara[2], Martina Koneracka[2], Martina Kubovcikova[2], Vlasta Zavisova[2], Martina Kmetova[1], Eva Baranovicova[1], Dusan Dobrota[1]
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In this study, we analysed the physico-chemical properties of positively charged magnetic fluids consisting of magnetic nanoparticles (MNPs) functionalised by different amino acids (AAs): glycine (Gly), lysine (Lys) and tryptophan (Trp), and the influence of AA-MNPs' complexes on the MRI relaxivity. We found that the AA coating affects the size of dispersed particles and isoelectric point, as well as the zeta potential of AA-MNPs differently, depending on the AA selected. Moreover, we showed that a change in hydrodynamic diameter results in a change to the relaxivity of AA-MNPs' complexes. On the one hand, we observed a decrease in the relaxivity values, r1 and r2, with an increase in hydrodynamic diameter (the relaxivity of r1 and r2 were comparable with commercially available contrast agents); on the other hand, we observed an increase in r2* value with an increase in hydrodynamic size. However, the relaxivity values were different for all amino acids used, allowing them to be distinguished from each other. These findings provide an interesting preliminary look at the impact of AA coating on the relaxivity properties of AA-MNPs' complexes, with a specific application in molecular contrast imaging originating from magnetic nanoparticles and magnetic resonance techniques.

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This research was funded by the Ministry of Health of the Slovak Republic (2018/11-UKMT-7) and by the National Grant Agency VEGA 2/0033/19.

# Digitizing Malaria Case Management Protocol in Ghana: A pilot Study

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Background: It has been a common practice in Ghana for patients to seek first aid medical attention from community pharmacies or chemical shops. Management of malaria cases is no exception to this, as many patients who experience symptoms of malaria visit pharmacy shops to seek medical attention. The Ghana Health Service guidelines for malaria case management ensure that all persons presented with malaria symptoms at any health facility are tested through microscopy or malaria Rapid Diagnostic Test (mRDT). Malaria case management interventions such as point of care testing using mRDT kits ensure accurate diagnosis and effective treatment and can be well monitored through a real time data capturing solution. This study evaluate the use of a mobile health technology platform, known as the Fionet Platform to remotely monitor mRDT testing and understand issues faced by healthcare workers in using the malaria diagnosis test kits.
Methods: To ensure adherence to malaria case management protocol of 'Test, Treat and Track (3Ts), a mobile phone installed with the Fionet App was deployed. Under this pilot study, 28 pharmacy shops were selected from Greater Accra Region and 13 Over the Counter Medicine Shops (OTCMS) from Central Region were selected. The pharmacists and Medical Counter Assistants from these facilities were trained to use the Fionet mobile phone App for malaria testing. The shops were also supplied with RDTs through the National Malaria Control Programme. Inventory of RDTs supplied to these shops were tracked to ascertain whether some tests were conducted without using the Fionet App and to understand the motivations behind the bypass through interviews.
Results: A total of 5312 RDT tests were recorded through the Fionet platform, out of which 3972, representing 74.7% were malaria antigen negative and 1286 (24.2%) were malaria antigen positive. The uploaded records also reported 1.05% tests as error. 91.91% of malaria positive cases were treated with ACTs, where as 14.85% of malaria negative cases were also treated with ACTs. Of the malaria negative cases that were treated, 9.1% of patients insisted they want ACT treatment and 91.8% were given ACT treatment because the patients were showing malaria symptoms according to the caregivers. For the RDTs that were not processed through the Fionet platform, the caregivers indicated that the incubation period is too long when they use the Fionet platform, as it compels them to stick to the incubation period.

# Directional freezing of cell-seeded electrospun fiber mats for tissue engineering applications

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As novel tissue engineered constructs (TECs) are developed, current tissue banking practices need better control over ice formation and growth to prevent cryodamage to cells and a scaffold. Directional solidification demonstrates benefits in adhered cells and native tissues cryopreservation through controlled heat transfer. Therefore, this study aims to investigate the feasibility of using this technique for cryopreservation of cell-seeded electrospun fiber mats as model TECs. Fiber mats were produced using blend electrospinning of polycaprolactone (PCL, 200 mg/ml) and poly-L-lactic acid (PLA, 100 mg/ml) dissolved in 2,2,2-Trifluoroethanol. The fiber size and morphology was characterized using scanning electron microscopy. Specific heat measurements were conducted using differential scanning calorimetry. The square-shaped fiber mats were seeded under static conditions with HeLa cells and cultivated for 24 h. Samples were directionally frozen in a sandwich format either in 10% DMSO or culture medium with the sample movement at 30 $\mu$m/sec through the predetermined temperature gradients along a 2.6 mm slit. After directional solidification, samples were gradually frozen at 1 K/min down to -80 ° . Crystal shape was visualized using cryomicroscopic system. Before freezing and 24 h after thawing, cell viability was assessed using live-dead assay. Within randomly orientated PCL-PLA fibers, HeLa cells exhibited typical shape and attachment with higher than 90% viability prior to freezing. While up to 80% of HeLa cells were alive on fiber mats after freezing using DMSO with or without directional solidification step. The demonstrated controlled freezing may assist optimizing the freezing of more sensitive cells. The results suggest that directional freezing becomes a viable option for cryopreservation in tissue engineering applications.

# Distinguishing Aortic Stenosis from Bicuspid Aortic Valve in Children using Intelligent Phonocardiography

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This paper presents a machine learning method to detect and discriminate between Aortic Stenosis (AS) and Bicuspid Aortic Valve (BAV) based on heart sound analysis. Differentiation between the two heart conditions is clinically important, but complicated if relying merely on the conventional auscultation. A novel form of the Time Growing Neural Network (TGNN) is introduced for the classification purpose. The method is applied to a dataset comprised of 87 children referrals to a university hospital, from which 50 individuals are healthy (with and without innocent murmur), and the rest are abnormal with either AS (15 individuals) or BAV (22 individuals). The baseline for comparison is a Time-Delayed Neural Network (TDNN) with the same size of the feature vector and the temporal frame. We used our original validation methods, named A-Test, which provides valuable in-formation about structural risk and also learning capacity of any supervised classification method. A-Test is an elaborated version of K-Fold validation method, in a rather profound way. Performance of the TGNN is superior comparing to the presented TDNN, with an accuracy of 85.8% against 81.5%. This method can be integrated with our intelligent phonocardiography to serve as an enhanced assessment tool in hands of nurses or practitioners at primary healthcare centres.

# Distributed Access control for Cross-organizational Healthcare Data Sharing scenarios

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Sharing information between healthcare organizations is a must for the next-generation healthcare systems. Despite the huge advantages that have been lately associated with it, organizations are still reluctant to its adoption due to the related privacy issues. In this work we propose a distributed access control system that relies on Garbled Circuits to perform a XACML-like policy evaluation, where attributes required for the evaluation are spread across organizations, ensuring that no attributes of one organization can be learned by others. Since Garbled Circuits is used as underlying protocol, an analysis of the complexity of the proposed method is provided in terms of Non-XOR gates. Some examples of the cost of using this method with different policy sizes is also provided with an estimation of the achievable amount of evaluations per second. The obtained results are promising but further research is still needed to determine which real-world scenarios would be suited for the proposed system.

# DMAIC approach for the reduction of healthcare-associated infections in the neonatal intensive care unit of the University Hospital of Naples ‘Federico II’

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Improvements in the obstetrical and neonatal management have allowed children to survive. These enhancements have showed, anyway, a general increased incidence of healthcare-associated infections, one of the most influent causes of morbidity and mortality in neonatal intensive care units. The aim of this paper is to suggest corrective measures to reduce sentinel germs colonization and identify the relationships between bacteria colonization with the number of procedures and the length of hospital stay. The Lean Six Sigma methodology was used to tackle this issue using a tailored Define, Measure, Analyze, Improve, and Control problem-solving strategy. An increased number of procedures and an extended length of hospital stay demonstrated a statistically significant influence on newborns’ possibility to be infected by sentinel germs. These findings could guide the clinical staff to improve the management of neonates in neonatal intensive care units reducing the number of infected patients, their length of hospital stay and the costs for the hospital.

# DMAIC approach to reduce LOS in patients undergoing oral cancer surgery

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Introduction. Oral cancers, especially the maxilla and mandible, represent the sites where cystic and neoplastic conditions, of a benign or malignant nature, can occur. In general, for patients undergoing surgery to remove cancer of the oral cavity, the administration of oral antibiotics can affect the Length of Stay (LOS).
Objective. This study compares the administration effects of two antibiotics in patients undergoing oral cancer surgery (mucosa / bone) at the Department of Maxillofacial Surgery of the University of Naples "Federico II".
Methods. The comparison was made considering the postoperative LOS for two different group of patients according to the Six Sigma (SS) methodology that follows the DMAIC cycle (Define, Measure, Analyse, Improve, Control). To this aim different variables were analysed through statistical tests performed, in the phase Analyse, to verify the influence of the variables considered for each antibiotic.
Results. Results reports the significance on postoperative LOS for each category of each variable between the two samples of patients treated with antibiotics. A weak statistical significance in favour of Ceftriaxone are patients not undergoing lymphadenectomy and patients not exposed to surgical site infections. In addition, a demographic study was conducted by applying the chi square test for each variable. A statistically significant different was obtained according to the American Society of Anaesthesiologists score.
Conclusions. This study showed the validity of the SS methodology to evaluate the introduction of the postoperative prophylactic antibiotic protocol for patients undergoing surgery for oral cancer.

# Dynamics of resting state topology in MEG: methods and applications

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In the latest years, pushed by the fMRI Resting State Networks (RSN), MEG provided important findings on the dynamics of ongoing interactions and their topology. However, with standard low Tc SQUID-based systems, the resolution of source-space MEG is affected by spatial leakage [1]. We here discuss the effects of leakage correction on the topological properties of MEG connectivity, during resting state. We then apply our pipeline to analyze the effect of task on the spectral dynamics of topology at rest.
Using a standard 153 channel MEG system, we recorded the ongoing activity from 13 subjects during fixation, before and after a self-paced finger tapping task. MEG data were preprocessed using temporal ICA to remove artifact components. The spatial maps of the non-artifact ones were projected into the source space [1]. To evaluate the effect of leakage correction, we estimated the activity of a set of 155 voxels comprised in 9 fMRI RSN through the linear combination of IC weighted by their source space maps in 3 conditions [1]: i) no correction; ii) corrected by the Geometrical Correction Scheme (GCS), preserving 0-lag correlation; iii) corrected by the Orthogonalization Scheme. We then estimated static Pearson's correlation matrices from the power timecourses in the theta (4-8 Hz), alpha (8-13 Hz) and beta (13-25 Hz) bands. After selecting the correction scheme, we evaluated the effect of task on ongoing connectivity, comparing pre- and post-finger tapping interaction evaluating differences of: i) correlation values; ii) global architecture; iii) binary Betweenness Centrality (BC). To obtain binary graphs, we selected the threshold providing the largest average BC. Finally, we identified hubs by comparing BC with random graphs with similar degree.
We obtained that leakage correction reduced the local interactions and, for the GCS only, increased the inter-hemispheric connections and the Global Efficiency. Overall, the role of important hubs in the anterior and posterior cingulated cortex was preserved. Thus, we selected GCS as the leakage correction scheme. When comparing pre- and post-finger tapping connectivity, we found that, in addition to task-invariant hubs, a set of hubs in the Motor and Default-Mode Networks were modulated mainly in the alpha and beta bands. In summary, these task-induced changes of spontaneous centrality resemble learning-related fMRI changes during motor task [2], possibly representing a short-term plastic mechanism to sculpt the brain state.

References:
[1] Della Penna S et al., Frontiers in Neuroscience 2019 13:1114
[2] D.S. Bassett et al., Nat Neurosci. 2015 18:744

# EAMBES working group on medical devices nomenclature and regulatory sciences

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In May 2019, the World Health Assembly of the World Health Organization (WHO) decided to start working on a free international nomenclature of medical devices, including IVDs, for facilitating and harmonising the work of regulators, procurers, supply and user around the globe. According to the WHO, this nomenclature must be a "Public Good", not subject to copyright, freely accessible to everyone, and designed to consider the real need of healthcare professionals (e.g., nurses, clinical engineers), facilitating their daily work. For instance, WHO considered aligning the nomenclature with the International Classification of Diseases 11th Revision (ICD11). This does not seem to be the case for the 2 major international nomenclatures: GMDN, developed by the European GMDN Agency, which is widely used internationally and UMDNS, developed by ECRI.
The European Union has decide to change its official nomenclature adopting the Italian nomenclature, which will be renamed EMDN (European Medical Devices Nomenclature).
However, a lot of work remains to be done, in order to male this nomenclature accessible and universal, especially to protect users from LMICs.
In order to offer a support to WHO and to the EU Commission, the EAMBES set a working group. This presentation will offer a preliminary view of the conclusions achieved from this working group.

# Early Diagnosis and Prediction of Skeletal Class III Malocclusion from Profile Photos using Artificial Intelligence

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A growing market of healthcare mobile applications is emerging in a wide range of areas including decision support systems for clinicians towards better treatments and home-use apps for raising awareness of the patients for early diagnosis. In the current healthcare mobile application market, there are several dental mobile applications. Current applications are mainly developed for patient education about general dentistry[1], braces, invisalign and oral health[2]. A recent artificial intelligence-based program marks landmark points on cephalometric images[3]. Among skeletal deformities, Class III is the one that orthodontics gives more importance compared to Class I or Class II, because growth modification is possible only before pubertal growth spurt. Class III malocclusion is especially difficult to treat with braces frequently requiring surgical intervention. In orthodontics clinics, cephalometric evaluation is the first line of test for the detection of Class III malocclusion. Yet the software required for cephalometric evaluation is expensive and not widely accessible by orthodontists in the developing countries. In this study, we assessed the potential of a computational model for detecting Class III Malocclusion using the profile images of patients as a cheaper and more patient-accessible alternative. The main purpose of our project is to develop this model into a mobile application for parents seeking a second opinion on whether to reach out to an orthodontist at an early stage of developmental bone growth with a warning of Class III malocclusion risk.

For detecting Class III malocclusion, we utilized several different angles from literature to mark the points on the profile (e.g. chin tip, nose tip) and discriminate skeletal status from each other. In this study, a test dataset consisting of 60 profile images of patients is used to evaluate the performance of several different heuristic criteria. After normalizing all images (renaming, resizing and formatting), facial landmarks on face images are detected by using Python face-alignment library[4]. Among 68 points that the library detected on faces, seven of them used to test different methods, which are G, Prn, Sn, Ls, Li, Sm and Pg.

We devised three heuristic methods to evaluate the performance on our patient test data. In all three methods, if the calculated angles match ClassIII angle mean+-standard deviation intervals, patients are categorized as “ClassIII”. If the angles are outside the standard deviation intervals, we assigned the category as “not ClassIII”. The most successful method so far was the third method, categorizing the 49/60 images correctly (85% in Class I, 100% in Class II and 60% in Class III).

# Early diagnosis of aortic aneurysms based on the classification of transfer function parameters estimated from two photoplethysmographic signals

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Cardiovascular diseases are the leading cause of death worldwide. Particularly aortic aneurysms are problematic: they affect 12-14 % of the population, early diagnosis is challenging because of the lack of symptoms, and in case of rupture, mortality is high. Aortic aneurysms are underdiagnosed: Existing diagnostic techniques, such as Doppler sonography, transesophageal echocardiography, computed- or magnetic resonance tomography, either lack sensitivity or require specialized expertise, are invasive and costly which hampers effective screening. The objective of this study is to develop an easy-to-use, non-invasive diagnostic method, based on the classification of two peripheral photoplethysmographic signals, to generate suspicious facts about the presence of aortic aneurysms at the family physician level.

Computational models of the cardiovascular system typically make it possible to simulate blood pressure and flow waveforms based on changes in the anatomy of the arterial network, e.g. bifurcations, aneurysms or stenoses. The attempt of this study, however, is to inversely deduce the underlying network morphology from peripheral pressure time series. In our previous study, we considered in-silico pressure-pressure transfer functions between two peripheral and sensitive measurement locations, by estimating parameters of an AutoRegressive-MovingAverage (ARMA)-model using a subspace Gauss-Newton search method. Parameters allowed to distinguish the pathological state of the underlying network morphology for three cases of aortic aneurysms.

Within this study, however, a similar approach is applied to in-vivo data, which was collected in a clinical study including 55 patients performed at the Tübingen University Hospital. ARMA-coefficients were estimated using baseline-corrected, zero-mean signals from the arteria brachialis and femoralis in two cases: besides the control group, the estimations were performed on signals arising from aneurysms located in the thoracic and abdominal aorta. Four best ARMA-coefficients were identified by maximising a mean distance measure to pre-select high quality classification features. Subsequently pathological states were identified using a naive Bayes classification algorithm, achieving sensitivity and specificity of greater than 75 %. Classification quality was compared for different pre-processing methods, other signal-based transfer-function and feature selection techniques to improve diagnostic precision in terms of location and degree of the disease.

The new approach has shown basic classification quality in a proof-of-concept clinical setting, however to overcome remaining uncertainties, training of the classifier with a larger number of patients is necessary. Nevertheless, we assume, that the method will improve the interpretation of cardiovascular signals in the early diagnosis of aortic aneurysms in near future.

# Eccentric vs. Concentric Coronary Lesions in idealized vessels: a parametric study

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The estimation of the hemodynamic severity of coronary lesions is a non-trivial matter in clinical practice. The functional assessment of coronary lesions is usually performed using a pressure wire, by measuring pressure values throughout the vessel, thus calculating the Fractional Flow Reserve value. In the current study, we try to investigate the effect of a certain geometrical factor (i.e. eccentricity or concentricity of the lesion etc.) on the hemodynamic parameters such as wall shear stress and smartFFR by performing blood flow simulations using the Finite Element Method on six idealized 3D arterial models which have a single stenosis of various severities (i.e. 25%, 50% and 70% diameter reduction). From the obtained results we can draw the conclusion that the eccentricity of the lesions exhibits higher WSS values and lower smartFFR values when compared to the concentric ones.

# Effect of left atrial appendage occlusion on intracardiac flow patterns during left ventricular assist device support

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Introduction: Thromboembolic events and consequently stroke are devastating complications of left ventricular assist devices (LVADs) therapy. Atrial Fibrillation (AF) is a common comorbidity in LVAD patients and has been identified as a risk factor for stroke. Blood stasis inside the Left Atrial Appendage (LAA) can be a main source of thrombosis during AF. Previous clinical studies suggest that occlusion of LAA may prevent thromboembolism in LVAD patients with AF, however the rationale behind is unknown. Therefore this study aims to investigate the effect of LAA occlusion on thrombosis-related parameter using Computation Fluid Dynamics (CFD) simulation.

Method: Left ventricular and left atrial models of an LVAD patient with AF were obtained from Computed Tomography (CT). Hemodynamic data of a typical LVAD-patient were generated by Lumped Parameter Model (LPM) and used as boundary conditions for CFD simulations of 6 cardiac cycles (total cardiac output 5 L/min). Mass flow rate and pressure boundary conditions were applied at the pulmonary veins and pump outlet, respectively. Ventricular and atrial volumes were independently modified based on LPM. A first simulation was performed for the atrium with LAA, while in the second LAA was occluded. Mean velocity magnitude, stagnation regions (where mean velocity <5mm/s), Wall Shear Stress (WSS) at the atrial wall, and blood washout with virtual-ink technique were calculated.

Results: The ventricular flow pattern was similar for both simulations, however, occlusion of the LAA leads to +8% higher average velocity within the atrium and consequent increase of +13% WSS at the atrial wall. Also, atrial stagnation volume decreased around 35% by occluding the LAA. After 6 cardiac cycles 99% of the blood was cleared from the atrium without LAA compared to only 91% clearance for the atrium with LAA.

Conclusion: This study revealed high stagnation volumes in the left atrial appendage of a LVAD patient with atrial fibrillation. Blood stagnation in the LAA and low WSS are potential sources for thrombus formation. Occlusion of the appendage in a LVAD patient with AF significantly reduced the thrombus-related flow mechanical parameters and seems to reduce the risk of thromboembolic events from the appendage.

# Effect of pulsed electric field pretreatment on the essential oil stabilityextracted from Lavender

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In the recent years, pulsed electric field (PEF) technology emerged as an important method for the extraction of natural bioactive compounds. Essential oils are one of the agro-industrial products with an increasing demand as alternative for artificial additives in food, cosmetics as well as pharmacological applications. Herein, we present pulsed electric field along with the conventional method to extract essential oils from Lavender. The lavender plant was subjected to a PEF-pretreatment with different electrical parameters (Electric field intensity, pulse number) before the hydrodistillation extraction. The PEF treatment resulted in an increase of the yield of the essential oil as well as the reduction of the distillation time. Taking into account the susceptibility of essential oils to conversion and degradation reactions, we investigated the effect of pulsed electric field one the stability of essential oils. We used analytical methods to assess long term stability under heat and air conditions that cause essential oils degradation. Interestingly, the essential oils extracted by PEF pre-treatment have better stability in terms of pH, refractive index, air interaction. Our results, prove for the first time the long stability of PEF extracted essential oils.

# Effect of resection line shape in pulmonary resection

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One of the surgical treatments for primary spontaneous pneumothorax is to partially remove the lung tissue together with the affected area. However, new pulmonary cysts may develop near the suture resection line after treatment and may recur. The risk of recurrence is considered to be affected by the resection line shape, which is thought to be due to the change in tension near the resection line depending on the resection line shape. To confirm these effects, simple models with different resection line shapes were created. One is a model with a straight resection line shape used for resection of spontaneous pneumothorax. The other model has an angled resection line used for resection of lung tumors. As a result of the stress analysis using finite element analysis, the stress distribution at the apex of the lung on the resection line changed depending on the angle.

# Effective Models for Microwave Antennas in Thermal Ablation

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Thermal ablation in cancer therapy refers to a set of minimally invasive treatments, which induce thermal damage to the target tissue, i.e. tumor and safety margin. Tissue necrosis can be achieved with different technologies. In this work, we focus on microwave (MW) ablation. Ensuring the full ablation of the tumor can be challenging, since there are significant deviations of the performed ablation from the expected one. The physician needs to take into account the effects of heat transfer by large blood vessels, tissue type, and state of tissue, on the size of the ablation. Failure to sufficiently estimate these effects and devise a treatment plan to correct for them, can lead to tumor recurrence close to the ablation.
Different imaging modalities (MR thermometry, Ultrasound, CT imaging) can be used to track the ablation zone growth, and allow for a better understanding of these effects. MW antennas are typically not MR-compatible, whereas CT imaging is typically used for positioning the ablation probes, but not for tracking the ablation, to reduce the exposure of the patient to radiation. Hence, using biophysical models can be meaningful for planning the treatment and estimating its outcome. Such models include the heat produced by the antenna and the diffusion of heat in living tissue.
In models for MW ablation, the exact geometry and components of a MW antenna have a significant effect on the electromagnetic field around the antenna, and thus on the heating of tissue. However, it is very difficult to identify this information from publications, white papers, and patents. In addition, even when modeling the antenna is possible, it comes with a significant computational cost, which is a bottleneck for real-time planning. We propose the use of simplified formulations of the heat source around the MW antenna, which can be derived from general information about the type of MW antenna and its size. We combine shapes that represent the essential features of an antenna. We fit the approximate description to available data to reproduce the expected treatment outcome. Typical data include the manufacturer ablation zones, literature or data measured in an experimental set up. Using an effective heat source further simplifies the treatment model and its computational solution, and increases the computational efficiency, without deteriorating the accuracy of the predictions. We present a method for estimating an antenna specific heat source, and numerical results regarding the accuracy of the effective formulation.

# Effects of Mirror Therapy on Motor Imagery elicited ERD/S: An EEG study on healthy subjects

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The human central nervous system integrates different sensory modalities with the visual information to produce a coherent mental representation of our own body, making us capable not only to process sensory events but also to plan and executes movements in the surrounding space. The basis of Mirror Therapy (MT) is the use of a mirror to create a visual reflection of an affected limb to create an illusion of movement of the paretic part of the limb. One of the uses of the MT is in motor recovery in post-stroke hemi-paresis and even thought that it is valuable rehabilitation tool, its underly-ing neurophysiological manifestations and interaction with Motor Imagery (MI) are still unknown. Our study applies Forearm Bisection Test (FBT) and EEG measurement of the Event-related (de)synchronisation (ERD/S) to as-sess the effect the MT on 18 healthy subjects. Our results shows that FBT scores were significantly higher in experimental (MB) group compared to control (CN) group (median 13.54 vs 0.00, respectively; $p = 0.003$). Fur-thermore, $\Delta$ERD/S (post-pre) differed significantly between the hemi-spheres in the MB group in the Mu, betalow and betahigh EEG bands, whilst did not differ in the CN group in the Mu and betalow bands. The results demonstrate improvement in ERD/S MI and an update of the body represen-tation caused by MT. Moreover, findings suggest that the reflection of the moving hand in the mirror created an illusion of concomitant movement in the opposite hand that modulate the arm length representation which is de-tectable even during MI at EEG level. Our findings of neural basis and link of the MT and MI supports MT as favourable neurorehabilitation tool for motor recovery affecting not only the areas governing the moving hand but also the corresponding regions of the other hemisphere.

# EIT Based Time Constant Analysis to Determine Different Types of Patients in COVID-19 Pneumonia

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Purpose: To evaluate the lung compliance variation over the course of COVID-19 pneumonia, and to classify the patients into different types described as re-cruitable and non-recruitable, which lead to different ventilator support treatment. Method: Two ICU admitted COVID-19 patients, who were mechanically venti-lated for more than 7 days, were included into this investigation. During a daily recruitment maneuver - a PEEP trial - they were monitored by Electrical Imped-ance Tomography (EIT). Deflation time constants were calculated offline from EIT data to determine the type of patient and to observe the transition of different types over the course of pneumonia. Result: The first patient was recruitable and had the tendency of transition to the other type. The second patient is non-recruitable. Both patients showed low lung compliance, but the first patient start-ed in a better condition (higher compliance). Conclusion: EIT-based breath-by-breath time constant analysis can classify COVID-19 pneumonia into different classes of patients. The deterioration of lung mechanics can be monitored online by EIT which may help to find proper ventilation treatment.

# Electric Current Detection by T2* Relaxivity Change: a Feasibility Study

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Precise detection of electric current flowing in a conductive liquid sample by MRI (current density imaging technique – CDI) is often challenging due to required special hardware for application of electric pulses, need for sample reorientation during the experiment or for multiple current injections, and lastly, need for special pulse programs. In this study, another, much simpler approach of current detection, which based magnetic resonance spectroscopy (MRS), is considered. It is shown first theoretically and then by experiments on a phantom, that it is possible to detect currents, by change in T2* NMR relaxation time, with a comparable or even lower detection threshold as with CDI. In an image voxel T2* relaxation time changes due to magnetic field change induced by electric currents. The sensitivity of the method is proportional to the voxel linear dimension and to T2* relaxation time and the signal-to-noise ratio (SNR) of the signal from the voxel. While the proposed method cannot be used for an exact current determination and is sensitive only to the current component perpendicular to the static magnetic field its main advantages are simple implementation and good sensitivity that stems from an excellent SNR of proton MRS.

# Electrical Impedance Tomography with Box Constraint for Skull Conductivity Estimation

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Unknown electric conductivities of human tissues is a common issue in medical engineering. Electrical impedance tomography (EIT) is an imaging modality that can be used to determine these conductivities in vivo from boundary measurements. In this paper, we demonstrate that local conductivity values of different skull segments can be solved from EIT measurements with the help of a box constraint. Based on our numerical results, the accuracy of the results depended on the locations of the current carrying electrodes and the signal to noise ratio of the measurements. Particularly, the conductivity values of the skull segments that located below the current carrying electrodes were reconstructed more accurately.

# Electro-gene transfer of a synthetic gene encoding the Glycogen Debranching Enzyme as a possible therapeutic approach for Glycogen storage disease type III

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Glycogen storage disease type III (GSDIII) is a rare metabolic disease caused by the lack of the "Glycogen Debranching Enzyme" (GDE), a large cytosolic protein with two distinct enzymatic activities, involved in glycogen degradation. Mutations along the Agl gene, encoding for the human GDE, are associated with loss of enzymatic activity. As a consequence, abnormal glycogen accumulates in both skeletal and cardiac muscle and/or liver, with great variability in the resultant organ dysfunction. No cure exists and the unique available treatment is based on a strict diet.

The most frequent form of GSDIII (type IIIa) is considered a muscular dystrophy: muscle disorders, may become evident in adults with progressive weakness and distal muscle deterioration, with some patients requiring the use of a wheelchair for mobility.

A synthetic, patented cDNA, coding for the human GDE, was inserted into a mammalian expression vector, and used to develop protocols for in vitro and in vivo electro-transfection.

We will show results of introduction of the gene in GDE-defective human fibroblasts and preliminary results on electroporation of mice muscles with the long-term goal of contributing to an alternative non-viral gene therapy approach for GSDIII.

# Electrochemotherapy for high-grade prostate cancer

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Introduction: Electrochemotherapy (ECT) combines the use of reversible electroporation and a chemotherapeutic drug to ablate cancerous tissue. Its clinical effectiveness has been proven in several types of cancers, but is still novel to prostate cancer (PCa). As one of the main advantages of ECT lies in tissue selectivity and overall low adverse event rates, it is a potential therapeutic candidate for high-grade and/or locally advanced PCa. We present initial retrospective data on genitourinary outcomes of ECT in patients with metastatic and non-metastatic high-grade PCa.

Materials/Methods: 13 patients (pts) were treated with ECT with a Gleason Score distribution of 2x7a, 2x7b, 4x8, 4x9, 1x10. TNM stage was 2xT2c, 1xT3b, 1xT3c, 5xT4, 4xTxN1/TxM1. All pts were classified high-risk by D'Amico. 10 pts had previous therapies related to PCa: 3xTURP, 3xIRE, 2xHIFU, 1xradiotherapy, 1xchemotherapy. 9 pts were on ADT at ECT. Treatment planning was based on MRI. The procedure was under general anesthesia and US guidance and was performed with the Cliniporator (IGEA). An average of 5.5 electrodes (17G, IGEA) were used. Median treatment time was 132±40min. Follow-up was based on MRI+PSA. The median follow-up time for the cohort was 178d (min: 25, max: 373). Functional outcome was assessed by IIEF5/IPSS.

Results: The median age of pts at treatment was 68.8±9.2y. Median iPSA was 79.3ng/ml. All treatments were performed without complications. Adverse events were dysuria (4x), mild hematuria (3x), urinary retention (2x), indigestions (1x), testicle swelling (1x). Three pts complained about painful sensations in the perineum for up to 4w. 8 pts correctly filled out the questionnaires before and after treatment. Half the pts (4x) had an improvement in urinary function, and half (4x) had a score that showed a worsening of the condition. The median IPSS score difference was +1. IIEF5 Score decreased in average by 2±4.6p. In 4 pts, a recurrence was detected during the follow-up time.

Conclusion: ECT of high-grade PCa is safe and feasible. All occurring adverse events were manageable. Sexual/urinary functions slightly worsened in average at last follow-up. These results imply a low toxicity profile of ECT of PCa. Recurrence rates are in the statistical corridor of RPE for high-grade PCa. A longer follow-up time and additional prospective clinical trials are necessary to evaluate the clinical potential of ECT for PCa.

# Electrochemotherapy in Head and Neck: historical background and recent innovations

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Rationale: Electrochemotherapy (ECT) is an effective local treatment for cutaneous, subcutaneous, mucosal and deep seated tumor nodules and metastases, with percentages of objective response close to 100%, especially for basal cell carcinoma.
The use of ECT in the head and neck area entails the need to manage different pathological conditions: cutaneous tumour nodules located in the upper or lower face; subcutaneous or deep seated tumours near to vital structures; mucosal nodules of the oral cavity or the oropharynx. Moreover, the standard doses of bleomycin in very old people can lead to more severe side effects. Recently, new electrodes have been developed to overcome the difficulties related to the treatment of these anatomical subsites and reduced doses of intravenous bleomycin or intratumoral Calcium have been introduced to reduce the side effects, maintaining the same cytotoxic efficacy.
Materials and methods: The indications and contraindications to ECT in the head and neck area will be presented as well as the different treatment typologies according to the site, side and number of the tumour nodules. Moreover, the new electrodes with fixed geometry for the treatment of the mucosal lesions and the methods for the application of the single electrodes for the variable geometry will be exposed. Finally, the indications and the modalities of administration of the reduced doses of bleomycin or Calcium will be explained.
Results: The literature data about the efficacy of ECT in the head and neck area will be commented as well as the preliminary results of the reduced doses of bleomycin and Calcium. Some explicative experimental and clinical cases will be further presented regarding the new electrodes with fixed geometry or the variabile geometry.
Conclusions: The development of new electrodes and new methods, the improvement of the procedures will allow to significantly increase the efficacy and safety of ECT for the treatment of difficult areas or old frail patients, who are the main targets of this therapy.

# Electronical and Physical Requirements for Setting up a Biomedical Simulation Tool in Rhinodiagnostic

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In this project, we investigate the possibility to evaluate Computational Fluid Dynamics (CFD) in ENT, especially in rhino diagnostic, using pressure measurements on 3D-printed physical models in a testbed with artificial breathing.
We are using the same set of individual segmented DICOM data (STL-format) for CFD analysis as well as to generate additive manufactured models, latter extended with a set of local pressure points.
Using sensors to realise smart 3D printed models for an ENT testbed requires certain considerations. Difference pressure measurements must meet high requirements in terms of sensitivity, noise, offset and gain stability. Pressure drop along the nasal cavity is in the range of 300 Pascal for healthy subjects but may exceed several times in subjects with respiratory obstruction. On the other hand, comparison with CFD requests a resolution in the single digit Pascal range and below. Therefor a high dynamic range of the sensor and data acquisition system is required.
The selection of the test point is determined according fluidic interesting places like before and after bifurcations, in strong bending or near an ostium. Additive manufacturing enables to implement fine curved tubes in the bone substitute to reach places in the model who normally are not accessible for pressure measurements. In the design of the in-bone tubes, the process of cleaning after additive manufacturing plays a dominant role. To find geometrical limits we also did calculation about the distortion of the signal due to connecting tubes (fluid or air filled).
Design of the breathing simulator: The main arguments to choose an axial Francis pumping turbine instead of a conventional piston pump are: size and costs; enabling of steady state flow; in combination with a changeover valve inspiration and expiration is realized with the same sense of rotation of the pump; various breathing contours and protocols respectively are possible by controlling the speed of the pump turbine. Special control of the valve allows also asymmetric breathing, as well as cough.
The entries of the model are equipped with additional pressure sensor as well as with high-resolution mass flow meter (Sensirion SFM3300) to measure the Impedance of the model. Loop control circuit that drives the pump turbine is able to combine pressure and flow control and may address specified constant values for steady state operation as well as individual breathing pattern that recorded from subjects with a standard Rhino manometer.

# Electroporation of Cell-seeded Electrospun Fiber Mats for Cryopreservation

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We have recently reported on the high practical utility of using electroporation of clinically relevant cells with sugars for their xeno-free cryopreservation in suspension. This paper extends our earlier approach to in situ electroporating attached cells for their robust cryopreservation on artificial scaffolds. Using CAD modelling, a two-electrode setup has been designed and in-house constructed allowing for simultaneous electroporation in multi-well cell culture plates. Blend electrospinning process has been optimized in order to manufacture porous fibrous mats made of polycaprolactone (PCL, 100 mg/ml) and polylactide (PLA, 50 mg/ml) with a thickness of 100 µm. Chinese hamster ovary (CHO) cells were grown and directly electroporated in nanofibrous blend electrospun fiber mats. An electric pulse was applied in the presence of propidium iodide and CellTracker Green to determine viable permeabilized cell counts using fluorescence microscopy. Cell recovery was evaluated using metabolic MTS assay 24 h post-electroporation. Electric field intensity and distribution within a 3D reconstructed fiber mat was simulated and visualized using COMSOL software. The results demonstrate that with developed setup it is feasible to electroporate around 80% of attached cells with 80% viability after electroporation when electric field strength was 1.7 kV/cm. COMSOL simu-lations showed local increases of electric field at intersection points of numerous fibers which may in part contribute to the observed drop in cell viability post-electroporation. Future studies anticipate implementation of the developed approach in effective biopreservation of stem cells on electrospun fiber mats as a model of tissue-engineered constructs.

# EMC Challenges

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EMC (Electromagnetic compatibility) is the ability of electrical device or system to work as intended in their electromagnetic environment. EMC testing covers two types of testing. Emission testing covers measurements of unwanted emissions emitted from the electrical device. Immunity testing covers several immunity tests which simulate real phenomena in a real life. Some of them have continuous character, some with transient character.
Nowadays, Electromagnetic (EMC) requirements are becoming more and more extensive. Electronic devices are becoming more comprehensive and more complicated in terms of features, usage of special accessories and usage of RF modules. If we combine comprehensive device, extensive requirements together with medical device, the challenge for compliance become even more complex.
New standard includes safety aspect with regarding to electromagnetic disturbances and requires manufacturers' different approach for insurance of patient and operator safety. Main focus of the manufacturer shall be done prior to the testing procedure. Test plan should be based on the risk analysis procedure, knowledge of the medical equipment or device, and must contain all information needed for the test procedure. Test plan shall be provided to the test laboratory prior to the testing.
Medical EMC standard divides medical devices into three different groups depending on the intended environment – HOME, PROFESSIONAL or even SPECIAL. Manufacturer should know for which environment medical device is intended. Immunity test levels for professional environment are lower as for HOME environment because it is more controlled as HOME environment. Due to the fact that EMC testing does not cover all possible EMC phenomena, manufacturer should consider if additional tests or tests with higher test levels are needed to ensure patient and operator safety.

# Establishment of a Multimodal Imaging Pipeline to track the course of cervical to cardiac Vagus Nerve

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Introduction: Heart transplantation is the gold standard treatment of patients with end-stage heart failure. However, patients suffer from negative side-effects of cardiac denervation after heart transplantation, such as sympathico-vagal imbalance at rest and insufficient chronotropic response during exercise1.
Within this project, we are addressing this clinical problem by first mapping the anatomy of the cardiac Vagus Nerve to establish a multimodal imaging pipeline to enable selective stimulation of the cardiac VN allowing for restoration of the cardio-vagal activity.
Four different imaging modalities, i.e. coherent anti-Stokes Raman scattering (CARS)2, optical coherent tomography (OCT)3, micro-computed tomography (µCT)4, and high-resolution episcopic microscopy (HREM)5 were used to provide essential 3D- information of the Vagus Nerve on anatomical, biochemical and histological level for development of a regenerative neural interface of the cardiac VN.
Material and Methods: Cervical Vagus Nerve (CVN) and subsequent cardiac branches were carefully isolated from the cadavers of New-Zeeland female rabbits (n= 6) and a female sheep (n=1). Further cervical and cardiac VN samples were obtained from human cadavers (n=3) and mini-pigs (n= 2). VN samples were first imaged using CARS2 microscopy and OCT3, which provide access to detailed information about tissue structure and molecular composition in a fast, label-free manner. Vago-topographical relevant information was obtained after fixation of the VN samples and scanning with contrast-enhanced µCT4 and HREM5. Based on the data obtained, a 3D model from the cervical level to the cardiac branch of VN was rendered.
Results: Our Multimodal Imaging Pipeline provides anatomically and morphologically relevant information of the Vagus Nerve, such as the course of single fascicles from cardiac branches up to CVN as well as their main features, such as diameter, myelination, fascicle number, fascicle area, internal branching, and twisting. Inter-species comparisons showed that the pig model was closest to humans, for example in respect to size and diameter of the VN. However, our study approach was the first one that was mainly focusing on mapping the course of the CVN down to the cardiac branches to create an anatomical model for selective stimulation of the cardiac VN. Anatomical inter-species differences, such as the course of the CVN down to the heart, should be taken into account with regard to translational research for human medicine.
Conclusions: This imaging pipeline provides anatomical and structural information for selective cardiac Vagus Nerve Stimulation to support the development of a novel, cardiac neuroprosthesis for HTx patients.

# Estimation of Blood Velocity from Cardiac Angiography

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Atherosclerosis is a frequent disease in developed countries. Any vessels' morphological impairments lead to blood flow changes. Even if vessels' hemodynamic patterns extraction from X-ray fluoroscopic angiography has stimulated many scientists for 60 years, there is not a robust method to be im-plemented into angiography software to be used in daily clinics such as in the catheterism laboratories.
A new algorithm is implemented into a graphical user interface for estimating blood velocity of the vessel's segments selected from coronary monoplane angiography. The method is not invasive except from the medical imaging ac-quisition.The method includes the detection of the absolute vessel length, the blood transit time and hence, velocity estimation for a vessel segmentfrom 20 patients.
The validation is done using the measurements from the medical scientific literature. A further validation with a blood vessel phantom is considered.

# Ethylene glycol improves cryopreservation of cell-seeded electrospun scaffolds in cryobags

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Cryopreservation of functional three-dimensional tissue-engineered constructs (TECs) is an inevitable step in ensuring their on-demand availability for clinical applications. Currently used protocols for TECs cryopreservation would greatly benefit from implementing efficient technological steps assuring improved heat and mass transfer, low toxicity and high cell cryoprotection. Therefore, we developed and validated an integral approach based on “in air” freezing in cryobags, optimization of thawing procedure and freezing solutions for efficient cryopreservation of cell-seeded electrospun scaffolds. Porous scaffolds were produced from polycarpolactone and polylactic acid (ratio 2:1) using blend electrospinning under previously optimized process parameters. The scaffolds (diameter 16 mm, thickness 100 um) were UV sterilized and seeded with human primary osteogenic sarcoma cell line SAOS-2 according to a modified protocol yielding homogeneous cell distribution. On day 3 of cultivation, the scaffolds were loaded for 10 min either using 10% (v/v) dimethyl sulfoxide (DMSO) or ethylene glycol (EG), and their combination with 0.3 M sucrose and frozen in polypropylene/polyethylene in-house made cryobags. For sucrose containing CPA cocktails, cell pretreatment with 0.1 M sucrose 24 h before freezing was also evaluated. Cell-seeded scaffolds were frozen using 1 K/min cooling rate down to -100°C in a Planer programmable freezer. The samples were stored at -140°C for 7 days and thawed in two steps using water bath and pre-warmed culture medium. Heat transfer during thawing was simulated using ANSYS software. On day 1, 3 and 7 before freezing and after thawing, functionality testing was performed using live-dead as well as metabolic activity assays, respectively. In addition, mechanical properties of cell-free scaffolds were analyzed using an Instron machine. Preservation of cell-cell and cell-biomaterial interactions was evaluated using scanning electron and confocal laser scanning microscopy. Mechanical testing revealed that our cryopreservation approach does not affect the properties of unseeded scaffolds. Both microscopic techniques showed the preservation of cellular integrity, cell-scaffold and cell-cell interaction post-thaw independently of the CPAs used. Quantification of the viability data demonstrated significantly higher cryoprotective effect of EG as compared to DMSO in combination with sucrose in the freezing solution. The results on metabolic activity of cells after thawing correlated with viability data. In summary, our work suggests that using controlled cryopreservation steps and EG as a non-toxic CPA, efficient cryopreservation of TECs in cryobags becomes feasible.

# Evaluating the role of pH changes in lesion development during conventional and high-frequency irreversible electroporation

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Introduction: For years, it has been well known that electrochemical effects play a role in lesion development during non-thermal ablation with irreversible electroporation (IRE), and modified waveforms have been introduced that maximize ablation volumes by intentionally eliciting electrolytic byproducts after IRE treatment. However, in certain electroporation-based applications (e.g. electrofusion) or ablations in sensitive organs (e.g. brain), deviations from physiological pH can cause unwanted side effects such as direct tissue injury, vasodilation, and increased respiration. High-frequency irreversible electroporation (H-FIRE) – which distributes electrical energy among short pulses (~1 µs) of alternating polarity – has been introduced to address procedural limitations of IRE. While pulses of alternating polarity limit production of electrochemical waste for reversible electroporation therapies, there is no established relationship between IRE/H-FIRE waveforms and electrolytic tissue changes. Here, we utilize collagen hydrogels and tissue phantoms to investigate pH changes during IRE and H-FIRE.
Methods: Malignant astrocytes were suspended in type I rat tail collagen and incubated for 24 hours prior to treatment. H-FIRE pulses (99 bursts, 800 V) with widths of either 2 or 10 µs (energized time = 100 µs/s) and interpulse delays ranging from 1 µs to 10 ms, and IRE pulses (99 pulses, 800V, 100 µs) were delivered via needle electrodes. One day after treatment, a live/dead stain was introduced and confocal microscopy was used to quantify ablations. Concurrently, agar tissue phantoms were created and incubated with bromothymol blue before pulsing. After treatment as above, photographs were captured with a CCD camera and the area of pH change was quantified.
Results: H-FIRE waveforms resulted in significantly reduced areas of pH change versus IRE ($p = 0.006$). 2 µs pulse widths yielded lower ablation areas ($p < 0.0001$) but similar areas of pH change ($p = 0.5515$) in comparison to 10 µs pulses. The effect of delay on the ablation area was obscure, but increasing delays amplified pH changes. IRE treatment produced increases in cathodic acidity and anodic basicity while H-FIRE treatments caused a slightly basic shift at both electrodes.
Discussion: These data offer insight into electrochemical byproducts resulting from treatment with IRE and H-FIRE. Reduced pH changes with H-FIRE treatments indicate that shorter bipolar pulses may be preferable for certain applications. Additionally, specific electrochemical signatures could at least partially account for different cell death dynamics, immune activation, and ablation efficiency between IRE/H-FIRE.

# Evaluation of 3D printed C1 and C2 model for use in a Cervical Fixation Experiment

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Abstract. Posterior fixation of C1 and C2 vertebra is a technique for restoring the stability of the C1 and C2 joint. Normally, this operation is done by placing one pair of screws at the lateral mass of C1 and other pairs at either the pedicle or the laminar of C2. After that, a stabilizing plate is attached to the screw head. Thus, the surgeon needs to drill holes into the vertebra with the risk of damaging the spinal cord or blood vessel. In order to reduce risk during the operation, the 3D print drill guide is being proposed as a navigation tool. Still, an experiment to compare normal free-hand operation and a drill guide operation requires multiple samples of the same subject. Therefore, this experiment proposes and evaluates the use of the FDM 3D printed model as a substitute for cadaver. The 3D file of C1 and C2 are reconstruct-ed from the Dicom file of 1 mm slice thickness and increment. 20 C1 and 40 C2 models were 3D printed using ABS materials. Then, they were 3D scans and measures for the error in the shape and size of the drill guide attachment area. The results show that there is less than 1mm in average error and standard deviation in the observed areas for both C1 and C2. The author concludes that the accuracy of the 3D printed model sufficient for use in future drill guide experiments.

# Evaluation of dZ/dt complex subtypes vs ensemble averaging method for estimation of Left Ventricular Ejection Time from ICG recording

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Impedance cardiography (ICG) was discovered nearly half a century ago, being proposed as noninvasive monitoring method for estimation of several hemodynamics parameter. Despite of nearly 5 decades of clinical research and use there is still certain controversy about its performance when estimating Left Ventricular Ejection Time (LVET). This work present a comparison between us-ing the different ICG subtype waveform and the ensemble averaged (EA) method to calculate the LVET. The ICG has been recorded from four volunteers, and the LVET parameter has been calculated using the two approaches. The result shows that each volunteer have different percentage of subtypes, and the mean relative error between the two approaches for estimation of LVET varied between 0.62 to 2.9% with an average mean absolute percentage error of 18,02% ranging be-tween 13.82 to 18.42 %.

# Evaluation of Embeddings in Medication Domain for Spanish Language Using Joint Natural Language Understanding

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Word embeddings have been widely used in Natural Language Processing as the input to neural networks. Such word embeddings can help in the understanding of the final objective and the keywords in a sentence. As such, in this work, we study the impact of different word embeddings trained with general and specific corpora using Joint Natural Language Understanding in a Spanish medication domain. We generate data using templates for training the model. The model is used for intent detection and slot-filling. We compare word2vec and fastText as word embeddings and ELMo and BERT as language models. We use three different corpora to train the embeddings: the training data generated for this scenario, the Spanish Wikipedia as general domain and the Spanish drug database as specialized data. The best result was obtained with word2vec continuous bag of words model learned with Spanish Wikipedia, obtaining a 71.77?-score for intent detection, an intent accuracy of 69.37% and a 74.36?-score for slot-filling.

# Evaluation of Interhemispheric Synchronization during Hemodynamic Oscillation in Acute Stroke Patients

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In stroke, vascular pathology is related to the remodeling of the neurovascular and profound change of capillary flow pattern. The cerebral autoregulation (CA) is hypothesized to be damaged by these processes. Thus, stroke may cause the imbalance in synchronization of hemodynamic oscillation within two hemispheres. Among various neuroimaging techniques, near-infrared spectroscopy (NIRS) is a promising neuro-imaging technique to explore the changes of inter-oscillatory synchronization in both resting and motor task conditions. The aims of this study was to evaluate the interhemispheric synchronization during hemodynamic oscillation in acute stroke patients.

A twenty-channel NIRS system was used to measure the concentration of hemoglobin at prefrontal cortex (PFC), supplementary motor area (SMA) and primary motor cortex (M1) in both hemispheres. The measurement in resting state and during motor task were conducted for acute unilateral stroke patients at day 7th and day 14th after stroke onset as well as normal subjects. In resting state condition, subjects were asked to sit comfortably with minimize movement for 5 minutes. In addition to magnitude coherence function, the phase coherence (PC) of NIRS data was utilized to estimate the phase synchronization of both hemispheres. Our data showed that the PC value in 14th day post stroke has major lower than those of 7th day and healthy control. In motor task condition, subjects were asked to perform the finger taping in a self-pace fashion using their affected index finger and middle finger alternatively. The tasks were executed at 10 repetitions of 10-second active followed by 20-second of resting. We observed that the oxy-hemoglobin response time to the motor task in stroke patients was delayed than that of normal subjects. However, there was no significant difference between stroke subjects at day 7th and day 14th.

In conclusion, we examined the cerebral autoregulation and neuron activity in acute unilateral stroke patients at two different times and normal control group. Our preliminary results indicate that interhemispheric synchronization after stroke onset in different timeline might reflect the effects of brain neuron damage and response to the event-related optical signal.

# Evaluation of medical training courses satisfaction: qualitative analysis and Analytic Hierarchy Process

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The implementation of the training courses is remarkable in the field of education, in order to analyze and observe individual's perception of the experience. Aim of this work is the combination of two methods, the Likert scale and the Analytic Hierarchy Process (AHP), to evaluate the quality of the training activities offered at Centre of Biotechnology of the National Hospital A.O.R.N. "A. Cardarelli" of Naples to improve its service. In particular, through the application of the AHP we get a hierarchy of needs but not information about user satisfaction, which is obtained with Likert scale. The synergistic application of both methods provided the necessary information to improve the service quality, allowing to identify the most valuable service features and, in case, improve them in order to meet users' satisfaction. However, a continuous collection of users' opinions is necessary.

# Evaluation of Surface Hardness of Biocompatible Material using Digital Microscope Image Analysis

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The most frequently used method for hardness testing is the progressive loading test. This test measures surface hardness and requires direct measurement of the indentation's depth. However, the diameter of the impression left by an indent can also be used to determine surface hardness. The authors designed a method and have custom-written a program for measuring and evaluating surface hardness using a digital microscope and digital microscopic image analysis. The proposed procedure and software are based on the calculation of an impression's diameter left by an indent from digital microscopic images. The evaluation procedure and the software were tested on Ti and TiN samples of biocompatible surfaces. Measurements demonstrated that the calculated hardness results were largely similar in five different operations for measuring the sample. As a result, it seems that evaluation using surface hardness measured by three test operations appears to be sufficient. The new software and procedures proposed allows for the evaluation of surface hardness in a wide range of metal surfaces, while providing credible results. The advantage of this design is the possibility of using existing cheap systems, which can create an indenter imprint, but do not have the ability to directly determine the hardness. The disadvantage of our solution is the need to use a microscope, but the price of electronic microscopes is very low today and they are commonly available on the market.

# Evaluation of Thermal Properties of Ex Vivo Kidney up to Ablative Temperatures

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Thermal ablative techniques have been used in kidney tumour treatments; these treatments use electromagnetic energy to increase the temperature of the target tissue in order to destroy it. Dielectric and thermal properties influence the deposition of electromagnetic energy and the heat distribution into the tissue, respectively. Accurate knowledge of dielectric and thermal properties permits accurate modelling of the therapeutic results. Extensive research has been conducted on dielectric property characterisation of tis-sue, while significantly less data are available in literature on thermal property characterisation. The aim of this study is to experimentally investigate the kidney thermal properties in ex vivo ovine models (n=4) in a temperature range from room to ablative temperatures (95-96 ºC). Results show changes in thermal properties at temperatures approaching the water transition to gas, i.e. above 95 ºC.

# Experimental and computational study on estimation of wall viscoelasticity of PDMS artery phantoms

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It has been known that plaque wall with large contents of smooth muscle cell (SMC) were stable and the SMC content affected the viscous nature of arterial wall. Therefore, estimation of viscoelastic characteristics of plaque wall would provide indirect measure of plaque rupture risk.

Artery phantoms were manufactured using polydimethylsiloxane (PDMS), and viscoelastic property of PDMS was controlled by changing mixture ratio of PDMS, curing agent and pure silicone oil. Pulsatile flow was generated using a mock circulation system with a pulsatile blood pump, and pressure and flow were measured. Pressure and diameter waveforms in the artery phantom were measured to estimate wall viscoelasticity. Elasticity was assessed using diameter distention over the pulse pressure, and viscous nature was evaluated using the energy dissipation ratio of pressure-diameter loop and the phase lag between pressure and diameter waveform. Computational analysis of arterial wall motion using a standard linear model was also performed, and parameters of viscoelastic model were determined.

PDMS phantom with 20:1 and 25:1 mixture ratio of resin and curing agent showed viscoelastic wall characteristics similar to those of young and old human carotid artery, respectively. Adding pure silicone oil further softens the silicone elastomer while decreasing viscous nature. Viscoelastic parameters of a standard linear model were determined from the pressure-diameter relationship of PDMS artery models. Computational analysis could simulate the arterial wall motion of various PDMS phantoms under pulsatile pressure.

# Experimental evaluation of physical breast phantoms for 2D and 3D breast x-ray imaging techniques

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Anthropomorphic phantoms are models of real or virtual parts of the body, organ or tissue, represented by tissue-equivalent materials that aim to provide a realistic and accurate representation of their anatomy and properties. The aim of this study is to evaluate experimentally the suitability of 3D printed materials in the production of both, physical breast phantoms and abnormalities, to be used in optimization tasks in breast imaging. For this purpose, we designed three software breast models, composed of skin, duct tree, adipose compartments and lesions. Subsequently, they were printed by using two 3D printing technologies and different printing materials, which were previously studied in details. The physical phantoms were scanned at a mammography machine, which allows 2D and 3D mammography (tomosynthesis) modes. The images were evaluated from an experienced radiologist. The results showed that tomosynthesis images are characterized with better realism compared to 2D mammography images. Next step is improvement in the printing quality of tumour formations as well as quantitative evaluation of the obtained results.

# Experimental Validation of Conductivity Tensor Imaging (CTI) using a Phantom with Giant Vesicle Suspensions

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Electrical conductivity of a biological tissue at low frequencies can be approximately expressed as a tensor. Noting that cross-sectional imaging of a low-frequency conductivity tensor distribution inside the human body has wide clinical applications of many bio-electromagnetic phenomena, a new conductivity tensor imaging (CTI) technique has been lately developed using an MRI scanner. Since the technique is based on a few assumptions between mobility and diffusivity of ions and water molecules, thorough validations are needed before applying it to clinical studies. We designed two conductivity phantoms with three different compartments. The compartments were filled with electrolytes and/or giant vesicle suspensions. The giant vesicles were cell-like materials with thin insulating membranes. We controlled viscosity of the electrolytes and the giant vesicle suspensions to change ion mobility and therefore conductivity values. The conductivity values of the electrolytes and giant vesicle suspensions were measured using an impedance analyzer before CTI experiments. A 9.4 T research MRI scanner was used to reconstruct conductivity tensor images of the phantoms. The CTI technique successfully reconstructed conductivity tensor images of the phantoms with a voxel size of 0.5 * 0.5 * 0.5 mm3. The relative L2 errors between the conductivity values measured by the impedance analyzer and reconstructed by the MRI scanner was between 1.1 and 11.48 %. The accuracy of the new CTI technique was estimated to be high enough for most clinical applications. Future studies of animal models and human subjects should be pursued to show the clinical efficacy of the CTI technique.

# Facial skin temperature during deception

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Measuring peripheral tissue temperature is a well known methodology to assess different physiological states of the body. It is also widely used in clinical environment. On the other hand, measuring facial skin temperature for the purposes of identification of psychological state of a person is not so common. This article will provide information on non-contact measurements of facial temperature in comparison with established psychophysiological measuring systems (electrodermal activity and hearth rate) for 24 participants. Experiment consisted of two different states of cognitive loads which were expressed through narration of a true and an untrue stories. During narration, on selected regions of interest (ROI), subjects were monitored using thermographic camera. Although the results did not show statistically significant differences between the true and untrue story for facial thermal measurement (in inter-person and intra-person comparison), some differences did appear. Results of this study showed, critical approach using information on camera's accuracy, human skin properties and other technical concerns) is needed when using facial temperature measurements with thermographic camera for a reliable evaluation of different psychological states or loads.

# Finite Element evaluation of the influence of extracellular matrix in electric field distribution in inhomogeneous environment

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This abstract presents the study of the effect of the electrical characteristics of the extracellular environment on the electric field distribution in the electroporation conditions by means of the Finite Element simulation. In particular, it shows how the inhomogeneities at electrical characteristic point of view can condition the electric field distribution around the cells with respect to a homogeneous media using the same boundary conditions. This is the case of in vitro experiments that include the fibrous extracellular matrix compared with cell electroporated in suspension. In particular, it is highlighted how an accurate simulation of the extracellular environment can more accurately predict the outcome of the cell membrane permeabilization due to the application of the electric field.

In fact, it is known that the distribution of the electric field in a non-homogeneous material changes with respect to the one obtained in a model with homogeneous electrical properties. The distribution of the electric field can be assessed by finite element models (FEM). In this case, the electric field was simulated in a region where conductivity can be considered homogeneous or non-homogeneous. The electric field within the analyzed volume is generated by applying two different potentials to two parallel faces of the region in order to obtain an electric field with intensity equal to 1000 V/cm in the homogeneous model. In the homogeneous model the simulated region is described with a homogeneous conductivity; whereas in the non-homogeneous model, the simulated region includes inhomogeneity described as circular area with a discontinuity in electric conductivity. Then, a two materials region is simulated. The electrical properties are those characteristic of the materials used in the experimental validation and in particular between 0.2 Sm-1 and 1.3 Sm-1. The numerical model assesses the intensity of the field in the examined region containing areas of non-homogeneity and compares it with the field obtained in the same areas under conditions of homogeneity. In particular, the electric field distribution obtained shows an increase in the intensity of the field near the areas with internal conductivity highlighted by the circles.

The difference in this case is given by the presence of a material whose lower electrical conductivity allows the local electric field to rise. This local effect could improve the electroporation efficiency for the same applied electric field. The data obtained showed that the cellular organization and the presence of extracellular matrix can modulate the local electrical properties influencing the efficiency of electroporation.

# Finite element simulation of the rupture of tendons

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Abstract. In the case of the transplant surgery of ligaments, it is common prac-tice to use tissues from other parts of the body with similar properties. Although they have similarities, there are some distinct properties, some of which may have serious effects on the success of the operation. These properties can be measured and compared to each other so that the surgeon can choose the best option.

The goal of the present research is to validate the measured data of the tensile tests of tendons and the theoretical results on fibrous materials, with special re-gard to the rupture phase. The mechanical properties of the tendon vary signifi-cantly, so in the case of a static tensile test, the material's rupture is not instanta-neous, but consisting of multiple steps, as the different groups of fibres are tear-ing. The main objective is to model this behavior and to compare it with previous results.

Our model is based on the results of in-vitro measurements and fibre bundle models describing the behavior of compound fibrous materials. Then by using fi-nite element simulation, the realistic process of the rupture is approximated by a bilinear debonding process. The fibres' mechanical properties can be set with dis-tribution functions, representing the real variance of the tissue. In the method used, the tensile strength of the fibres is represented by contact stiffness, like stat-ic friction, practically separating the fibrous body examined into two parts. With the proper modelling of the fibrous structure's stochastic behavior, it is possible to validate the previous in-vitro results. The method can be used in other areas, such as the examination of ligaments possessing similar properties, or in the de-scription of the behavior of fibre-reinforced composites.

# First array of Helium 4 Optically Pumped Magnetometers (He OPM) for on scalp MagnetoEncephaloGraphy (MEG) at ambient temperature

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SQUID sensors have been extensively used for biomagnetic recordings during the last decades and are still the reference sensors in this domain. Emerging new technologies such as high temperature SQUID or alkali optically pumped magnetometers (OPM) have been recently applied for recording brain magnetic fields (Boto et al, 2018; Pfeiffer et al, 2019). We work on another kind of OPM, based on helium 4 gas. These 4He OPM present several advantages. Helium 4 gas requires any heating or cooling, three axis measurement of magnetic field is possible, they have a large bandwidth (from DC to 2 kHz) and they are operated in closed loop. This operating mode consists in continuous cancelling of the three components of the magnetic field at each sensor by applying an opposite compensation field with tri-axial Helmholtz coils. Therefore, an optimal stability of the transfer function and a high dynamic range (up to 200 nT) of the sensor are guaranteed and no additional nulling field coils inside the magnetic shielded room is required for operating these sensors. In addition, 4He OPM can be placed directly over the scalp, without thermal insulation or discomfort for the patient, reducing the brain source - sensor distance. These characteristics make 4He OPM a very good candidate for MagnetoEncephaloGraphy (MEG). In the last years, a first proof of concept of brain and cardiac magnetic fields recordings have been reported (Morales et al 2018, Labyt et al, 2019). These first recordings were performed with sensors whose intrinsic noise was limited to 200 fT/Hz1/2. Recently, this noise has been largely improved to less than 50 fT/Hz1/2 and the 1/f noise rise in low frequencies has been also reduced. The sensor is packaged in a 3D printed mount made from a photosensitive resin, with a footprint of 2 x 2 cm2. A first array of four 4He OPM has been built and the first measurements revealed that collective closed-loop operation was possible with the sensors set side-by-side. Cross talk matrix coefficients were in close agreement with the theoretical predictions from Biot-Savart law . This first 4He OPM array offers a new alternative for on scalp multichannel MEG recordings. First MEG recordings in healthy subjects and epileptic patients are already planned from spring 2020 through several collaborations with hospitals.

# First steps toward automated classification of impedance cardiography dZ/dt complex subtypes

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The detection of the characteristic points of the complex of the impedance cardiography (ICG) is a crucial step for the calculation of hemodynamical parameters such as left ventricular ejection time, stroke volume and cardiac output. Extracting the characteristic points from the dZ/dt ICG signal is usually affected by the variability of the ICG complex and assembling average is the method of choice to smooth out such variability. To avoid the use of assembling average that might filter out information relevant for the hemodynamic assessment requires extracting the characteristics points from the different subtypes of the ICG complex. Thus, as a first step to automatize the extraction parameters, the aim of this work is to detect automatically the kind of dZ/dt complex present in the ICG signal. To do so artificial neural networks have been designed with two different configurations for pattern matching (PRANN) and tested to identify the 6 different ICG complex subtypes. One of the configurations implements a 6-classes classifier and the other implemented the divide and conquer approach classifying in two stages. The data sets used in the training, validation and testing process of the PRANNs includes a matrix of 1 s windows of the ICG complexes from the 60 seconds long recordings of dZ/dt signal for each of the 4 healthy male volunteers. A total of 240 s. As a result, the divide and conquer approach improve the overall classification obtained with the one stage approach on +26% reaching and average classification ration of 82%.

# Four-point impedance as a biomarker for bleeding during cochlear implantation

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The preservation of cochlear structures and natural hearing has become the standard of care for cochlear implantation (CI). Currently in cochlear implant surgery, there is no method for real-time detection of cochlear injury, such as the infiltration of blood from the lateral wall if damaged. Blood in the inner ear creates a hostile environment, causes a larger inflammatory response, and may lead to the loss of natural hearing. Four-point impedance (4PI) can be used to distinguish different biological mediums and may be useful to detect intra-cochlear bleeding as it occurs. The aim of this work is to monitor four-point impedance, directly from the intra-cochlear electrodes on the implant, to correlate these measurements with hearing preservation and cochlear injury. Fifty-one adults with some natural acoustic hearing prior to surgery underwent cochlear implantation. Real-time intra-operative monitoring of hearing was undertaken during implantation, and four-point impedance was measured immediately after insertion. Thirteen of these patients had elevated 4PI values and these patients not only lost their natural hearing, but also experienced dizziness in the perioperative period. 4PI was then measured in 13 ears from 9 tri-colour guinea pigs, before and after blood injection into the cochlea. The results showed the 4PI instantaneously increased after blood injection, similar magnitude seen in clinical patients, and remained high, whereas the control ears did not experience this increase. An alternative explanation to elevated 4PI values is the geometry of the cochlea, which has a decreasing diameter from base to apex. 4PI was measured throughout insertion of a clinical cochlear implant into a 3D-printed human cochlear model and the 4PI had a slightly increasing trend as the implant was inserted further in. However, this increase was an order of magnitude too small to explain the clinical results.

# Four-point impedance measurements of blood and its constituents in saline and localisation of blood during cochlear implantation

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Cochlear implants provide a way of hearing for adults and children who experience hearing loss. More recently, cochlear implants are being offered to those with some natural hearing and preserving this hearing during cochlear implantation leads to better outcomes for the patient. Unfortunately, more than half of these patients lose this hearing after implant insertion, and the cause of this is still not well known. A potential reason for this loss could be due to intra-operative trauma during cochlear implantation, leading to blood entering the cochlea and causing a hostile environment. Therefore, a method for detecting blood in the cochlea may open therapeutic avenues during and after implantation. Four-point impedance can offer information regarding the bulk resistance of the immediate fluid/tissue surrounding the electrode. It can distinguish between bodily fluids, such as blood compared to perilymph, the conductive fluid in the cochlea. Here we present four-point impedance measurements from different concentrations of whole blood, red blood cells, and plasma in saline, which is similar to the conductive fluid in the cochlea. Two systems were used to measure four-point impedance. The first was a commercially available device that can measure both the reactance and resistance component of impedance, providing the magnitude and phase angle of the sample. The second system used the impedance measuring capabilities of a cochlear implant, which can only measure the resistance of the sample. The results showed that both systems succeeded in differentiating concentrations of blood, as little as 5%, in saline, and that resistance alone was sensitive enough for this purpose. Lastly, an in-vitro study was conducted where four-point impedance was continuously monitored using a cochlear implant, during its insertion into a 3D printed cochlear model. The model was primed with artificial perilymph followed by an injection of blood after insertion to emulate surgical events. These results demonstrated four-point impedance from a cochlear implant can instantaneously detect the addition of blood in a cochlear structure, magnify the amount of blood, and localise it on the electrode array.

# Fourier Transform vs. Graph Fourier Transform for EEG-Based Emotion Recognition

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Electroencephalogram (EEG)-based feature extraction for emotion recognition is a very challenging task. The vast majority of the feature extraction approaches are based on the frequency characteristics of the EEG signals which are extracted using, e.g., the traditional Fourier Transform approach. Lately, a new approach for processing signals in graph domains, namely Graph Signal Processing (GSP), has provided new means of feature extraction by exploiting the oscillations across the vertices of the graph domains instead of the time oriented oscillations of the signals. In this work we are investigating the effectiveness of a fused feature vector for emotional state recognition comprised both of the Graph Fourier Transform and the traditional Fourier Transform features over the DEAP dataset. Support Vector Machines classifier was used in order to classify the extracted features resulting in over 69% and 68% of classification rates for the arousal and valence dimensions, respectively. The fused feature vector outperformed the single GFT- and FT-based feature vectors revealing the need for feature vector approaches that combine graph- and time-based oscillatory features for emotion recognition from EEG.

# Gait perturbations with the RYSEN body weight support system: A proof of concept study

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Using mechanical perturbations during gait is a common way to assess balance in humans. For rehabilitation training and stability studies, it is important to reliably and safely produce gait perturbations. Body weight support systems, like the RYSEN, offer a safe environment and allow patients to train gait in an early stage of rehabilitation. The aim of this study was to assess whether the RYSEN is also able to apply perturbations for balance assessment during gait. Based on experimental bandwidth evaluation, the fastest expected perturbation with the RYSEN was 300ms. The preferred perturbation from literature is around 150 ms, which results in a step width variability of 5-6 cm. To determine whether long perturbations could be used, a separate experiment without the RYSEN was performed. In this experiment an experimenter manually pulled on a passive spring-rope system connected to the pelvis of a walking subject, in such a way that perturbations of a controlled duration and force could be applied. The experiment showed that even long perturbations of approximately 500 ms perturbation still led to a step width variability of 5 cm, indicating that long perturbations are also viable. In a second experiment the RYSEN was tested, using a 120 kg test dummy, over a range of vertical unloading of 15-60 % body weight; a perturbation duration between 50-500 ms and a perturbation peak force of 5-10 % body weight. We analyzed performance in terms of how well a reference impulse, peak force, and final displacement were achieved. The results showed that the performance of the RYSEN was adequate when the ratio of vertical unloading force to peak perturbation force was 5:1 or larger, which occurred approximately at a vertical unloading force of 30-40 % of body weight for the best force-duration trade off that could achieve the desired impulse of 0.024 %BW*s, which was a force of 8 % BW and 300 ms duration. Below this ratio, small mechanical adjustments to the RYSEN are required to reach the desired perturbation peak force. This is important to note because it is known that around 30% vertical unloading subjects tend to change gait behavior. These preliminary results indicate that the RYSEN could be used for perturbation studies.

# Gene Electrotransfer of Plasmid DNA as an Effective Delivery Approach for Multiple Therapeutic Applications

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Gene therapy has the potential to be utilized as an effective therapeutic approach for a variety of disorders. While there have been some major advances, there are still many issues that need to be resolved. One of the critical aspects to advance the field of gene transfer is controlled delivery to the appropriate target. While viral vectors have dominated the field for quite some time, non-viral gene delivery systems including the use of physical delivery approaches have seen tremendous growth and success. Our group has explored the use of electroporation (gene electrotransfer; (GET)) and have developed several protocols for a variety of tissues. The focus has been to find the correct parameters that deliver the transgene in a manner that yields a reproducible expression pattern with minimal to no adverse effects. Expression of the transgene can be controlled by manipulating the delivery parameters. This control of the expression profile is a key element in developing successful therapeutic applications. One area of focus has been to demonstrate that GET is an effective tool for delivering plasmid DNA to the skin. While use of GET has been effective, we have recently established that the addition of moderate heat (43oC) in combination with GET can significantly enhance delivery. We further evaluated the combination of moderate heating and GET for delivering a DNA vaccine against Hepatitis B Virus. Guinea pigs were injected intradermally with a plasmid encoding Hepatitis B viral surface antigen followed by GET with or without moderate heating. After a prime/boost vaccination, $\alpha$HBSAg serum titers indicated a 12-fold increase in antibody levels up to 30 weeks post-vaccination in those animals receiving GET combined with moderate heating compared to GET alone. In addition, a single dose vaccination generated titers significantly higher than injection of plasmid DNA alone. We also investigated delivering a plasmid encoding Human Factor IX as a protein replacement therapy for treating Hemophilia B. A guinea pig model was also used for this work and elevated Factor IX protein serum levels were detected. In addition to DNA vaccine delivery and protein replacement, GET has also been tested as a potential therapeutic approach for accelerating wound healing or for inducing reperfusion of ischemic tissue. Work has also been focused on developing an immune gene transfer approach for the treatment of cancer. This approach has now been successfully tested in multiple clinical trials.

# Graphene- and Graphite-based Polyorganosiloxane Composite Ligaments forSensory Feedback in Upper-Limb Prosthetics

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The hand is a sophisticated enabler of many of our regular daily activities. When it is lost, e.g. due to disease or trauma, it has a significant effect on the amputee's quality of life. Prosthesis users regularly report the desire for more sophisticated prosthesis technologies that provide sensory feedback to the body, and are more intuitive to use. This would lessen the requirement for visual feedback, for instance to determine if enough pressure has been applied to lift an object. Sensory feedback requires sensors that can respond to different stimulation in real-time. Graphene-based composites have many interesting electrical, mechanical and thermal properties, and have a conductivity that changes with applied pressure, movement (e.g. grasping) and temperature stimulation. We have developed a working proof of concept for a low-cost sensory feedback system using graphene-based composites and commercial-off-the-shelf technology. Prototype graphene- and graphite-based composite sensors were fabricated using a polyorganosiloxane matrix, and eight ligaments were mounted onto a reduced scale hand with four moving fingers each with three phalanges. After temperature, pressure and/or movement stimulation, the signal from each sensor was digitized and then characterised by a bespoke algorithm running on a Raspberry Pi to provide real-time electrotactile stimulation 10mA to the body. When identifying between different stimuli combinations, the algorithm has an accuracy score 95%. In this paper, we outline the synthesis of prototype graphene- and graphite-polyorganosiloxane composite sensors, and discuss the classifying algorithm used to discriminate between different combinations of stimuli. We present initial results from our upper-limb prosthesis demonstrator, and outline further developments such as introducing the magnitude of the stimulation into the classifying algorithm, and the direct scalable chemical synthesis of other graphene- and graphite-composite sensors.

# HB-HTA: Evaluation and Prioritization of Medical Equipments - Pilot study

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One of the key issue of health technology management is to evaluate medical equipment lifecycle and to determine the necessity for the equipment replacement in time.
Aim of the study: The main objective of this pilot study is to create an approach for assessment of medical equipments and their prioritizing in the decision-making process concerning their purchase for a medical facility within their replacement on the basis of factors effecting the length of their lifecycle.
Methods: On the basis of discussions with experts in respective fields of expertise (technical, clinical, user-operational), by using multicriteria decision methods, we determined the weights for individual criteria and areas necessary for calculation of the replacement priority index (PI).
Results: Methodological approach was tested in a outpatient helthcare facility specialized in radiodiagnostics. 3 medical equipments were tested while all of them was X-Ray equipments: RTG GE Discovery; RTG DRGEM; Opera 500C, U rameno Polistat – M.
Conclusion: This easy-to-apply methodology procedure may provide healthcare facilities with relevant information necessary for a decision-making process in the field of medical equipment replacement planning and thus to facilitate better investment planning.

# Health Apps: Opportunities and Challenges

Paulo Carvalho
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The current health provision paradigm is acute illness driven, i.e., it focuses itself in handling acute situations. It is believed that the focus should be redirected towards (1) preventive healthcare, mainly by promoting healthy lifestyle changes, and (2) shifting from acute-disease treatment to disease management in NCDs. This requires a completely new approach of health organization, putting the patient in the centre, developing a continuous process of care and shifting the care from a hospital-driven approach to a home-driven (or more generally, a pervasive) approach. Some countries are rapidly moving towards this new paradigm; e.g. in Germany Physicians will be able to prescribe Heath Apps starting in 2020/21.

From the technological point of view, new low cost and accurate solutions for remote patient management are required. Mobile technologies and Apps are excellent enablers for this paradigm shift: globally 66% of the world population has a mobile phone subscription (44% with mobile data), furthermore currently there more than 325 000 health Apps available in App Stores which are downloaded over 410 000 times per hour (3.6 billion downloads in 2017). This poses a huge opportunity, but also some significant risks as most of these Apps might pose significant security, privacy and safety risks. In this talk we will overview some of the most relevant challenges in using Health Apps both for the industry, health provision systems and end-users.

# Health care equipment management with ICT tools in Burundi and Rwanda

Marc Nyssen
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One of the principal elements, contributing to ensure the quality of medical service to the patient in the health system is the management and maintenance of medical equipment. To assist in the development of a country-wide management and follow-up system, guidelines exist and ICT tools are available to be implemented. This presentation focuses on the country-wide developments in two central-African countries who apply similar strategies, with some implementation variants: Rwanda and Burundi. We will therefore give an overview of the guidelines and ICT tools that were applied and explain the implementation strategy that has been defined for both countries. In conclusion we make some recommendations that can be useful for future developments.

# Health Technology Assessment of Laboratory Medicine

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Objective: Recent studies have been sustaining the re-organization and automation of a Laboratory medicine as a challenge for the hospital in terms of costs reduction, turnaround time and workload, human and technological resources optimization, and safety improvement. The purpose of this study was to update and to follow up the results of the HTA evaluation, previously conducted in 2017, assessing the real impact that the re-organization and automation of the Laboratory medicine, has had on Bambino Gesù Children's Hospital, after 9 months from its implementation.
Methods: The previous HTA process was conducted applying the Decision-oriented HTA (Do-HTA) method. , w It is an analytical instrument, which involves the integration of the EUnetHTA CoreModel and the Analytic Hierarchy Process, for the identification of the main evaluation criteria of a decision problem and the attribution of their weights and performances Scores. Twenty-one professionals have been involved to define tender specifications related to the adaptation works of the new dedicated rooms and to the automatic technologies and organizational solutions for the new Laboratory Medicine
After an accurate analysis, evaluating the two manufactures 'companies proposals, with respect to all evaluation criteria defined (safety, clinical efficacy, cost, organization & technical criteria), the hospital's decision-makers decided to implement the technological solution that resulted, in terms of performances score, slightly higher (2.5%) than the other. After 9 months from its implementation, it was followed- up, measuring the real impact of the technology solution use after 6 and 9 months from its implementation, with respect to the same evaluation criteria elaborated in the HTA process. More specifically, a detailed analysis on the impact that the automation has had on the hospital organization was carried out taking into account the processes management, the productivity and the quality of the processes, the risk management and the safety.
Results: Preliminary results confirmed the HTA results, highlighting the benefits previously evaluated especially from clinical and organization points of view.
Conclusions: Monitoring and following-up the Laboratory Analysis automation impact on hospital context over time is pivotal to highlight the importance of conducting an HTA study before the implementation of those health technologies that have significant organizational and economic impact.

# Health Technology Assessment of Medical Devices in the Global Health Context

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The diffusion of medical devices is expanding at an astonishing rate. This created an unprecedented global need for well-trained experts who can help healthcare systems to assess them. However, the wide majority of the global population is still diagnosed and treated in low-income settings, in low- or middle income countries (LMICs). In LMICs, the need for HTA is even higher, given the limited and scarce budget for healthcare, the chronic lack of specialised personnel, the quasi-absence of prevention programmes, the inadequacy of medical devices, which are mainly designed for huge-income countries and rich healthcare setting. The International Federation for Medical and Biological Engineering (IFMBE), NGO in official relations with the United Nations World Health Organisation (WHO), has been very active in promoting the role of the biomedical engineer in Health Technology Assessment (HTA). The University of Warwick had supported the IFMBE Health Technology Assessment Division (HTAD), performing field studies in Africa, promoting studies, projects and activities to foster the growth of HTA of medical devices in global contexts. This included summer schools, training material, an HTA eLearning platform and hosting workshops for the preparation of HTA guidelines for medical devices. This article describes the work done in the past years.

# Health Technology in the Prevention and Management of Diabetes

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In the management of healthcare in our societies, especially one with an aging population, the proactive approach of "prevention is better than cure" is always regarded as superior. Even though the responsibility of disease prevention and general well-being lies in the hands of individuals, there has been increasing efforts from governments and institutions to promote healthcare and improving health literacy amongst their citizens and stakeholders. There are good reasons for this trend. An obvious one will be the ever-rising healthcare cost and its increasing weightage in government spending. While there are several approaches towards improving health awareness, they can generally be grouped under efforts for education and compliance. Education of public on health and lifestyle is often the first step towards health awareness, but it is ineffective if the public is not convinced to adopt a heathier lifestyle. Based on the case study of how Singapore declares war on diabetes, and the multi-faceted approach taken through government intervention, technology and communication, we will try to understand how a country tries to improve health awareness for prevention and management of diabetes. An important aspect of prevention is public health promotion. Mobile communication technology, wearable devices and internet play crucial role in empowering individuals with health literacy. In particular, the extraordinary growth of mobile phones, fast growth of mobile networks, and technology. The use of information and communication technologies for health can transform medical and public health practice. For instance, the monitoring and motivation of daily physical activities and healthy food consummation. Diabetes Prevention Program study has shown that 30 minutes a day of moderate physical activity along with a 5 to 10% weight loss can produced a 58% reduction in diabetes. Development and use of technology in early screening, detection and diabetes management can certainly prevent onset of complications such as cardiovascular diseases, blindness and limb amputation.

# Health Trend Monitoring by Embedded Sensor Systems for Health

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Embedded Sensor Systems for Health (ESS-H) is a research profile where academia collaborates with healthcare organizations and industry with a focus to develop sensor systems for future healthcare. The overarching aim is that health monitoring should be possible to perform anytime, anywhere, using sensor systems for health monitoring and monitoring of humans.
A system-wide holistic approach is used, including end-user involvement and close collaboration with companies. This way, user relevance and user acceptance, together with industrial interests, are assured throughout the system design and implementation. The research results have a high potential to become adapted, deployed, and commercialized through this approach.
The work in ESS-H is focused within five subprojects:
Microwave technology systems, where microwaves are used to measure human tissue, with the aim to detect tumors and strokes.
Systems for prevention and monitoring of chronic diseases, where multiple physiological parameters are monitored, and the data is aggregated in order to diagnose and follow health trends. This also includes safe and secure communication, data aggregation and decision support.
Vehicle and driver monitoring systems, where the driver environment detects the status of the driver, e.g., regarding alcohol level, attention, and sleepiness.
Motion control and analysis, fall prevention, where motion parameters are captured and analyzed, e.g., in order to detect risk of falling or physical activity level.
IT-platform for monitoring health at home, where a platform for reliable acquisition of physiological data as well as management and analysis of this data is provided.

# Heart Rate Variability Analysis for the Stress Relaxation Effects of Oxygen-Light Therapy

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The oxygen-light therapy, which provides mild oxygen gas and LED light to the stressed person, are being popularized for the stress relaxation. Although commercial products for the therapy are available in the market, the effect of them is not clear. In this presentation, we illustrate the experimental results to show that the therapy relaxes the user's stress.

In the experiment approved by the Institutional Review Board of Dong-Eui University in Korea(DIRB-201803-HR-E-26), healthy 148 adults(72 males and 76 females) with mean age 29.5 years and range 18-60 years volunteered to participate. All participants had not ophthalmic or mental disease and signed informed consent forms. A commercial product, OxySpa(NF Co., Ltd., Korea) was used to supply the oxygen of concentration 30% and visible lights to the participants. Color of the light was chosen by the participants.

To study physiological effects we acquired the electrocardiograph(ECG) signals of the participants with the BIOPAC MP150(Biopac System Inc., USA). The signals were measured using the bipolar lead with the rate of 250 samples per second, and recorded for 40 minutes with the therapy.

To figure out stress relaxation effect, we analyzed the heart rate variability (HRV) of the signals reflecting the autonomic regulation states of the participants. We extracted the R-peaks of the signals by the Pan-Tompkins algorithm and calculated the intervals between the neighboring R-peaks(RRI). We performed the HRV analysis with the features including heart rate, standard deviation of RRI, square root of the mean squared differences of successive RRIs, and power spectra of RRI time series in low and high frequency bands. All features were calculated with data for 5 minutes at every 5 seconds.

We extracted some stress indices including Stress Resistance(SR), Stress Index(SI), Autonomic Balance(AB), and the Baevsky's Stress Index (BSI) from the features, and estimated the increasing or decreasing rates of them during the oxygen-light therapy leading to 0.74, -0.17, 0.35, and -1.3 per minute, respectively. The number of participants whose stress indices got better were 128, 123, 92, and 125 among 148 for SR, SI, AB, and BSI, respectively. We also estimated the time of the therapy required for meaningful stress reduction resulting in 15 minutes.

In conclusion, the experiment showed that the oxygen-light therapy reduced the stress level of participants.

# Heart Rate Variability Calculation Using Heart Periods Measured Between Consecutive Ponset Points

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Heart rate variability (HRV) is a widely used measure to assess emotional arousal and stress level. HRV is a measure of the variation in time between two consecutive heartbeats. If HRV is determined using the ECG signal, the beat-to-beat intervals (duration of heart cycles) are conventionally calculated as the time difference between successive R-peaks. However, the heart cycle begins with atrial depolarization, therefore, the onset of the P-wave (Ponset) is a physiologically more appropriate fiducial point to define heart cycles. This paper investigates how the result of HRV calculation changes if the duration of heart cycles is measured using the onset of P-waves instead of R-peaks. Measurements containing ECG signals recorded in Einthoven II lead and one measurement containing simultaneously recorded intracardiac electrograms and surface ECG signals were used. Our results suggest that HRV values are different depending on whether the onset of P-waves or R-peaks are used as fiducial points.

# High-frequency asymmetric bipolar pulse generator, which enabled first in vivo high-frequency electrochemotherapy

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Currently, high-frequency electroporation is intensely investigated, but limited to a few research groups with custom made prototype electroporators. Previous studies indicated that the advantage of high-frequency electroporation (HF-EP) pulse characteristics might be in reducing muscle contraction and pain sensation during high voltage pulse delivery. Additionally, it is assumed that HF-EP renders electric field distribution in tissue more homogeneous. Therefore, we developed an asymmetric bipolar pulse generator with a maximum voltage of 4 kV, minimum pulse duration 200 ns, with theoretical maximal current 131 A, maximal pulse repetition rate 2 MHz and burst maximal repetition rate 1 MHz, which enables in vivo evaluation of biological effects of HF-EP.

First high-frequency electrochemotherapy (HF-ECT) was performed in vitro, by Scuderi et. al., the authors determined that 2.5-times higher electric field should be delivered in case of HF-ECT to obtain comparable cytotoxicity as with "classical" ECT. The newly developed device enables the translation of HF-ECT also to in vivo, thus in the scope of this study, we compared the effectiveness of "classical" electrochemotherapy (8 pulses, 1300 V/cm voltage-to-distance-ratio, 100 µs pulse duration, 1 Hz) and HF-ECT (100 µs long bursts of bipolar (1-1-1-1) µs pulses, 3250 V/cm voltage-to-distance-ratio , with burst repetition rate 1 Hz). Electric pulses were in both case applied by parallel stainless-steel plate electrodes (distance between the electrodes: 6 mm ) HF-ECT with bleomycin (intratumoral injection, Bleomycin medac, Medac, Wedel, Germany; 5 µg; 40 µL) proved at least as effective as "classical" ECT where 86 % and 50 % of complete responses were observed, respectively. Additionally, preliminary data on HF-ECT with cisplatin (intratumoral injection, Cisplatina Kabi, 1 mg/mL, Fresenius Kabi AG, Bad Homburg, Germany; 40 µg; 40 µl) (n=2) indicated that HF-ECT is as effective as classical ECT, resulting in 100 % of complete responses. Contrary to numerous reports, muscle contractions (measured with a triple axis accelerometer, taped with a micropore tape to the right hind foot during the pulse delivery) were comparable between the two protocols. In the future, the voltage amplitude should be optimized for in vivo HF-ECT, with plate electrodes, which could result in a reduction of muscle contractions.

The developed device operates in accordance with expectations and thus enables the research of still not completely understood effects in the range of poorly investigated µs range of pulse parameters in vivo.

# Holobalance: An ecosystem for managing balance disorders through guiding and persuasive virtual coaching

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Balance disorders involve the inadequate and problematic integration of visual, somatosensory, vestibular information and musculoskeletal function. Probably the most appropriate approach to cope with these disorders (which WHO characterizes as global epidemic) is balance physiotherapy programs. Yet, to this point, there is a total lack of personalized coaching solutions for patients with balance disorders. Bearing in mind the importance of the level of commitment required from these patients to such physiotherapy programs, Holobalance proposes an ecosystem which comprises sensing hardware, intelligent algorithms and cloud services, aiming to monitor, guide and motivate patients to correctly and safely execute their program on a tailored fashion.

Holobalance collects motion and emotional data, generated by wearable sensors, along with clinical profiles and provides guidance on the correct performance of the exercises, delivered by a virtual coach which has the form of a holographic physiotherapist surrogate presented to the user through an augmented reality environment. Motion analysis algorithms, inference mechanisms and behavioral models are deployed on a mixed edge-cloud environment, creating personalized activity and cognitive plans which are meant to maximize the participation of the patient to the program.

While at this point, the main pilot study is running, pre-pilot studies indicate that the Holobalance concept can improve not only the commitment of the patients to the physiotherapy program, but also the quality of the guidance and exercise assessment during the program execution at the patient's home.

# How imaging membrane and cell processes involved in electropermeabilization can improve its development in gene electrotransfer

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The use of electroporation to deliver cytotoxic drugs and nucleic acids in cells and tissues has been successfully developed over the last decade (1). This strategy used in clinics to treat cancers is promising for vaccination and gene therapy. Its safe and efficient use for clinical purposes requires the knowledge of the mechanism underlying molecules electrotransfer. Despite the fact that the pioneering work on electrotransfer was initiated many years ago, the mechanisms underlying DNA electrotransfer remain to be elucidated (2).
We will describe what is known about DNA electrotransfer into mammalian cells. If small molecules can freely cross the electropermeabilised membrane and have a free access to the cytoplasm, heavier molecules, such as plasmid DNA, face physical barriers which reduce transfection efficiency and engender a complex mechanism of transfer (3-5) . As will be presented, our strategy to address these processes is to use different biological models with increasing complexities and implement different imaging tools (4, 6, 7). We will give a survey of our latest works on gene electrotransfer in skin (8, 9), pre-clinical investigation of the effect of interleukin-12 gene electrotransfer and electroporation (10) and the use of hyaluronidase to improve gene electrotransfer (11).

References

1. M. L. Yarmush, A. Golberg, G. Sersa, T. Kotnik and D. Miklavcic, Annual review of biomedical engineering, 2014, 16, 295-320.
2. C. Rosazza, S. H. Meglic, A. Zumbusch, M. P. Rols and D. Miklavcic, Curr Gene Ther, 2016, 16, 98-129.
3. A. Paganin-Gioanni, E. Bellard, J. M. Escoffre, M. P. Rols, J. Teissie and M. Golzio, Proc Natl Acad Sci U S A, 2011, 108, 10443-10447.
4. C. Rosazza, A. Buntz, T. Riess, D. Woll, A. Zumbusch and M. P. Rols, Mol Ther, 2013.
5. C. Rosazza, H. Deschout, A. Buntz, K. Braeckmans, M. P. Rols and A. Zumbusch, Mol Ther-Nucl Acids, 2016, 5, 1-11.
6. L. Gibot and M. P. Rols, Curr Gene Ther, 2013.
7. M. Madi, M. P. Rols and L. Gibot, Curr Gene Ther, 2016, 16, 75-82.
8. L. Pasquet, S. Chabot, E. Bellard, M. P. Rols, J. Teissie and M. Golzio, Hum Gene Ther Method, 2019, 30, 17-22.
9. L. Pasquet, S. Chabot, E. Bellard, et al., Sci Rep-Uk, 2018, 8.
10. L. Pasquet, E. Bellard, S. Chabot, B. Markelc, M. P. Rols, J. Teissie and M. Golzio, J Immunother Cancer, 2019, 7.
11. M. De Robertis, L. Pasquet, L. Loiacono, et al., Cancers, 2018, 10.

# HTA and Africa – Challenges

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Health care technology assessment is one of the critical activities the health care delivery system. Despite the fact that HTA is important in the medical device, but in Africa the level and implementation of HTA is not developed. Globalization, international recognition of HTA can be taken as opportunities for HTA . Critical challenges for HTA in Africa include
- Lack of focus in HTA especially in Education sector- Most universities and educational system in Africa do not give focus for HTA and most of the idea of HTA is not provided as a curriculum
- Lack of awareness about HTA—Most professional working in Medical device sector use HTA and HTM like similar terminologies
- The rise and dynamism of new technologies- It became very difficult for a continent like Africa to cope up with the rise of technologies as HTA addresses the evaluation of properties and effects of health technologies.

Even though there are lots of challenges for the proper implementation of HTA in Africa, the above issues are very critical and need to be addressed properly.

# Human Umbilical Cord Blood-derived Secretome Enhance Endothelial Progenitor Cells Proliferation and Migration

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Endothelial progenitor cells (EPCs) plays an important role in the pathophys-iology of coronary artery disease (CAD). Secretome produced by human Umbilical Cord Blood-Mesenchymal Stem Cell (hUCB-MSC) shown to have neovascularization and angiogenesis effect. However, the effect of hUCB-MSCs-derived secretome treatment toward EPCS proliferation and migration is not yet elucidated. This study aims to identify the effect of hUCB-MSCs derived secretome treatment on the EPCS proliferation and migration capa-bility. EPCs were isolated and cultured from peripheral blood samples and cultured in the Stemline II medium for three days. Cultured EPCs were culti-vated in 6-well plates until confluence and incubated with hUCB-MSCs-derived secretome at a concentration of 2%, 10% and 20% in conditioned media. EPCS proliferation was determined using the XTT assay and migra-tion was evaluated using a Boyden chamber assay. Statistical analysis was performed using SPSS 25.0. EPCs proliferation and migration were signifi-cantly higher between hUCB-MSCs-derived secretome treatment group (2%, 10%, and 20%) compared to the control group ($p<0.05$). This study also showed that hUCB-MSCs-derived secretome increase EPCs proliferation and migration in a dose-dependent manner ($p<0.05$). hUCB-MSCs-derived secre-tome enhances EPCs proliferation and migration. Thus, showing its potential as a new candidate for regenerative therapeutic modality for a patient with CAD.

# Hyperparameter Algorithms in Electrical Impedance Tomography for Rotational Data

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Rotational electrical impedance tomography provides novel possibilities for multimodal imaging. This could be especially useful in tissue engineering studies where non-destructive and label-free imaging is needed. In difference electrical impedance tomography, the change in conductivity distribution between two samples or states is reconstructed from boundary measurements. Typically, regularization is employed in the solution to tackle the ill-posedness of the problem. The amount of regularization is controlled by a hyperparameter value that is commonly found by subjective and time consuming heuristic selection. In order to find an automatized method that works also with rotational data, three state-of-the-art methods for hyperparameter selection were investigated: BestRes, L-Curve and SNR. These were tested with conventional and rotational experimental data. The results show that SNR was the only method that provided good image quality with rotational data.

# Identification of Clinically Relevant Rules: An Interpretable Approach for CVD Risk Assessment

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The current health care paradigm clearly identifies prevention as a key element to an efficient disease management. In the context of cardiovascular disease, risk assessment models may be a valuable element in the support to clinical decision, contributing to that preventive care. Moreover, interpretability as well as personalization of risk assessment are decisive aspects to increase the physicians' acceptance and consequently the respective application in the clini-cal practice. The proposed work aims to create an interpretable and personalized model based on the proper combination of a set of simple rules resembling the clinical reasoning. Three main steps can be identified in this approach: i) derivation of simple rules based on available risk factors (isolated/combined); ii) identification/selection of a subset of meaningful rules that have more likelihood to contribute to a correct risk classification; iii) ensemble scheme (e.g. voting technique) considering from this subset only the rules that are more adequate for each particular patient. The implementation of this model relied on supervised learning techniques. This methodology was validated with one real patients testing dataset pro-vided by the Santa Cruz Hospital, Lisbon/Portugal, comprising of N=460 of Acute Coronary Syndrome (ACS-NSTEMI) with an event rate of 7.2% (Death/MI; 30 days). The preliminary results are encouraging, reaching a geo-metric mean of Gmean=0.86 for all patients, assuring simultaneously the clinical interpretability and the personalization of the model.

# Identifying challenges during colonoscopy procedure through the application of Latent Dirichlet Allocation (LDA) method to interviews with endoscopists

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Introduction: The high incidence and mortality rate of colorectal cancer require new technologies to improve early diagnosis of the disease. In order to improve the design and development of such new systems, it is important to previously identify the colonoscopy procedural constraints. For that, interviews to endoscopists, as the main actors involved in the colonoscopy procedure, are often performed. The aim of this study is to identify challenges during colonoscopy procedure through the application of Latent Dirichlet Allocation (LDA) method to interviews with endoscopists.
Methods: The LDA method is a statistical analysis technique widely used to identify latent topics in a collection of documents. LDA allows getting the most relevant words that appear in each topic and representing them in word cloud charts. In these charts, the larger the probability of occurrence of a specific word is, the bigger and bolder it appears in the chart. In this study, LDA method has been applied to interviews performed to endoscopists.
Results: Six endoscopists from two different Spanish hospitals were interviewed. After applying the LDA method, two topics that best describe the interviews have been found: polyps and patient. In fact, a histogram of the 100 most used words in the interviews shows them as the two most repeated words (36 and 22, respectively). A further detailed analysis of both topics in the interviews shows that one of the main problems during the colonoscopy procedure is the detection of polyps, and that the technical problems for that are mainly related to the patients (poor bowel preparation prior to colonoscopy, and anatomy of the colon).
Conclusions: Firstly, LDA method shows an interesting potential to identify hidden patterns within free-text data, including interviews, so far scarcely used in the health care area. Secondly, results shows that the most important challenge during colonoscopy procedure is to see what you cannot see. On the one hand, educational initiatives for patients to improve their compliance of bowel preparation should be encouraged, but also for health care providers. On the other hand, although mechanical add-on devices and accessory device-based systems are used to maximize the colon exposure, the challenge in polyp detection could be the achievement of an endoscopic tip with 360o of vision, either with a rotating tip or with a system that allows peripheral as well as focused vision, for the improvement of the visual field behind the colonic folds.

# Impedance Cardiography Method: The Old and New Applications

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Impedance cardiography (ICG) was developed to allow quantitative estimation of mechanical activity of the heart and large blood vessels basing on a rhythmic change of the electrical impedance, caused by cyclic activity of the heart. Changes in the thoracic impedance are evaluated using the tetrapolar method where an alternating current of 20-100 kHz (constant amplitude 1 mA) oscillates between application electrodes while the voltage (reflecting the impedance) is measured on the receiving electrodes. Using ECG signal and the trace of the first derivative of signal proportional to the impedance, obtained from the human chest, the following parameters describing the haemodynamics could be evaluated: heart rate (HR), stroke volume (SV), cardiac output (CO), left ventricular ejection time (LVET, ET) pre-ejection period (PEP), thoracic fluid content (TFC), velocity index (VI) and acceleration index (AI) describing ejection of blood from the left ventricle, Heather index (HI) and systolic time ratio (STR) describing heart muscle contractility. Also other derivative descriptors might be calculated when basic indices are normalized by body sur-face area (BSA) or combined with arterial blood pressure (BP) values (e.g. the peripheral vascular resistance -SVR, left cardiac work-LCW). There is a consensus between researchers that absolute values of indices derived from ICG traces, describing time relationship of different phases of cardiac cycle, might be considered as reliable. However, there are controversies in accepting the absolute values of SV estimated using ICG, while the analysis of changes in haemodynamic indices are considered as more adequate. The analysis of changes in stroke volume and systolic time intervals (including their variability) seems to be a possible source of diagnostic information regarding mutual coupling between the cardiovascular system and autonomic system dysfunction. The information might be derived from the response of cardiovascular system to several environmental and/or pathological factors. Thus, ICG could be used for monitoring the effects of neurodegenerative processes, analysis of sleep apnea disorders, monitoring the effectiveness of physical training and exercise and predicting orthostatic intolerance. So far, ICG method was mainly used in analysis of hemodynamic response to static and dynamic exercise, orthostatic test, mental stress, arrhythmia events (especially when ambulatory version is used), pacemaker control. Another field of application of ICG might be the analysis of the shape of impedance traces. The modifications in signal waveform may indirectly reflect physiological activity and pathological changes of the heart and its compatibility with arterial system.

# Improving drug supply chain model: a simulation-based analysis for a hospital district in Italy

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The present work, carried out at the MOLISE DATI SPA headquarters, arises from the need to collect data regarding the procurement and consumption of drugs at the ASREM with particular interest in the three main regional hospitals: the Cardarelli Hospital in Campobasso, the Veneziale located in Isernia and the San Timoteo site in Termoli. We propose an in-depth analysis of Supply Chain Management (SCM) focusing on how it has acquired over time an increasingly fundamental role in all industrial production processes. The list of the main configuration models of the Supply Chain (SC) will be immediately followed by a case of study that highlights the main advantages and disadvantages deriving from collaboration along the entire logistics-production chain. The final objective is to analyze a new Supply Chain model demonstrating the effective reduction of the overall business costs and the significant improvement of the service level ob-tainable through a more efficient management of materials.

# Improving Estimation of Mental Wellness Using Computer Games

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Due to ageing population, old age cognitive deficit is becoming an epidemic-like mass phenomenon. Some form of dementia occurs in 11% of men and 16% of women over the age of 71. Mental wellness is a major factor contrib-uting to the quality of life, therefore, the early detection of deterioration is a very important but hard task. Improving detection would allow ageing at home and more cost effective care. As clinical tests are infrequent and expensive, methods applicable for regular home monitoring have to be developed. Esti-mation of mental wellness based on voluntary game playing has been investi-gated in the last years, serious computer games are especially suitable for that purpose. One of the main problems is that popular games are not well fitted for measurement, regular tests are not entertaining enough. The basic was applied in a research project, and it worked well, but some improvements are suggest-ed based on the experience gathered. The most important one is that the com-bination of the game playing with special tests is proposed for better estima-tion capability. Consulting with end-users, the participation level and the feed-back system is suggested to be improved. Basic considerations, challenges, po-tential solutions, presentation of preliminary analysis results are described in the paper. The work is performed in the FROm empoweriNg To Viable Living (FRONT-VL) project supported by the Celtic-Plus Programme.

# In-vivo electrical conductivity and field mapping for transcranial electrical stimulation (tES) using deep learning strategies

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Transcranial electrical stimulation (tES) is a non-invasive neuromodulation technique indicated to treat depression and chronic pain. In tES, low amplitude current is delivered to the brain through surface electrodes. The best contemporary estimates of electric fields delivered by tES are estimated from computational models of the head. However, these models rely on literature values for tissue conductivities and do not include electrode contact impedances. Therefore, this approach cannot correctly predict subject-specific fields.

Magnetic flux densities induced by tES currents can be measured from MR phase and used to reconstruct current density, electric field and conductivity tensor distributions, using diffusion tensor magnetic resonance electrical impedance tomography (DT-MREIT). DT-MREIT has been used to produce electrical conductivity tensor images by imaging of a scale factor ($\eta$) relating MRI diffusion and conductivity tensors. Stable reconstruction of conductivity tensor C via DT-MREIT requires two independent current administrations. Here, we use data from an in-vivo human experiment to demonstrate that it is possible to use DT-MREIT to reconstruct conductivity tensors and electric fields using a single experimental current administration via a deep learning approach.

Experimental protocols were approved by the Arizona State University Institutional Review Board. Data obtained from a 58-year old volunteer male human subject was used to demonstrate method performance. Structural, diffusion tensor and two projections of MREIT data were obtained and corrected for wire fields. A dual-loop method was used to reconstruct DT-MREIT data within the brain from one current projection, producing conductivity images with streaking contamination. A deep neural network was trained to recognize and correct data based on a training set constructed using multiple different values of gray matter, white matter and cerebrospinal fluid conductivities. Simulated data from a second electrode projection were used to complete reconstructions. Electric field distributions were calculated following conductivity tensor reconstruction.

Reconstruction performance was verified using relative L2-differences from standard scale-factor images obtained using the DT-MREIT algorithm and another set of data measured using a T7-T8 electrode pair. Relative L2-differences between single-current injection and standard, two-projection reconstructions and derived electric fields were found to be 0.15 and 0.20 respectively.

We conclude that stable conductivity tensors can be reconstructed using only one current injection.

# Increasing the Temporal Resolution of Dynamic Functional Connectivity with Ensemble Empirical Mode Decomposition

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Understanding the functional organization and execution mechanisms of the brain is one of the key challenges of neuroscience. Functional connectivity emerging from phase synchronization of neural oscillations of different brain regions provides a powerful tool for investigations. While the brain manifests highly dynamic activation patterns, most connectivity work is based on the assumption of signal stationarity. One of the underlying reasons is the problem of obtaining high temporal and spectral resolution at the same time. Dynamic brain connectivity seeks to uncover the dynamism of brain connectivity but the common sliding window methods provide poor temporal resolution, not detailed enough for studying fast cognitive tasks. This paper proposes the use of the Complete Ensemble Empirical Mode Decomposition followed by Hilbert transformation to extract instantaneous frequency and phase information, based on which the phase synchronization between EEG signals can be calculated and detected in every time step of the measurement. The paper demonstrates the suboptimal performance of the sliding window connectivity method and shows that the instantaneous phase based technique is superior to it, capable of tracking changes of connectivity graphs at millisecond steps and detecting the exact time of the activity changes within a ten millisecond margin. These results can open up new opportunities in investigating neurodegenerative diseases, brain plasticity after stroke and under-standing the execution of cognitive tasks.

# Influence of extracellular environment on electroporation efficiency

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In this work, the effects of extracellular environment, in terms of both electro-poration (EP) medium and extracellular matrix (ECM), on EP efficiency were evaluated in a 3D in vitro model composed of HCC1954 cells cultured on hyalu-ronic acid (HA) hydrogels enriched with self-assembling peptides carrying IKVAV motifs. The results from 3D cultures were compared to those derived from cell in suspension and adherent cultures. EP was carried out by using either RPMI (high conductivity medium) and electroporation buffer (low conductivity medium) and applying 8 rectangular voltage pulses at 700 V (electric field strength 1000V/cm with plate electrode with 7 mm gap). Collectively, our data highlighted that cell organization and the presence of ECM modulate local electri-cal properties, thus affecting EP efficiency.

# Influence of the Backpack on School Children's Gait: A Statistical and Machine Learning Approach

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Studies and reviews show that the vast majority of students around the world use heavy and uncomfortable backpacks, which could negatively affect their skeletal-muscle development or at least generate a non-physiological functional overload and a change in the kinematics of gait. The purpose of this study is to investigate the role of the school backpack during the execution of the Walk test trying to identify if and how much it affects walking in terms of space-time parameters considering whether it might be correlated to potential spine disorders during the development age. A population-based sample of 98 students (60?male) aging from 10 to 12 years old was studied; gender, age, weight and lower limb length were recorded. Kinematic data were computed using a wearable inertial device for gait analysis: G-WALK System by BTS Bioengineering and analyzed using ANOVA test and Machine Learning. Overall, concerning ANOVA test between free walk and walk with backpack, it emerges that there is a significant statistical difference on 9 out of 10 kinematic parameters, of which 6 with maximum statistical significance (p-value<0.0001). Concerning Machine Learning analysis carried out through Linear Discriminant Analysis, Naïve Bayes, AdaBoost and Random Forest algorithms considering free walk and walk with backpack as two different classes, it emerges high values in the evaluation metrics: Accuracy and ROC Area for all the algorithms employed. The best performances have been reached with Linear Discriminant Analysis to an accuracy of 85.71% and a ROC Area of 0.92. Study results suggest that there is a drastic change on kinematic related to the gait because of the backpack. This con-clusion should be taken in correct account to safeguard children's health wearing backpack for prolonged periods.

# Influence of the gender on the relationship between heart rate and blood pressure

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Blood Pressure (BP) and Heart Rate (HR) provide information on clinical condition along 24h. Both signals present circadian changes due to sympa-thetic/parasympathetic control system that influence the relationship be-tween them. Moreover, also the gender could modify this relation, acting on both control systems. Some studies, using office measurements examined the BP/HR relation, highlighting a direct association between the two varia-bles, linked to suspected coronary heart disease. Nevertheless, till now such relation has not been studied yet using ambulatory technique that is known to lead to additional prognostic information about cardiovascular risks. In or-der to examine in a more accurate way this relation, in this work we evaluate the influence of gender on the BP/HR relationship by using hour-to-hour 24h ambulatory measurements. Data coming from 122 female and 50 male normotensive subjects were recorded using a Holter Blood Pressure Monitor and the parameters of the linear regression fitting BP/HR were calculated. Results confirmed those obtained in previous studies using punctual office measures in males and underlined a significant relation between DBP and HR during each hour of the day in females also showing a different trend in the BP/HR relation between genders only during night-time. Moreover, the circadian rhythm of BP/HR presented similar trends in both genders but with different values of HR and BP at different times of the day.

# Inhibition of vesicle formation at the Golgi apparatus delays membrane resealing after electroporation in vitro

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Electroporation is a method in which cells are exposed to external electric field of sufficient amplitude and duration to achieve transient destabilization of the cell membrane (1). Brefildin A (BFA) is a fungal metabolite that inhibits vesicle formation at the Golgi apparatus and induces tubulation of endosomes and lysosomes (2). Since lysosomes are reported to be involved in cell membrane resealing after membrane destabilization (3) we tested if BFA treatment has any effect on membrane resealing after electroporation in vitro.

CHO cells in suspension were incubated with 5 µg/ml of BFA (Life Technologies, USA) for half an hour, 1 hour or 2 hours before exposure to 8 pulses of 100 µs duration and 1.6 kV amplitude in 4 mm cuvettes (VWR International, Belgium). Cell recovery after electroporation was detected by adding propidium iodide (Life Technologies, USA) immediately before pulse application, immediately after pulse application or 2 to 16 minutes after pulse application in 2 minutes intervals. Incorporation of propidium iodide into cells was detected with flow cytometry (excitation 488 nm, emission 574/26 nm band-pass filter).

We observed delayed membrane resealing after electroporation if cells were exposed to BFA prior electroporation, compared to cells that were not pretreated with BFA. The longer the cells were exposed to BFA the greater was the delay in membrane resealing after electroporation. In conclusion, our results indicate that inhibition of vesicle formation at the Golgi apparatus and tubulation of endosomes and lysosomes can lead to delayed membrane resealing after electroporation in vitro and that lysosomes are involved in membrane resealing after electroporation in vitro.

1. Kotnik T, Rems L, Tarek M, Miklavčič D. 2019. Membrane Electroporation and Electropermeabilization: Mechanisms and Models. Annual Review of Biophysics, 48, 63 − 91.
doi: 10.1146/annurev-biophys-052118-115451

2. Klausner R. D, Donaldson J. G, Lippincott-Schwartz J. 1992. Brefeldin A: insights into the control of membrane traffic and organelle structure. The Journal of cell biology, 116(5), 1071–1080. doi:10.1083/jcb.116.5.1071

3. Castro-Gomes T, Corrotte M, Tam C, Andrews N. W. 2016. Plasma Membrane Repair Is Regulated Extracellularly by Proteases Released from Lysosomes. PloS one, 11(3), doi:10.1371/journal.pone.0152583

# Inspection of the Efficacy of the Screening Behavior Support Program for Colorectal Cancer Organized Screening

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The purpose of this study including the questionnaire survey is to perform the colorectal cancer screening behavior support program developed preliminary by the authors and to inspect the efficacy of the program. The subjects were male and female persons who lived in the Kinki area of Japan and were older than 40 years. The subjects were divided as the intervention group and control group. The program was applied to the intervention group. The questionnaire survey was carried out before and after the intervention for all subjects. However, the results of the intervention group are shown and discussed in the text.

The ratios of men to women and the youngers (40-59) to the olders ( 6o) were about one to one in the intervention group. Almost subjects lived not alone. The proportion of the persons whose screening history is “yes”, increased after the intervention. It is considered that the intervention is effective to raise awareness of screening test and lead to screening behavior. As a whole, women respect time and financial convenience for screening behavior more than men do. The olders ( 6o) are concerned about their health, while the youngers (40-59) prioritize work and family. Such differences after the intervention. On the comparison be-fore and after the intervention, the differences were found in “12. I think it is difficult to have the test at early time, because self-screening of colorectal cancer is impossible.”, “17. I don’t like to have detailed test after screening test in which abnormality is found, because I don’t want any medical treatment.” and “29. I have the test, because my family members often talk about the test.”. These results are considered to be caused by the intervention.

The results of this study suggest that the screening behavior support program is useful as an educational the intervention for raising awareness on colorectal cancer screening behavior. Further improvement of the program is necessary for more effective the intervention.

# Integrating real world data and statistics in Multiple Criteria Decision Analysis for Health Technology Assessment of Medical Devices

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Over the last decades, the use of Multi-criteria Decision Analysis (MCDA) methods have been spreading in several fields, even though very few applications in health care have been recorded, so far. Notwithstanding the integration of MCDA in Health Technology Assessment (HTA) offers the possibility to obtain relevant and easy to interpret data there are several issues, which affect MCDA results. Firstly, no historical time series data are explicitly taken into account for the Organizational and Economic aspects, which are instead evaluated, through experts' hypothetical previsions. Secondly, the numerical values of the technologies' safety and effectiveness performances, usually gathered from scientific literature, cannot be always measured and they are affected, indeed, by the robustness of the evidences, which supports them. To overcome these problems an innovative method, which integrates real-world data and statistics in MCDA is here proposed, resulting in a useful tool for decision makers to make investment choices with greater awareness.
A Montecarlo simulation (taking into account the MCDA results as input) is introduced as an integral part of the MCDA assessment process, in order to improve the reliability of technologies' performances expected values. We distinguished between safety and effectiveness data, which are gathered from literature review and those obtained from hospital registries and databases (Organizational and Economic) for which historical time-series data are usually available. The former are modeled by Gaussian distributions built on the relative GRADE level. The higher the GRADE level, the lower the related standard deviation is, indicating the high reliability of sources of information. The latter, thanks to the availability of their historical time series, are analyzed through the application of forecasting algorithms. Obtaining their forecast values and the confidence intervals, it gives the possibility to design the related Probability distributions, providing short-term expected values with high accuracy.
Conclusions: The statistical method allows decision-makers to rationally evaluate the technologies under assessment, providing a different and more detailed way to carry out an accurate analysis, quantifying the error rates around the judgements. Before the acquisition of a technology, it is considered essential to make the best, most rational and reliable decision. Carrying out an evidence based approach, which integrates literature review and real world data from context analysis with an analytical and statistical method, significantly improve the robustness, the reliability and the reproducibility of the solution, recommending decision makers the best solution available within the modern-day technological market.

# Interactive Process Mining Exploiting Digital Health Transformation to Provide High-Value Care to Achieve the Quadruple Aim of Healthcare

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Burden of longer life expectancy with a prevalence of chronic diseases and increasing multimorbidity is together with a rise in patient expectations from healthcare processes requires certain healthcare transformation. The vision of the quadruple aim of healthcare leads such transformation adding sustainability by incorporating the experience of healthcare professionals.

To be able to provide the high-value care expected by the population, all aspects influencing on outcomes and experiences must be taken into account. Fortunately healthcare digitalization is making its way through healthcare and technologies for advanced analytics like Artificial Intelligence are available to support identifying the best way to provide high-value care in a sustainable manner long-term.

Process mining is a technology adopted in production and manufacturing settings used to optimize the processes to achieve the final result with the highest quality in reasonable time and cost that facilitates a sustainable future. For the last decade, process mining has been tested in dozens of different healthcare settings across the world. The valuable insights obtained suggest the usefulness of process mining for healthcare improvement, but the accumulated experience clearly indicates that for clinical adoption a specific methodology and a dedicated tool are required.

With the goal to create evidence about the usefulness of process mining the project VALUE, a consortium of industrial and academic partners led by the clinical need from six hospitals, was born (http://valueproject.eu/). Creating VALUE through clinical pathways & care flow optimization is a 3 years innovation project supported by the EIT Health (pnr 20238), aimed at creating a market ready solution to deploy interactive process mining in healthcare settings by developing a methodology of use, producing an Medical IT tool and implementing a healthcare improvement service.

In VALUE, a software tool providing process mining and data analytics including interoperability with clinical data repositories and Hospital EPR is being developed to implement a lead six-sigma approach to healthcare process improvement boosted by the IPM (Interactive Process Mining) methodology. A total of six pilots are being planned targeting improvement on Management of Heart Failure chronic patients, Stroke care flow, Musculoskeletal disease care flow, myocardial infarction emergency care pathway and optimization of Emergency Care department with and without support from Real-Time Location Solution data.

If VALUE project is successful the IPM methodology will be truly available for clinical adoption across EUROPE in 2023.

# Intermittent Non-Invasive Blood Pressure Measurement: Gaps and Clinical Needs

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The accurate measurement of blood pressure (BP) is essential for the diagnosis and management of several medical conditions. Intermittent non-invasive blood pressure (NIBP) is regularly used in different care units, as it is a readily available method to ascertain BP. This study aims to identify and interpret the current gaps and needs in clinical practice regarding NIBP monitoring.

Based on a review of the literature on current BP monitoring protocols, a set of questions were prepared, and 12 interviews were conducted with health professionals. The interviews were followed by shadowing work in the hospital. The results indicate that there are some problems associated with NIBP that can have both human and financial negative consequences. It was found that the difficulty in establishing thresholds for defining clinically relevant changes in BP dynamics and the unreliability of NIBP readings in several clinical contexts, namely hypotension, are the most considerable problems in need of intervention.

In conclusion to this work, a list of suggestions to future research is summarized, among which stand out the improvement of NIBP accuracy and NIBP adaptive sampling frequency.

# Intraoperative electrochemotherapy of colorectal liver metastases, a prospective phase II study

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Background and objectives: Previous pilot study proved feasibility, safety and efficacy of electrochemotherapy in treatment of colorectal liver metastases. The aim of this study was to evaluate long-term safety and effectiveness of electrochemotherapy in treatment of unresectable colorectal liver metastases.

Patients and methods: In prospective phase II study, patients with metachronous colorectal liver metastases were included. In all patients, at least one metastasis was unresectable due to the central location, or too small future remnant liver volume. Patients were treated by electrochemotherapy using intravenously administered bleomycin, during open surgery. Treated were 84 metastases in 39 patients. Local tumor control, progression free survival and overall survival were evaluated.

Results: Objective response was 75% (63% CR, 12% PR). Median duration of the response was 20.8 months for metastases in CR and 9.8 months for the tumors in PR. The therapy was significantly more effective in metastases smaller than 3 cm in diameter than larger ones. There was no difference in response according to the metastases location, i.e. metastases in central vs. peripheral location. Progression free survival was better in patients who responded well to electrochemotherapy, compared to tumors that had partial response or progressive disease. However, there was no difference in overall survival, with median 29.0 months.

Conclusions: Electrochemotherapy has proved to be safe and effective in treatment of colorectal liver metastases, with durable response. It provides local tumor control that enables patients with unresectable metastases further treatment modalities.

# Investigation of Drug Eluting Stents performance through in silico modeling

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Coronary artery disease is one of the most dominant factors of mortality worldwide. The stenting procedure has been adopted as an effective means of blood flow restoration in the diseased part of the artery. Producing improved clinical outcomes compared to Bare Metal Stents (BMSs), Drug-eluting stents (DESs) have been widely accepted in the field of cardiovascular intervention. In this study, through the BioCoStent in silico stent deployment platform, three different stents (two DESs and one BMS) are comparatively analyzed with respect to the prediction and assessment of their mechanical performance in realistic, patient specific arteries. The results demonstrate the nearly identical behavior for all three stents, with minor differentiations. The differences in the results are attributed to the incorporation of the thin drug-eluting coating on the metal core of the stent, eventually inducing an insignificant increment in the post-deployment stresses. Furthermore, the strut peaks, the end rings of the scaffolds and the stenosed part of the arteries experience the highest stresses.

# Investigation of Magnetic Sensor for Intra-oral Continuous Jaw Tracking

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Currently available jaw tracking methods require large accessories mounted on a patient and thus are utilized in controlled environments, for short-time examinations only. In some cases, especially the evaluation of bruxism, a non-restrictive, 24-hour jaw tracking method is needed. This study explores the possibility to use a permanent magnet and a 3-axial magnetometer to track mandible's spatial position in relation to maxilla. An algorithm for determining the sensor's coordinates from magnetic field values was developed and verified via analytical and finite element modelling of a magnetic field surrounding a magnet and by using a 3D positioning system. The trajectory of natural masticatory movement (10 x 7 x 5 mm) was replicated, and coordinates from sensor data were calculated with RMSE of $0.267 \pm 0.023$ mm. Estimation of the coordinates of cubic ($a = 10$ mm) trajectory resulted in RMSE of $0.325 \pm 0.009$ mm. Errors due to the Earth's magnetic field were shown to increase exponentially with magnet–sensor distance. Possible compensation techniques and sensor positioning possibilities were discussed. Despite the limited working range and large uncertainties in the periphery, it is a strong advantage of the method to be increasingly accurate and robust and when approaching occlusion.

# Investigation of Muscle Imbalance

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Sedentary occupation and lack of exercise lead to the gradual muscle wasting and thus shortening of the whole body and also the development of muscle imbalance which involves weakening of muscles, shortening of muscles and impaired spine statics and dynamics in a long-term sitting position. Prevention of muscle imbalance should be aimed at eliminating their causes. Myotonometric parameters were measured using MyotonPro device before and after a physiotherapeutic exercise aimed at strengthening and stretching the deep muscular system. Eight females (age: 56.9±8.4 years) volunteered to participate in this study. Six muscles were selected for measurement on both sides of the body and symmetry index was calculated. Overall, symmetry improved in 119 cases out of 240. In 55 cases the right-left symmetry changed to left-right or vice versa. A graphical user interface has been designed for better understanding and visualization of results. The physiotherapist can choose an individual proband and compare the results before and after exercise. In the next exercise it can focus on individual muscle parts where the symmetry was not achieved.

# Large Liver Blood Vessels and Bile Ducts Are Not Damaged by Electrochemotherapy with Bleomycin

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Electrochemotherapy has been reported to be feasible and effective for treatment of centrally located liver tumors which could not be treated surgically or with thermal ablation techniques. However, damage to normal small diameter blood vessels and bile ducts has been observed in resected tissue specimens. As damage to major liver blood vessels and bile ducts can lead to serious complications, we conducted an animal model study to evaluate changes in normal liver tissue after electrochemotherapy with bleomycin. Based on previous findings, we hypothesized that electrochemotherapy would not cause clinically significant damage to normal liver tissue and/or adversely affect liver function. Electrochemotherapy with bleomycin was performed during open surgery in six female domestic pigs, two additional pigs received electrical pulses only to serve as controls for possible toxic side effects of bleomycin. We selected pigs as our experimental animals due to the similarities between porcine and human liver. Electrical pulses were delivered in four locations in each liver with a risky treatment strategy including intraluminal electrode insertion. Both variable linear and fixed hexagonal geometry electrodes were used. Bleomycin dosing and electrical parameters were consistent with previously described standard operating procedures for electrochemotherapy. Study endpoints were euthanasia of pigs with specimen collection on post-operative days two or seven. Examination of tissue specimens, computed tomography and blood sample analysis were used to determine the effects of electrochemotherapy on the normal porcine liver. The study was approved by the Ethical Commission for Animal Experimentation at the Administration of the Republic of Slovenia for Food Safety, Veterinary and Plant Protection. We found no signs of thrombosis or other clinically important damage to large liver blood vessels and bile ducts. No differences between the use of electrochemotherapy or electrical pulses only were observed. Four zones of changes in liver parenchyma were seen where the electrodes were inserted. Damage to small blood vessels was observed near the electrodes due to irreversible electroporation. Regenerative fibrotic changes were already seen seven days after the procedure. Computed tomography demonstrated areas of decreased liver blood flow due to vascular lock, however no thrombosis or bleeding was observed. No clinical or biochemical signs of liver failure or systemic inflammatory response were observed. In conclusion, electrochemotherapy with bleomycin does not cause clinically important changes in normal liver parenchyma. Our study confirms its safety for use in treatment of patients with irresectable liver tumors near major blood vessels and bile ducts.

# Lean Six Sigma approach to implement a Femur Fracture Care Pathway at ”San Giovanni di Dio e Ruggi d’Aragona” University Hospital

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Timeliness in the treatment of fracture of the femur, through surgery, is crucial in the elderly patient as it reduces the risk of mortality and disability. Here we pro-pose a Lean Six Sigma (LSS) approach to reduce the preoperative length of stay for patients with femur fracture. Through the LSS, a tailored Diagnostic and Care Pathways (PDTA) for these has been inmplemented and monitored over time. A significant reduction of the length of stay has been achieved, in compliance with the national recommendations to guarantee the quality of care.

# Level of awareness of developers and start-up companies on legal requirements and management system standards for medical devices

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To “put medical device to service” or “placing it on the market” in EU, the manufacturer shall follow particular legislation. Significant number of start-ups fail to fulfill requirements of legislation for developed products prior their termination. Many incredible ideas are left behind due to inappropriate approach to the project. Two main technical causes were recognized in this relation: the ignorance of legislation and improper implementation of the development. Nevertheless, fulfilling requirements of legislation to gain pos-sibility of marketing the medical device does not ensure success. Thus make medical device available, where marketing and sales jump in.

# Linear and Nonlinear Features for Myocardial Infarction Detection using Support Vector Machine on 12-lead ECG Recordings

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The development of non-invasive techniques to assess cardiovascular risks has grown rapidly. In this sense, a multi-lead electrocardiogram (ECG) provides useful information to diagnose myocardial infarction (MI), the leading cause of death worldwide. In this paper we used a support vector machine (SVM) to detect MI by exploiting temporal, morphological and nonlinear features extracted from 12-lead ECG recording from the PTB Diagnostic ECG database. Temporal features correspond to QT, ST-T and RR intervals, morphological features were extracted from P and T waves, and QRS complexes, and nonlinear features correspond to the sample entropy of QT, ST-T and RR intervals. A 10-fold Monte Carlo cross-validation was implemented by randomly splitting the data set into training (70 %) and test (30 %) sets with balanced classes. Sensitivity of 97.33 %, specificity of 96.67 %, and accuracy of 97.00 % were obtained by jointly exploiting temporal, morphological and nonlinear features by the SVM. The inclusion of entropy favors the detection of healthy control cases because the information of signal regularity improves the specificity of classification.

# Localization and classification of intracranial hemorrhages in CT data

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Intracranial hemorrhages (ICHs) are life-threatening brain injures with a relatively high incidence. In this paper, the automatic algorithm for the detection and classification of ICHs, including localization, is present. The set of binary convolutional neural network-based classifiers with a designed cascade-parallel architecture is used. This automatic system may lead to a distinct decrease in the diagnostic process's duration in acute cases. An average Jaccard coefficient of 53.7 % is achieved on the data from the publicly available head CT dataset CQ500.

# Lossy Compression Should Also Be Used in Functional MRI Research

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The amount of functional MRI (fMRI) data processed in research is growing, yet no practice or protocol to store them in a lossy format exists. Many researchers are struggling with limited storage space, and speed of common processing tools are often bound by storage speed. In this work, we present a lossy compression framework for fMRI data with user adjustable trade-off between compression ratio and root mean squared error (RMSE). Our goal is to demonstrate the usability of on-the-fly lossy compression for fMRI data. On one hand, the storage footprint and processing speeds both benefit from higher data compression rates achieved with lossy compression. On the other hand, data quality for functional analysis remains effectively the same. With this short demonstration we encourage the research community to develop a lossy data standard for fMRI data.

# Loudness Compression and Speech Understanding in Bone-Anchored Hearing Systems

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Bone-anchored hearing systems (BAHS) transmit sound via an osseo-integrated implant behind the ear to treat patients with conductive or mixed hearing loss. In recent years, digitally programmable audio processors for BAHS have been introduced. These enable, among others, the adjustment of the compression threshold (CT) and the maximum power output (MPO) of the sound processor. However, it is still unclear whether and how these parameters provide benefit to BAHS users in everyday life, in particular in pa-tients with an additional cochlear hearing loss. Therefore, the presented prospective study aims to systematically investigate the effect of CT and MPO on the speech intelligibility of BAHS users.

Twelve adult BAHS wearers with bilateral conductive hearing loss exhibiting varying degrees of additional cochlear hearing loss participated in the study. The audio processors of the participants were programmed with two different CTs (50 and 65 dB sound pressure level) and two MPO levels, resulting in four test conditions. Speech intelligibility was measured in quiet and noise using a multi-loudspeaker test setup.

As expected, the results of the speech tests show that speech intelligibility in quiet and noise decreases with increasing cochlear hearing loss. Speech understanding in quiet was not affected by either the CTs or the MPOs. However, with noise present, the lower CT in combination with the higher MPO level significantly increased the speech reception threshold by an average of 1 dB SNR ($p = 0.001$), which corresponds to an improvement in speech understanding of approximately 17% compared to the other processor settings.

# Machine learning and data mining methods for managing Parkinson's disease

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Artificial intelligence (AI), specifically machine learning (ML), has found numerous applications in computer-aided diagnostics, monitoring, and management of different pathological states including Parkinson's disease. Parkinson's disease ( PD) is a long-term, neurological disorder that specifically targets the central nervous system region used to regulate motor function. Individuals affected experience many symptoms that include imbalances in breathing, body coordination and muscle strength. ML algorithms are of use in the management and treatment of Parkinson's disease patients, enabling the detection and classification of tremors. This paper presents a comprehensive, high-level overview of AI applications in diagnosis, monitoring, and treatment of Parkinson's disease (PD) based on scientific publications published in the period 2015-2020.

# Machine Learning based Image Segmentation with Convolutional Neural Networks

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In recent years, machine learning algorithms have lead to significant improvements in medical image analysis by outperforming techniques which were previously considered state-of-art. For image segmentation in particular, fast and accurate results have been obtained using a particular type of deep learning algorithm called a Convolutional Neural Network (CNN). According to a survey by G. Litjens et al. (2017) which included over 300 publications on applications of deep learning to medical image analysis published from 2012 to 2017, CNNs have been the most frequently used deep learning algorithm in the field during this time period, especially for image segmentation. CNN architectures have, for example, been applied to segment brain tissues and lesions in MRI, substructures of the heart in cardiac US, fluid abnormalities in OCT, retinal vasculature in fundus photographs as well as pancreas and liver tumors in CT images. In otorhinolaryngology, more specifically in rhinology, techniques have so far been lacking to generate anatomically accurate segmentations of the sinonasal cavities from CT images automatically and rapidly. Semi-automatic or manual segmentation is laborious and does not constitute a viable basis for large-scale data analysis. In this work, results are presented for a CNN architecture which was developed specifically to classify different segments in CT images of the nasal cavity and paranasal sinuses automatically and accurately. This approach makes it possible to generate high quality segmentations of the frontal, maxillary, and sphenoid sinuses on both sides of the body, the oral and nasal cavities, bone, tissues, as well as the air outside the head surrounding the patient's body in order to remove the latter conveniently. With this CNN architecture, CT volumes of arbitrary patients can now be segmented accurately and in a fully automated manner within minutes. The obtained segmentations can then be used for, e.g., 3D model generation, computational fluid dynamics simulations, 3D printing, volumetry, or automated pathology detection.

# Management of the diabetic patient in the diagnostic care pathway

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Diabetes is one of the most common chronic diseases in the world. The data reported by ISTAT statistical yearbook 2015 indicate that diabetes affects 5.4% of Italians, equal to over 3 million people. Diabetes is a complex pathology both for the affected patients and for the medical specialists who follow them. Furthermore, since diabetes is a pathology with a high prevalence and incidence, it is essential to intervene effectively in therapeutic actions through the application of common guidelines. Therefore, in order to improve the management of the diabetic patient, the aim of the work is to define a possible Diagnostic Therapeutic Assistance Pathway (PDTA, Italian Acronym).

# Mechanical Investigation of Decellularized Cartilage Scaffold Using Two Different Protocols: In-Vitro and In-Silico Evaluation

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Tissue engineering is rapidly emerging as a promising therapeutic strategy to repair, enhance, or regenerate diseased or damaged tissue. Design and manufacturing of an appropriate scaffold, which provides the structural support for cell attachment and subsequent tissue development, are key to successful tissue regeneration. Numerous studies have investigated the possibility of using synthetic and natural scaffolds combined with chondrocytes or mesenchymal stem cells for cartilage tissue engineering, a tissue with limited potential for self-healing. Recent investigations demonstrated that scaffolds derived from decellularized cartilage matrices have the potential to provide a highly organized structure. The objective of this study was to investigate the biomechanical response of two decellularization techniques using both in-vitro and finite element (FE) modeling techniques. Cartilage specimens were harvested from the femoral condyles of mature bovine within 4 h after demise. Forty five Specimens were punched (D=5 mm, h= 7mm) and equally assigned into 3 groups (i.e., (1) control (C) (N=15), Decellularized using (2) Triton X-100 (TX) (N=15), and (3) Sodium Dodecyl Sulfate (SDS) (N=15)). The C group did not receive any forms of defects nor treatments. TX and SDS groups were decellularized according to the instructions in literature and all steps were conducted under continuous shaking. All 45 specimens were mounted in a chamber filled with phosphate-buffered saline (PBS) and underwent a stress-relaxation test using a mechanical testing apparatus (Zwick/Roell, Ulm-Germany). A validated inverse poroelastic FE methodology in conjunction with the in-vitro experiments were used to determine the mechanical properties. The results of the FE models were well comparable with the in-vitro experiments (Error of 5.49 ($\pm$3.67) %). Compared to the C group, the Elastic modulus significantly decreased for the SDS ($p<0.001$), however no significant differences were observed in the TX group ($P=0.084$). The permeability increased for both the TX ($p=0.016$) and SDS groups ($p<0.001$), which enhanced the fluid flow capability. It is therefore concluded that from a biomechanical perspective, TX Decellularization creates mechanical support and provides enough time for regenerating during the healing process of cartilage tissue and can hence be considered as a promising candidate as a scaffold for cartilage tissue engineering applications.

# Mechanical modeling module - In silico mimic all the in vitro mechanical tests required by technical standards to assess a drug-eluting BVS

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Stents (endovascular prosthesis) are a solution for treating many health disorders and cardiovascular diseases. One of the problems in stent implantation is a process called in-stent restenosis (ISR). The state of the art in-stent industry is the new era of BVS (bioresorbable vascular scaffolds) devices. InSilc is an in-silico clinical trial (ISCT) platform for the development and assessment of drug-eluting BVS. InSilc platform provides insight on the performance of drug-eluting BVS in their short term and medium/long term through the Mechanical Modelling Module, the Deployment Module, the Fluid Dynamics Module, the Myocardial Perfusion Module, the Drug-delivery Module, and the Degradation Module. The stent should fulfill specific performance requirements such as (i) high radial strength, (ii) flexibility, (iii) good fatigue properties, (iv) low elastic radial and longitudinal recoil and, (v) optimum scaffolding. For validating stent performance is necessary to be performed several different mechanical tests described and de-fined by ISO 25539 standard. Mechanical Modelling Module is developed for mimicking in-silico those tests and compare two or more different stent designs or the same design with different materials based on the three-dimensional (3D) finite element model. The new PLLA for BVS non-linear material model implemented, in an open-source code FE solver. BVS material is very specific and “memorize” all previous exposed loading conditions, so for achieving god precision solver keep from previous simulation results of all residual stress and strain field and use them like boundary condition at the beginning of next simulation. Also, contacts and boundary conditions were updated and adapted for the non-linear problem. Results show that FE simulations are the fast and reasonably accurate numerical approach for designing and optimizing stents with a significant reduction of time and costs for designing and developing a BVS implantation system. **Research supported by the InSilc project that has received funding from the European Union’s Horizon 2020 research and innovation program under grant agreement No 777119. This article reflects only the author’s view. The Commission is not responsible for any use that may be made of the information it contains.

# Medical device inspection - Analysis of machine learning for performance prediction

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Medical devices are highly complex apparatuses whose regular maintenance is mandatory in order to ensure proper functioning. Prediction of failure and overall performance is crucial for both cost reduction in terms of effective maintenance strategies and guaranty of safety for the patients. As the era of digitalization advances, novel methodologies can be used for this purpose, such as collection of data and using it in machine learning. This paper highlights the potential that machine learning has in the field of performance prediction of medical devices. Searching the papers in Google Scholar repository indicated that there are only a few papers focused strictly on using machine learning for performance prediction of medical devices. The review of reports of effective utilization of these strategies in performance assessment and prediction indicates that this field has a significant potential for development. On the other hand, the review of current state of the art, using Web of Science, across scientific disciplines points out the gap in utilization of machine learning for medical device performance prediction and the need for cooperation be-tween medicine and engineering in order to bridge this gap.

# Medical Equipment Procurement Practices and Maintenance Mismatch

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Background: Health service delivery is predicated upon the availability, appropriateness, affordability and acceptability of medical devices. Research evidence suggests that between 40% and 70% of medical devices/equipment in low resource settings are broken, unused or unfit for purposes. In Ghana, it is common to hear that medical equipment like X-ray, CT Scan or MRI in public hospitals are not functional. Patients are denied access to healthcare due to breakdown of medical equipment. Improper procurement practice has been cited as one of the major causes of medical equipment breakdown or service unavailability in Ghana. This study assesses whether procurement decisions rightly support the other aspects of the medical equipment management life-cycle.
Methods: The study was conducted to assess the procurement practice and management of service contracts on medical imaging equipment (X-rays, MRI, CT scan). Structured interviews and questionnaire was administered to BMETs who play significant role in medical equipment management at Teaching Hospitals and Regional Health Directorates for data collection. Ten (10) Regional Equipment Managers and Heads of BME Units in 3 Teaching Hospitals were selected participate in the survey.
Results: Warranty Service Management (Good Practice)
The study shows that supplier/third party service provider prepare PPM schedule and in-house BMETs remind the service contractor when a scheduled maintenance is due. The in-house BMETs sometimes supervise and verify a scheduled maintenance performed by service contractors.
Challenges: The study also revealed that there is monopoly on supply of spare parts and spare parts cost. Other issues emerged from the study are: Contract details are not easily accessible by in-house BMETs, manufacturer's after sales service resources cannot be directly accessed by in-house BMETs, there is little or no access for in-house BMETs to perform first-line maintenance and repair services, Some supplier secure service contract and outsource to third party which makes it more difficult to manage. In-house BMETs have little or no details of the service contract and are also not well resourced to manage service contracts. It was also identified that there is lack of coordination in managing third party contract. Medical equipment are sometimes procured and installed without the involvement of in-house BMETs.
Recommendation: Medical equipment management decisions are normally taken during procurement. Therefore, procurement decisions must be rightly taken to support the medical equipment maintenance life-cycle to ensure equipment availability for patient care.

# Medical technologies procurement, management and maintenance in developing countries: the case of health challenges in Africa

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Biomedical technologies are the basis of a functioning health system, in particular, medical devices are essential for the prevention, diagnosis, treat-ment of diseases. However, while developed country hospitals are renewing their fleet of machines by divesting large quantities of biomedical equipment annually, there is a chronic lack of biomedical technology in developing countries to support clinical activities, which could be met by the re-use of used equipment, adapted to the new hospital environment. However, even if the donations of biomedical technologies are generally made with good in-tentions and not-profit making as in the case under study, obtained results aren't what we expected also due to a not perfect communication between donors and recipients and a lack of culture about technology maintenance in the developing countries. At the moment, there is little documented evidence to support these statements. For this reason, the aim of this paper is to quan-tify the donated medical equipment that are out of service in two different hospitals in Benin. Furthermore, the information was collected on the type of communication existing between donors and beneficiaries and on the type of support that donors provide in terms of staff training, manuals and mainte-nance.

# MEHR: A Modular Exoskeleton for Hand Rehabilitation after Stroke

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Stroke is one of the leading causes of death worldwide. Among the survivors, 60% present some impairment associated with their hand and after 6 months of the incident, more than one third of the patients depend on assistance to manage activities of daily living. Spasticity is one of the most common disabilities in stroke patients and there are several spastic hand patterns. Clinical rehabilitation methods are still not close to restore normal limb functions and, during the last decades, there has been an increase in robotic training aimed to restore motor function. Nevertheless, most upper limb robotic devices are designed for elbow and shoulder training. In order to accomplish the criteria of a comfortable light-weight device, aimed for rehabilitation, that provides enough force to overcome spasticity, capable of measuring patient evolution and applicable in a wide range of patients, this work presents a modular exoskeleton, actuated by 1 to 4 linear servos, the force is transmitted to the distal phalanx by bowden cables that moves inside cable sheaths, which allows the device to perform both fingers flexion and extension. The device can be mounted to exercise the wrist, 1 to 4 fingers inde-pendently or actuate middle finger and moves index, ring and little fingers pas-sively. It is also available a splint-like component to immobilize wrist and meta-carpophalangeal joints. Load cells are placed between the servos and the bowden cables to measure tension and the software allows the therapist to control the dis-placement of the actuators, the number of actuators, number of cycles of exten-sion/flexion needed for the task and the wait time between beginning and end of each cycle. Association of design and software tools allows the device to achieve the device purpose.

# MEHR: A Modular Exoskeleton for Hand Rehabilitationafter Stroke

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Stroke is responsible for a large amount of injured limbs. The hand is of major importance for activities of daily living and any malfunction can result in difficulties to handle the simplest tasks. Current clinical strategies are still not close to fully restore patients' limbs. During the past decades, several devices have been developed to assist hand rehabilitation, although only few are designed for finger rehabilitation. This work presents a prototype of a modular hand exoskeleton, cable actuated, able to overcome spasticity and track patient's evolution. In order to evaluate the device, the resulting angles of fingertip, distal and proximal interphalangeal joints with respect to the metacarpophalangeal joint during free index finger flexion and extension were compared to the same movements when the finger was actuated by the exoskeleton. Result showed that the device is capable to achieve 46% and 48% of free hand fingertip workspace during flexion and extension, respectively.

# Metal Artifact Reduction in Dental CT Images using Deep Learning Generated Prior Images

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Metal artifacts in dental CT images, stemming from highly x-ray absorbing objects such as dental implants, often jeopardize reliable diagnosis and surgical planning in dental clinical practice. To efficiently reduce metal artifacts using the well-recognized NMAR (normalized metal artifact reduction) technique, generating accurate prior images is essential to separate out the metallic components from the CT projection data. In this paper, we generated high-quality prior images using a U-net based network. To make reference images for the network training, we applied manual segmentation of teeth, bones and metal objects to 528 dental CT images and augmented the data, with image rotation, flipping and tilting, to increase them to 2,112 images. In manual segmentation of metal objects, teeth, and bones, we heuristically exploited prior knowledge of tooth and bone shapes to avoid erroneous segmentation caused by severe metal artifacts. After generating the prior images, we applied the NMAR to the CT projection data and reconstructed final CT images. The metal artifact reduction performance of the proposed method is 74.6?tter than the conventional linear interpolation method. We expect further performance improvement in the following studies employing more dental CT images for the network training.

# mHealth to securely coach chronic patients

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This paper aims to summarize and discuss the privacy, security, interactions and safety challenges for the case study of a mobile Health application (mHealth app), for chronic obstructive respiratory diseases, namely AIRDOC - a Smart Mobile Application for Individualized Support and Monitoring of the Respiratory Function and Sounds. mHealth apps create opportunities for improving health outcomes of patients with chronic diseases. However, privacy and security features need to be much improved. Social/behavioural (interactional), technical and legal aspects need to converge to provide a more comprehensive privacy protection when patients interact with mHealth apps. By guaranteeing privacy, more secure, safer and better health results can be achieved, with patients more empowered and in control of their personal health data protection. An embedded security infrastructure, with GDPR compliance and controlling data access, usage and sharing functionalities, together with a continuous risk assessment and enhancement from user and interactions profiling feedback, can help provide useful and long-life trusted mHealth solutions.

# Microbubbles as safety issue of novel catheterization ablation methods

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Gaseous microbubbles release is the main complication of left sided cardiac catheter ablation. Cerebral vessel occlusion results in subclinical "silent" ischemia or manifests as stroke, however other organs may also be affected. Active search for gas formation (caused by either manipulation or nature of energy application) is essential in developing and established catheterization methods. Radiofrequency (RF) ablation causes macroscopic gaseous bubble formation during excessive heating, while, pulsed electric field (PEF) electroporation was reported to elicit microbubbles during milliseconds of application.
We aimed to describe gaseous bubbles formation during catheter RF and PEF energy application using customized quadripolar ablation catheters with/without active flushing and high-speed video microscope mounted camera (ORCA- Flash4.0 LT, Hamamatsu). Dynamics of gas formation was followed up to 20 seconds after the ablation energy application. The experiment was performed in circulation tubing and custom-made microfluidic chamber (1.2 cm x 1 cm, PDMS), allowing precise readouts even in relatively high fluid flow, above 100ml/min. The open system with an elevated fluid level (1330 mm above catheter position) mimicked human average blood pressure of 98 mmHg. The system was filled with 0.9% (9g/l) sodium chloride or human plasma and perfused by a peristaltic pump, generating flow conditions equivalent to left coronary artery, calculated for 3mm diameter tubing, used in experiment.
Two application catheters were introduced into the flowing fluid, spaced 8mm and their distal electrodes were connected to custom made DC generator, AC generator (patent PV2019-400 CZ) Inc) or RF generator (Smartablate, Biosense Webster). Distal electrodes and the microfluidic chamber, were alternatively monitored for eventual bubble formation. Background flow of bubbles was recorded as negative control and agitated saline injection as positive one. A bubble trap and 0.4 µm filter were placed along the circuit to prevent bubble recirculation. Size, volume, and number of microbubbles were quantified using image processing methods.
Results and Conclusion: Monophasic DC PEF elicited large number of bubbles – proportionally to applied energy, persisting more than 20 seconds, in clinically safe dimensions 3-8µm, up to size of an erythrocyte, thus capable of permeating through capillary network. When not flushed, smaller bubbles on cathodic tip of PEF catheter merged during repetitive pulse application into larger gaseous clusters. AC PEF did not elicit traceable microbubles, only heating as demonstrated by phase contrast microscopy. RF created detectable bubble stream in case of constrained irrigation, quickly vanishing, possibly due to entirely vapor content.
Ref.: Wojtaszczyk, A, Irreversible electroporation ablation for atrial fibrillation. J Cardiovasc Electrophysiol. 2018; 29: 643–651

# Modeling approach of blood hemodynamics in the left ventricle

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The heart is a muscular organ, which pumps blood through the blood vessels of the circulatory system. The left ventricle is the main mechanical element of the human heart, as it receives low – pressure blood from the left atrium and “launch-es” the blood with high pressure through the aortic pump to the entire circulatory system. Computational modeling is widely used in cardiovascular research, rec-ognizing the cardiac malfunction as the most common cause of death worldwide. The aim of this work is the computational study of deformation, stress and strain distribution of left ventricle’s wall due to the effect of blood hemodynamics. We employ the Navier-Stokes equations considering fluid-structure interaction using the finite element method. We build initially, the geometry of the left ventricle us-ing computed tomography. The meshing, the creation of a framework and distri-bution of nodes for a more accurate solution of the given elements are examined through a mesh sensitivity analysis. We apply appropriate boundary conditions which simulate the pathophysiology of left ventricle. In this work the value of stresses are found within the range of values referring to a non-healthy left ven-tricle and especially in a ventricle after infarction.

# Modelling of electrochemical reactions at electrode-electrolyte interface during electroporation

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Electroporation is the process of electrically induced increase in the permeability of the cell membrane for molecules which otherwise cannot diffuse across the membrane barrier. Increased permeability occurs due to the structural rearrangements and chemical modifications of the cell membrane. Furthermore, electrochemical reactions take place at the electrode-electrolyte interface during the application of high voltage pulses. Electrical energy in the form of electron current in the electrode is converted to ion current in the electrolyte via electrochemical reactions. Toxic substances such as dissolved metal ions and gas bubbles are formed during the application of pulses, due to electrochemical reactions, which could be harmful to biological tissues.

Computer modelling can be used to describe electrochemical reactions at the electrode-electrolyte interface during electroporation. In this study a simplified computer model is described which consists of anodic and cathodic reactions occurring at the electrode-electrolyte interface during the application of high voltage biphasic pulses. The main chemical reactions at the anode are chlorine evolution, oxygen evolution and dissolution of the metal ions from the electrode. At the cathode, hydrogen evolution is the principle observed reaction. COMSOL Multiphysics was used with Electrochemistry module based on Nernst-Planck equations and Transport of diluted species. The model is constructed in 1D around a spherical gold electrode surrounded by aqueous solution of sodium chloride electrolyte. The electrolyte domain is bounded by an inner and outer surface; the gold electrode represents the inner surface while the outer boundary is positioned far enough to ensure that it does not affect the domain being studied. Different assumptions are made to ensure the simplicity of the model. Only diffusion and migration in electric field are taken into account to contribute to the transport of ionic species. Inputs to the model are the voltage and duration of the biphasic pulse, interphase delay and size of the electrode.

Obtained results present the concentration profiles of ionic species as a function of time. When pulse was applied to the model, dissolution of the anode metal electrode was observed, followed by diffusion of metal ions away from the electrode surface. Computer modelling provides a better insight into processes occurring at the electrode-electrolyte interface during electroporation. A validated computer model could help us optimize high voltage pulse application and minimize consequent damage to the surrounding tissue.

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# Modelling of microcirculatory dynamics with auto-regressive models

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Ageing adversely affects most physiological processes, including cardiovascular dynamics. Indeed, vascular ageing plays a major role in several cardiovascular diseases, currently deemed the main cause of death in the world. Vascular ageing produces measurable effects at cardiac level, on major vessels, but also at capillary level. While the effects on the first two components are well known, the dynamics of microcirculation still lacks a complete understanding. In this work, we analyzed the predictability of the pulse waveform at capillary level, using a linear model, aiming to relate the estimated prediction model with the subject age. The pulse waveform was described fitting each pulse with a sum of Gaussian curves, that showed good representation capabilities; each pulse was thus associated with a series of physiologically relevant parameters, derived from the Gaussian curves. For each subject, we estimated a set of auto-regressive models that represent the temporal sequence of each parameter. Then, a classifier was trained to discriminate auto-regressive models according to subject age.

Results indicate that, in accordance with literature, the parameter that presents the higher discriminative power is the cardiac cycle duration, with an accuracy in assigning individuals to their age group of 90%, and an area under the ROC curve of 0.915. However, we observed also good performances by modelling the sequence of pulse amplitudes.

# Modular control of kinematics in prosthetic gait: low-dimensional description based on the planar covariation law

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Amputation of a lower limb implies a re-organization in the strategies used to reach a stable walking pattern. The planar covariation law of elevation angles is a well-defined low-dimensional description of the kinematics of movement; accord-ing to this law, thigh, shank and foot elevation angle co-vary on a plane, defining a typical gait loop. However, a robust biomechanical interpretation of the out-comes of its related analysis is still missing. In this work, we tested the planar covariation law on a group of 14 trans-femoral amputees, comparing the results with the ones related to 12 healthy people. Moreover, by adopting a common co-variance plane for all the subjects, we checked whether the projection of the orig-inal elevation angles on this plane is able to yield biomechanically meaningful in-formation on the control of prosthetic gait. A common plane was able to describe the coordination of lower limb elevation angles in all subjects; on this plane, most of the differences among populations were identified on the time course of one principal component.

# Monitoring of mesenchymal stem cell migration in the extracellular matrix

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Cell migration and invasiveness play an essential role in a number of biological processes, such as embryogenesis, the immune response, wound healing, morphogenesis and inflammation. Thousands of publications have elucidated detailed molecular and biophysical mechanisms of cell migration cultured on flat 2D glass and plastic substrates [1, 2, 3, 4]. However, much less is known about cell behaviour in the 3D environment of living tissues. The migration of cells in a 3D environment is challenging because it requires the cell to be extruded through complex or dense extracellular structures. It also requires specific cellular adaptation to the mechanical properties of the extracellular matrix (ECM). Human mesenchymal stem cells (hMSCs) were chosen, to study migrations in the ECM of various compositions. To simulate this environment, a specifically prepared collagen gel in pure composition, or with the addition of fibronectin (FN), was used. In our experiment, sets of images of cell migrations in the ECM were obtained using a confocal microscope. We used the MATLAB software environment and custom prepared, semiautomatic algorithm for processing and evaluation of measured data.

# MR-based conductivity with Electrical Properties tomography: from cell to bedside

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Introduction: Cells of human tissue have sophisticated mechanisms to manage concentration of different types of ions (e.g., sodium), both for intra- as well as extra-cellular space. Any disturbance of the ion concentration bears the risk of severe pathologies and vice versa: many pathologies are reflected by disturbed cellular ion concentrations. Ion concentration is directly connected to electric conductivity, i.e., measuring tissue conductivity yields diagnostic information on tissue status.

Technical background: Electric conductivity can be measured with standard MR systems and standard MR sequence with "Electrical Properties Tomography" [1]. Without any patient, the complex RF transmit field of an MR system (so-called B1) is more or less flat, and is getting distorted by the presence of the patient and his/her conductive tissue. This distortion is described by Maxwell's equations, thus Maxwell's equations can be applied to reconstruct tissue conductivity from the measured distorted B1. For an accurate reconstruction of conductivity, both magnitude and phase of the complex B1 is required. For clinical purposes, however, measurement of B1 magnitude can be skipped, and measuring only B1 phase enables a sufficient approximation of tissue conductivity. This approximation is based on the second derivative of the B1 phase in all three spatial directions, describing the B1 phase curvature. A straight-forward numerical differentiation of the phase tends to be instable, and various advanced reconstruction approaches are currently under investigation to increase stability of EPT reconstruction.

Evaluation: EPT has been evaluated using phantoms of known chemical compounds as well as volunteers, yielding the expected conductivity values [2]. Via EPT, the expected conductivity dependence has been confirmed with respect to ion mobility, temperature, and frequency. Moreover, EPT has been evaluated by comparing conductivity of brain tumors before and after extraction [3].

Clinical studies: First clinical (predominantly oncologic) EPT studies have been performed. For instance, investigating breast [4], brain [3], and lung tumors [5], it turned out that tumors always show higher conductivity than corresponding healthy tissue. Moreover, more and more studies show that conductivity reveals correlation with specific features of tumors like malignancy and grade.

Conclusion: Conductivity as measured via EPT on standard MR systems might be able to provide a new biomarker, particularly useful for characterization of tumors.

References:

[1] Katscher U et al., NMR Biomed. 2017;30:3729
[2] Gabriel C et al., Phys Med Biol. 1996;41:2231
[3] Tha KK et al. Eur Radiol. 2018;28:348
[4] Kim SY et al. Eur Radiol 2016;26:2317
[5] Tha KK et al. EMBEC 2020, submitted

# MR-based Electrical Conductivity Imaging of Brain Tissue Response after Irradiation

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Radiation therapy (RT) has been widely used as a powerful treatment tool for cancerous tissue removal because of its ability to control cell growth. Ionizing radiation damages the DNA of cancerous tissue and leads to cell death. Medical imaging still has limitations on reliability of tissue response evaluation and prediction of treatment effect due to lack of contrast information on gradual and minute tissue changes after RT. Recent magnetic resonance (MR)-based conductivity imaging method may provide direct and highly sensitive information on tissue response because its contrast mechanism originated from the concentration and mobility of ions existing intra- and extracellular space. In this feasibility study using the mouse brain, we applied T2-weighted, diffusion-weighted, and electrical conductivity imaging using a MRI to map tissue response after the exposure to radiation. To quantify the degree of tissue response, we measured the T2 relaxation, apparent diffusion coefficient (ADC), and electrical conductivity of brain tissues before and after the irradiation. The conductivity images, which showed significantly high sensitivity than the other MR imaging methods, indicated that its contrast is distinguishable in a different way at different brain areas. Future studies are focused on the verification and long-term evaluation of conductivity changes by various irradiation methods for clinical application.

# Multi-run Differential Evolution Improves the Decomposition of Compound Muscle Action Potential in High-density Surface Electromyograms

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We assess the performance of previously introduced jDErpodifferential evolution (DE) algorithm in the decomposition of CompoundMuscle Action Potential (CMAP), recorded by High-Density SurfaceElectromyograms (HDEMG) and show that multiple runs of this stochastic algorithm results in the dispersion of Motor Unit Action Potential(MUAP) position estimates across different runs and in false exclusion of MUAPs in some of the runs. We then introduce a procedure that optimally combines the results of multiple runs and show that this additional optimization significantly improves the consistency and accuracy of the CMAP decomposition by jDErpo. On average, in noiseless signals, the proposed multi-run optimization correctly identified the firings of 31.6±6.3, 33.4±7.0 and 34.5±10.3 MUs on simulated CMAPs with136, 168 and 200 active MUs, respectively. When 20 dB Gaussian noise was added to the signals, the method identified 31.2±20.4, 33.9±27.5and 35.0±26.3 MUs, on average.

# Multimodal Guidance in Neurosurgery

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The overall aim is to combine intraoperative MRI and optical techniques for multimodal guidance in neurosurgery in patients undergoing brain tumor resection and biopsies. Further, in neurointensive care patients with subarachnoid hemorrhage or traumatic brain injury different MR modalities will be combined with optical techniques for measurement of cerebral perfusion and blood flow. The optical techniques will be transferred and integrated for use with a 3T MR scanner (Skyra, Siemens) and a new operation room (OR).
Brain tumor resection: The blue-light neurosurgical microscope has been evaluated together with the in-house developed 5-ALA induced fluorescence probe-technique which helps identify the infiltrative high-grade tumor border. Up till now the fluorescence technique has been used in more than 50 tumor resections at the Neurosurgical clinic (Richter et al., 2017). Further development by combing the fluorescence method with laser Doppler flowmetry (LDF) for biopsy procedures can help indicate vessels structure along the insertion trajectory. As a next step probes will be adapted for iMRI together with frameless intraoperative navigation.
Neurointensive care: A thin optical probe and corresponding software module for a LDF has been developed and adapted for use in the human brain (Rejmstad et al., 2018). Cerebral microvascular monitoring in the neurointensive care unit (NICU) has so far been done in two patients (EPN, 2099-01032). Each monitoring covered LDF information from more than four days and data was presented in real time in the NICU. Signal analysis methodology development for reduction of movement artifacts, and extracting signals representing e.g. vasomotion, microvascular level is ongoing. Correlation to routine parameters like intracranial pressure, microdialysis and EEG will be the next step in the development chain, together with monitoring of brain perfusion and blood flow in single vessels using MR techniques like ASL, BOLD and NOVA.

References:
Rejmstad, P., Haj-Hosseini, N., Åneman, O. & Wårdell, K. 2018. Optical monitoring of cerebral microcirculation in neurointensive care. Med Biol Eng Comput, 56, 1201-1210.
Richter, J. C. O., Haj-Hosseini, N., Hallbeck, M. & Wårdell, K. 2017. Combination of hand-held probe and microscopy for fluorescence guided surgery in the brain tumor marginal zone. Photodiagnosis Photodyn Ther, 18, 185-192.

# Multiple regression model to predict length of hospital stay for patients undergoing femur fracture surgery at ”San Giovanni di Dio e Ruggi d’Aragona” University Hospital

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The economic cuts suffered by public health have in many cases led to the reduction of beds. In order to optimize the available resources, the length of stay (LOS) can be used as an efficiency parameter. The objective of this study is to predict the value of LOS using the clinical information that is generally supplied by a patient who is hospitalized following a fracture of the neck of the femur and to make a comparison with results obtained after the implementation of the new diagnostic-therapeutic-assistance pathway (DTAP). The analysis was conducted on data extrapolated from the information system of the University Hospital ”San Giovanni di Dio and Ruggi d’Aragona” of Salerno (Italy). The results show promising outcome in the use of the proposed prediction models as a tool for determining an estimate of the LOS and support the decision making process and the management of hospital resources in advance. In addition, the comparison of between the two models can be used as an indicator to assess the efficiency of the implemented DTAP.

# Multiscale Poincaré plots analysis of nystagmus amplitude variability during rotation on Bárány chair

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This article describes the application of nonlinear methods in the form of Multiscale Poincaré plots for the purpose of evaluating the variability of the horizontal amplitudes of nystagmus during bilateral stimulation on Bárány chair. The evaluated parameters were areas of the 95 % confidence ellipses of amplitudes per- and post-rotational nystagmuses. 3D VOG glasses were used to assess the vestibulo-ocular reflex induced by the trapezoidial accel-eration stimulation. A total of 10 volunteers without neurological disorders involved in the pilot measurement (5 males: mean age 23.4 years [SD 3.8 years], 5 females: mean age 22.8 years [SD 1.5 years]. Jarque-Bera test did not show normal distribution of the data and results did not confirm the dif-ference between ellipses surfaces per- and post-rotational nystagmus ampli-tudes, even for different coarse grained parameters Σs (s = 1-4). Lowest p-value (Mann-Whitney-Wilcoxon) was found in Σ3: p-value = 0.1212). On the contrary parameter Σ4 showed highest p-value = 0.8501 therefore, for further research, it would be advisable to focus on lower coarse grained Σs parameters.

# Myoelectric signs of sustained muscular activity during smartphone texting

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The aim of the present study was to analyze the upper trapezius activity, and its relationship with muscular discomfort perceived, during prolonged smartphone texting. Seventeen healthy young subjects participated in the experiment; they were asked to use their own smartphone for texting (10 minutes), maintaining two different postures, sitting and standing. The muscular activity of the right and left upper trapezius was recorded, and the CR10 Borg Scale was administered af-ter each experimental section. To normalize the EMG signals, the maximum vol-untary contraction was acquired at the beginning of the experiment. The median, the 10th percentile (P10) and the range (difference between 90th and 10th) of EMG RMS, the relative rest time (RRT), the correlation between P10 and RRT and be-tween P10 and CR10 scale were calculated. The results showed no statistical dif-ference between the postures, and the body side. The value of RMS parameters was around the 2% of MVC, showing a constant muscular activity throughout the experimental section. A significant negative correlation between P10 and RRT suggested that the subjects with greater P10 showed a lower rest period; moreo-ver, the significant positive correlation between P10 and CR10 Borg scale, for both postures, suggested that the subjects with high P10 values perceived greater discomfort in neck and cervical zone. The results support the hypothesis that the prolonged use of smartphone for texting influences the upper trapezius activity and it is strictly linked with the absence of a period of muscular recovery, and with the perception of muscular discomfort: that may be a potential risk factor to develop neck pain and musculoskeletal cervical disorders.

# New Anthropometric Data for Bulgarian Females and 3D Biomechanical Model Results for Inertial Parameters of the Upper and Lower Extremities

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In the current article we do report anthropometric measurements of 107 Bulgarian women performed by our team, that complement the representative anthropological investigation (Yordanov et al., 2006) of 2855 Bulgarian females aged 30-40 years. Based on these data, we present an approach for evaluating the mass-inertial parameters of the thigh, shank, upper and lower arm via using 3D geometrical modelling. We model the segments with a geometrical body, called right elliptic stadium solid, having cross-sections of elliptic stadium. The comparison of our model results with data reported in literature shows that the suggested modelling is successful since it uses 3D bodies closer to the actual shape of the foreseen segments. he results obtained could be used for the design of systems and devices aimed to enhance the rehabilitation, to help disabled persons and in criminology to evaluate body fall problems, ergonomics, sports, robotics, computer simulations and other fields of research.

# New approach of numerical model for Hodgkin Huxley model using COMSOL

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Transcutaneous electrical nerve stimulation is a non-invasive method of treating patients who have indication of pain. Based on the gate-control theory, this treatment relieves pain by activating the sensory nerve, which is faster than the pain, by applying an electric stimulus. A number model for nerves based on the Hodgkin Huxley model has been studied a lot. In this study, the Hodgkin Huxley model is to be implemented using COMSOL to obtain the active potential of the nerves. The Hodgkin Huxley equivalent circuit was modelled using SPICE in COMSOL. And using the ODE and DAE interface, the differential equation about rates of ion channels and the voltage-dependent opening and closing rates of ion channels was solved by coupling the voltage of the node in SPICE. When the Hodgkin Huxley model is modelled using spice alone, it was inefficient to describe parameters about ion channel, but it was possible to perform the modeling efficiently by coupling the variables with each other using COMSOL. Thus, the Hodgkin Huxley model based on COMSOL was verified by comparing analytic solution of the Hodgkin Huxley model using the Kirchhoff law. In the future work, the Hodgkin Huxley model based circuit model considering myelin will be able to be implemented efficiently, and by modeling human body bodies and applying external applied electrodes, it will be easy to couple external current sources.

# Non-invasive Intracranial Pressure (nICP) Monitor for Traumatic Brain Injury (TBI)

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Head injuries are the most common cause of death and disability in people aged between 1-40 years in the UK. It is estimated that in England and Wales around 200,000 people are admitted to hospital following a head injury or 1.4 million people attend Emergency services due to a head injury. Among these people, up to 50 % are aged under 15 years and 20 % present a skull fracture or brain damage. It is estimated that head and traumatic brain injuries count as the 10% of all cases in emergency departments, resulting in providing care for approximately 1 million subjects per year in the UK, with an estimated cost of £15 billion. The medical treatment received after a head injury is paramount for the full recovery of the patient in order to avoid permanent brain damages, disabilities or death.

The intracranial pressure (ICP), defined as the pressure inside the cranial cavity and surrounding the brain, is one of the most important parameters monitored in head injuries. Elevated intracranial pressures for extended periods of times can cause severe brain injuries, leading to permanent disabilities or death. The current method to measure the intracranial pressure involves inserting a small pressure sensor inside the cranial cavity after performing a surgical opening in the skull. Although considered the gold-standard, the procedure requires highly skilled and qualified neurosurgeons to insert the sensor and introduces risks of infections or damages for the patients.

Currently, there is no other method to measure intracranial pressure. This research aims to develop a non-invasive intracranial pressure system. The non-invasive intracranial pressure (nICP) monitor works by shining harmless near-infrared light into the brain. The sensor is attached on the forehead and it records the brain pulsations inside the cranial cavity which are related to the intracranial pressure. Complex analysis techniques are then applied to measure the intracranial pressure non-invasively.

So far, the nICP monitor has been extensively tested on an in vitro model which simulated the intracranial brain cavity. When compared to a reference pressure sensor, the nICP system was able to predict the intracranial pressure with an accuracy of 2.4 mmHg, similar to a standard pressure sensor. At the moment, the nICP monitor is being tested on trauma patients at the Royal London Hospital. If successful, the nICP monitor will be developed in a commercial device for its adoption in the NHS. The invaluable advantages of using the nICP monitor could also be extended to other conditions such as hydrocephalus, stroke, migraine.

# Notified body certification – main challenges and findings of assessments

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In order to place a medical device of higher risk on the market or put it into ser-vice a manufacturer has to undergo a conformity assessment procedure at notified body. During the procedure deficiencies can be identified which has to be solved prior to issuing an EC certificate. With the statistical analysis of the conformity assessment procedures performed at SIQ as notified body in last 4 years we have found that knowledge of legal requirements and associated guidance, involvement of expert knowledge of specialists from different disciplines including medical doctors, thorough study of scientific literature prior design of product starts re-duces number of deficiencies in the conformity assessment procedure. Number of deficiencies is correlated with the time needed from first audit of technical docu-mentation to the EC certificate.

# Novel methods for assessment and training of dynamic balancing during walking after stroke

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Ability to adequately maintain dynamic balance during walking is essential task in human locomotion which is in most cases impaired after stroke. Thus, development of methods for assessment and training of balancing abilities are in focus of contemporary research.

We developed “Balance Assessment Robot on Treadmill” that enables movement of pelvis in six degrees-of-freedom during walking and application of perturbing pushes to pelvis. We performed several experimental studies in neurologically intact subjects during perturbed walking on an instrumented treadmill. The results have shown that balancing reactions to perturbations required well-coordinated response of central nervous system. Furthermore, the results also indicated that balancing responses to perturbing pushes greatly vary with speed of walking as well as with timing, magnitude and direction of perturbation. Control of center-of-mass (COM) was at very low speed of walking achieved predominantly through the action of hip abductors modulating horizontal component of ground-reaction-force while control of center-of-pressure was modulated through the action of ankle musculature (“in-stance strategy”). At higher speeds of walking predominant response following perturbing push consisted of adequately modulating location of next step (“stepping strategy”).

Contribution of ankle musculature to balancing responses during walking was investigated in a study involving subjects with trans-tibial prosthesis. Complete absence of “in-stance” response was noted when perturbation commenced at heel strike of amputated side resulting in much greater COM displacement as compared to the non-amputated side.

Further experimental study was done in a group of 40 subacute post-stroke subjects which were all independent walkers and were considered as a homogeneous group according to a battery of selected clinical outcome measures. Approximately one half of subjects displayed dynamic balancing responses following perturbations that were similar to those seen in neurologically intact subjects while the other half of subjects have shown responses that were subject-specific and asymmetric where “in-stance strategy” was to a great extent missing when perturbations occurred while paretic leg was in stance. Thus, balancing responses were delayed until the non-paretic leg entered next stance with step location adequately modulated resulting in much bigger displacement of COM.

Based on specific deficiencies we developed perturbed-balance training approach which was applied to a number of selected post-stroke subjects. The results of prolonged training with high volume, specificity and intensity brought about considerable improvement in balancing capabilities and overall walking performance.

# Nucleic acid sensing by B16F10 mouse melanoma varies based on cell environment during electrotransfer

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Pattern recognition receptors (PRRs) are nearly ubiquitous in immune and non-immune mammalian cells. PRRs detect molecular pattern molecules associated with pathogen invasion as well as internal damage markers. A subset of pattern-recognition receptors, found in the nucleus, endosomes or cytosol, detect nucleic acids. Recently, a number of cytosolic DNA-specific PRRs expressed in non-immune cells have been described. Binding and activation of these "DNA sensors" induces the production of Type I interferons and pro-inflammatory cytokines and chemokines. This signaling cascade may lead to cell death or, in vivo, inflammation.

Many cell types, including mouse B16F10 melanoma cells, respond to plasmid DNA (pDNA) electroporation or electrotransfer with the upregulation of specific PRRs on the mRNA and protein levels. Our group has demonstrated in multiple cells types that delivery of non-coding backbone pDNA or pDNA encoding reporter, not therapeutic, genes (1) has significant anti-tumor effects, (2) induces upregulation of DNA-specific PRRs in a cell-specific manner, (3) induces inflammatory biomarkers in vitro and in vivo, (4) several PRRs directly bind DNA after delivery, and (5) inhibition of p204, the mouse ortholog of Ifi16, inhibits PRR signaling.

The purpose of this study was to determine whether mouse B16F10 melanoma cells respond similarly to pDNA electrotransfer based on their environment during delivery. We delivered pDNA to cells in suspension, attached cells (2D), and to cells grown in a 3D collagen hydrogel model (3D). We found that the relative metabolism kinetics of 3D cells were similar to monolayers in culture. Significant transgene expression was observed after delivery to cells in suspension, 2D, and 3D environments. However, while similar PRR mRNAs were upregulated, including DAI/ZBP1, DDX60, and p204, the relative levels of upregulation differed significantly between cells in the three environments. Supporting these observations, the induced chemokine and cytokine profile also differed. These data emphasize the importance of testing multiple models before generalizing to tissue or in vivo responses.

# Numerical analysis of accumulation of residual transmembrane potential during high frequency electroporation

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Measurement of cell transmembrane potential (TMP) is complicated during fast charging and relaxation phenomena. Therefore, numerical methods are applied for evaluation of the TMP changes in cells. In this work, the high frequency ( 1 MHz) electric fields are studied and the phenomenon of rapid membrane charge accumulation, which is non-occurrent during conventional low-frequency electroporation is simulated using finite element method (FEM). It is shown that the medium conductivity has a strong influence on the electroporation phenomenon in the high-frequency range of electric fields. The study allowed to grasp the differences in polarization between 100 and 900 ns pulses and enabled successful prediction of propidium iodide electrotransfer into CHO-K1 cells. The conductivity-dependent patterns of MHz range electric field treatment outcome were determined. This work was supported by grant Nr. S-MIP-19-13 from Research Council of Lithuania.

# Numerical evaluation of the electric field distribution in an ECT-testing platform

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The electric and magnetic fields, although they have been the subject of discussions concerning their being harmful, can be usefully used in different applications: among all of them, they can be of considerable help in Electrochemotherapy (ECT). The Pulsed Electric field (PEF), in fact, facilitates the transport inside the diseased cell of drugs that normally are not permeating, allowing a localized harmful effect and consequently, a low chemotherapeutic content. ECT exploits the electroporation, also called electropermeabilization, that is a technique used to increase the permeability of the cell membrane. The electroporation (EP) is based on the use of an electrical field applied to cells in order to create temporary pores in cell membranes.
Depending on the intensity of the field and the nature of the tissue, the effects can be temporal (in this case the electroporation is called reversible (RE), in which the opening of the pores is temporary and allows the cell not to die, reaching the electrochemical balance of the cell in a final phase) or permanent (i.e. irreversible electroporation (IE) in which the electric field has a higher intensity than that used in the reversible process: the pores that are formed are permanent and lead to cell death).
Moreover the efficacy of the ECT treatments is strictly linked to the field uniformity in the tissue.
The development of new drugs involves several preclinical tests to verify their effectiveness, also in the case of drugs to use in ECT. The case of a 9 cells well-chamber is considered as experimental set-up for testing tissues subjected to the standard ECT protocols (8 pulses, 100usec Pulsed Electric Field of 500V/cm amplitude, 1Hz and 5kHz of frequency) in presence of different drugs amount. The hypotesys of powering one-cell at time with a parallel-plate electrodes is considered. The behaviour of the electromagnetic field in the wole platform is analyzed by means of a COMSOL developped 3d model. The field uniformity and the fringing effect of the powered cell is analyzed by time solving the electroquasistatic approximation of the Maxwell equation with the AC/DC module. The electric field in the unpowered cells is tested and evaluated in oder to numerically exclude the influence of the delivered PEF on the tissue-drugs combination here contained. The numerical results will be used to optimize and support the planned experimental phase.

# Numerical investigation of electroporation therapy on atrial fibrillation

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Cardiac electrophysiology describes and models chemical and electrical phenomena taking place in the cardiac tissue. The electric wave propagating in the cardiac tissue can be represented by a nonlinear reaction-diffusion partial differential equation –coupled with an ordinary differential equation representing cellular activity– called the bidomain model [1,2]. Atrial fibrillation is the most common serious abnormal heart rhythm, for which ablation is the main treatment. Generally, ablation is performed by thermal and centrifugal energy deposit such as radiofrequency or cryotherapy through a catheter, to destroy a small area of cardiac muscle in order to isolate the source of fibrillation and thus disrupt the arrhythmia. The drawbacks of such therapies lie in the fact that
it is difficult to estimate the boundaries of the treated region. This may lead to under treatment, or worse, irremediable burning of functional regions of the heart.
Recently electroporation has emerged as a promising alternative that may overcome the drawbacks of thermoablations.
In this paper, we investigate numerically the impact of electroporation on the atrial fibrillation. Electroporation is a complex phenomenon that occurs when biological tissues are subjected to electric pulses. It makes it possible to kill directly the cells in a target region. Numerical modeling of the electric field magnitude allows us to evaluate the impact of electroporation on the heart electric wave propagation. Thanks to well-designed partial differential equations [3,4], the computation of the distribution of the electric field is performed, providing a numerical evaluation of the electric field distribution. Our numerical study provides a numerical estimation of the influence of a local electroporation ablation on the propagation of the cardiac potential on realistic geometries.

References:
[1] L. Tung. A bi-domain model for describing ischemic myocardial d-c potentials. Massachusetts Institute of Technology. Dept. of Electrical Engineering and Computer Science, 1978.
[2] A. Collin, J.-F. Gerbeau, M. Hocini, M. Haïssaguerre and D. Chapelle. Surface-based electrophysiology modeling and assessment of physiological simulations in atria. FIMH, 2013. Lectures Notes in Computer Science. Volume 7945.
[3] G. Jankowiak, C.Taing, C. Poignard, A. Collin Comparison and calibration of different electroporation models - Application to rabbit livers experiments. To appear in ESAIM: Proc (2020).
[4] D. Voyer, A. Silve, L. M. Mir, R. Scorretti, and C. Poignard. Dynamical modeling of tissue electroporation. Bioelectro- chemistry, 119:98 – 110, 2018.

# Numerical modeling of DNA plasmid transfection by Electroporation

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Plasmid DNA vaccination combined with electroporation (EP) provides a promising approach for the prevention of infectious diseases and for cancer immunotherapy. This technology generates an immune response due to an enhancement in expression of specific encoded antigens. The use of pulsed electric field to vectorize the plasmid presents an efficient biophysical tool for DNA transfection without healthy risk as for viral gene transfection. Such gene transfection may be greatly improved by advanced numerical modeling. Indeed, in silico gene transfection can provide (theoretical) optimized protocols that can be tested in vitro and in vivo. The aim of this paper is to present recent advances that addresses gene transfection by EP at the cell scale and at the tissue scale.
At the cell scale, the passage of DNA plasmids from extracellular matrix into the cell cytoplasm thanks to the effect of the pulsed electric field is described as well as the intracellular traffic of plasmids enhanced by a network of microtubules, from the cytoplasm towards the nucleus [1]. We exhibit and quantify numerically the role of microtubules on the plasmid transport up to the nucleus. At the tissue scale we describe the intramuscular gene transfection protocol that combines EP with the injection an enzyme degrading the extracellular matrix [2]. The model combines the poroelastic theory of mixtures with the transport of enzymes and DNA in the extracellular space [3]. The protocol is then optimized numerically by nonlinear optimization procedure [4]. As a result, the numerically optimized protocol may improve the DNA distribution within the muscle of 30% the DNA distribution. These results have to be confirmed but they demonstrate the high potential impact of computational science in the field.

References:

[1] M. Leguèbe, M.G. Notarangelo, M. Twarogowska, R. Natalini, C. Poignard, Mathematical model for transport of DNA plasmids from the external medium up to the nucleus by electroporation, Mathematical Biosciences, Vol. 285, 2017.
[2] E. Signori, K. Wells, V. Fazio, D. Wells. Optimisation of electrotransfer of plasmid into skeletal muscle by pretreatment with hyaluronidase—increased expression with reduced muscle damage. Gene Therapy Journal. Vol. 8, 2001.
[3] M. Deville, R. Natalini, C. Poignard. A Continuum Mechanics Model of Enzyme-Based Tissue Degradation in Cancer Therapies. Bull. Math. Biol. Vol. 80, 2018.
[4] D. Peri, M. Deville, C. Poignard, E. Signori, R. Natalini. Numerical Optimization of Plasmid DNA Delivery Combined with Hyaluronidase Injection for Electroporation Protocol. Computer Methods and Programs in Biomedicine, Vol. 186, 2020.

# Numerical Modeling of Electroporation Process Using Endocardial Catheter

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This paper is about electroporation using an endocardial catheter. It is focused on numerical modeling of the electroporation process inspired by in vivo experiment. Two electroporation models are compared; model with electric conductivity dependent and independent on the electric field intensity. Further, it also demonstrates the effect of the flowing blood on obtained results.

# Numerical simulation of impedance cardiogram changes in case of type B aortic dissection to monitor false lumen thrombosis

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Aortic dissection is a hazardous aortic disease with high mortality. The formation of aortic dissection is commonly initiated by the dilatation of the aorta or high blood pressures which tear the intima, allowing blood to flow into the aortic wall. Due to the pulsatile pressure in the aorta, the layers of the aortic wall get separated. Thus, a false lumen develops while the true lumen remains for the usual passageway of blood. Subsequently, the local hemodynamic conditions in the false lumen may contribute to the formation of a thrombus. The stage of thrombosis affects patients' prognosis and survival. Therefore, an easy-to-use permanent monitoring method would be extremely beneficial. Impedance cardiography is proposed, which is a non-invasive method to evaluate several cardiodynamic parameters and allows identifying and quantifying conductivity changes by measuring the impedance on the thorax during a cardiac cycle. Since the conductivity of the blood-filled aorta is much higher than that of the surrounding tissue types, the changes in the measured impedance are strongly related to the changes in the aorta. Aortic dissection alters the aortic shape as well as the blood flow. The latter affects the blood flow-induced conductivity changes, which is one of the primary sources of the impedance cardiogram, i.e. the first time derivative of the electrical impedance.

A 3D numerical simulation model with simplified geometry of the thorax has been set up in COMSOL Multiphysics. Here, the impedance cardiogram changes on the thorax surface in case of a type B aortic dissection (the false lumen on the descending part of the aorta) are computed. Depending on the location and the size of the thrombus in the false lumen, i.e. the thrombosis stage, the portion of the volumetric flow rate can vary in the false lumen and true lumen. Besides, the electrical conductivity of the thrombus is much lower than that of the blood. Therefore, several stages of the thrombosis have been adopted to the false lumen in the simulation model. Impedance cardiograms are computed from the simulation models with different stages of the thrombosis. Comparison of these results shows that in the first stages of the thrombosis, the variation of the impedance cardiograms might not be noticeable. However, as soon as the thrombus grows and creates remarkable pathological changes in the cardiovascular system, it is possible to track the thrombosis by impedance cardiogram monitoring.

# Numerical Simulation of Langmuir-Hinshelwood Mechanism for Heterogeneous Biosensors in Microfluidic Channel

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Use of heterogeneous biosensors in microfluidic channels for diagnostic and detection of diseases in early stages, is a novel, relatively cheap and applicable solution for saving lives and health purposes. It has attracted great interest in experimental field and a lot of works are being done in order to reach better biosensors with reliable results and fast detection. A comprehensive numerical model of Langmuir-Hinshelwood mechanism would help speeding up the process of design and analysis of biosensors. For this means we have developed a code in Fortran to simulate flow inside a microfluidic channel combined with Langmuir-Hinshelwood reactions on the surface of the biosensor. Control-volume based finite-element method (CVFEM) with high order discretisation has been used to solve full Navier-Stokes equations with chemical reactions on the biosensor. Results has been validated with existing experimental data from literature. The influence of target concentration as well as the inlet velocity (flow rate replica) on the biosensor saturation time, moreover, investigated in this study. The results show that as the inlet velocity and concentration increases the time that concentration on the surface of biosensor reaches its asymptotic value decreases, although increase in inlet velocity does not have any effect on dissociation stage of binding cycle.

# Numerical study of safety and feasibility of electroporation-based treatments adjacent to implanted cardiac pacemakers

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The use of electroporation-based treatments is currently contraindicated for patients with implanted cardiac pacemakers if the treated zone is in proximity of the pacemaker. In this study we numerically investigated the influence of the presence of a metal-encased pacemaker on the effectiveness and safety of electrochemotherapy (ECT) and irreversible electroporation (IRE) ablation of a subcutaneous tumor. A simplified anatomical model was developed and separate electrode configurations and pulse delivery protocols were used for each treatment scenario. The effect of the pacemaker on treatment outcome was evaluated in three different situations for each treatment scenario: pacemaker is in electrical contact with one of the electrodes, pacemaker is present but without contact and a control situation without the pacemaker. A previously designed numerical framework for planning electroporation-based treatments was adapted for the computations of electric field distribution and heat dissipation in tissue. The presence of the pacemaker has a similar effect in both treatments (ECT and IRE ablation). Without contact with the electrodes the presence of the pacemaker does not significantly affect the delivered electric current when compared to control situation. Changes in electric field distribution are mainly observed in nearby healthy tissue, while electric field in the tumor remains mostly unaffected. Furthermore, no additional heating was observed in tissue. When the pacemaker is in electrical contact with one of the electrodes an additional current draw is observed, with the calculated electric current approximately 50 % higher when compared to control situation. In both treatments the resultant electric field is overall higher and a significant amount of IRE phenomenon is observed in healthy tissue adjacent to the point of contact. Higher temperatures are also observed in the vicinity of the electrodes in both treatment scenarios, however the temperature rise is much higher in case of IRE ablation. In this simple model geometry the presence of a metal-encased pacemaker does not negatively affect the outcome of ECT and IRE ablation in terms of sufficient tumor coverage. Electrical contact between the pacemaker and one of the electrodes however, results in a higher percentage of IRE phenomenon in both treatments and a significant rise in temperature near the electrodes. In clinical setting no critical anatomical structures are present in immediate proximity of an implanted pacemaker therefore, based on our preliminary results, we can conclude its presence should not impair treatment feasibility or safety. However, increased current draw may cause interruption of pulse delivery if the current exceeds the hardware limit.

# Objective usability validation of a learning management system for online training of laparoscopic cholecystectomy

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Introduction: An integrative Learning Management System (LMS) with the potential to connect external assets for technical and nontechnical skills training in minimally invasive surgery (MIS) has been implemented. Didactic contents for a laparoscopic cholecystectomy case study have being integrated in this LMS. This study aims to perform an initial objective usability validation (user-friendliness) of the LMS beta release.

Methods: Expert MIS surgeons were asked to complete a set of tasks on the LMS within a limited time to obtain the following Key Performance Indicators (KPIs): 1) average number of clicks to perform a task, 2) conversion rate (CR), defined as total number of users that fulfil the task divided by the number of users, 3) average time to perform a task, 4) average number of clicks to reach a function, and 5) efficiency, defined as the minimum number of clicks to perform the task divided by the number of clicks to perform the task.

Results: The KPIs obtained by three experts after performing the tasks in the LMS show that all participants (CR: 1.00) completed the steps of the procedure of the case study with high efficiency (0.62), as well as the logout (CR: 1.00, efficiency: 0.67). 2 out of 3 participants registered on the platform and logged in correctly (CR: 0.67), although needed more time and clicks than expected (efficiency: 0.41). The synchronization of external assets resulted in CR: 0.67. Finding a term in the glossary of anatomy was achieved by 1 out of 3 participants (CR: 0.33), with a high number of clicks and time (efficiency: 0.09). No participant completed the change of password neither created a topic in the forum within the time limit. The average number of clicks to reach each function was low, except for changing the password (10.67).

Conclusions: This objective usability validation has shown that the beta release of the developed LMS has contents and external assets easily accessible with a few clicks. While the registration, login and logout in the platform offer no problems, the access to the glossary, user profile settings and forum topics should be improved. With these improvements, and with the fact that this LMS allows programming training activities, having access to ubiquitous learning and monitoring progress on learning experience, one could use this LMS to standardize training across Europe, favouring mobility of professionals and the exchange and co-creation of knowledge in MIS.

# On the need for spatial whitening of high-density surface electromyograms in motor unit identification by neural networks

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In recent years, many new decomposition methods for identification of motor unit (MU) firings from high-density surface electromyograms (HDEMG) have been developed, with recent attempts focused on the use of different neural networks (NN). In this study, we evaluated the need for HDEMG signal whitening in NN-based MU identification. For this purpose, we analyzed the learning efficiency of two different types of NN, namely dense NN and long short-term memory (LSTM) NN, on the same HDEMG signals, with and without spatial whitening applied to them. All the HDEMG signals used were simulated with advanced HDEMG simulator, providing a full control of MU firing patterns and MU char-acteristics in our test environment. Spatial whitening of HDEMG signals signifi-cantly improved the precision of MU identification, regardless of the type of NN tested. For dense NN, precision of identified MU increased from 32.2 ± 20.2 % to 93.1 ± 8.7 %, whereas miss rate decreased from 48.4 ± 23.9 % to 12.0 ± 13.3 % when whitening of HDEMG signals was employed. For LSTM NN the preci-sion of MU identification increased from 59.7 ± 19.7 % to 99.4 ± 2.0 % whereas miss rate decreased from 43.1 ± 22.3 % to 12.7 ± 9.7 % with whitening.

# On the reuse of motor unit filters in high density surface electromyograms with different signal-to-noise ratios

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We test the reuse of motor unit (MU) filters estimated by the Convolution Kernel Compensation (CKC) method from high-density surface electromyograms (HDEMGs) with different signal-to-noise ratios (SNRs). During the learning phase the MU filters are extracted from HDEMGs with four different SNRs, namely $\infty$ dB, 30 dB, 20 dB and 10 dB. The MU filters are then applied to HDEMG signals at the different SNRs, yielding the MU spike trains. We report mean precision and miss rate of MU firing identification. In order to test the sensitivity of MU filter learning to the length of the HDEMG signals, we repeated the experiment at 5 s and 15 s long learning sets of HDEMG signals.

The number of identified MUs decreased from about 12 MUs, when using MU filters learned on 15 s long HDEMG signals with SNR of $\infty$ dB, to about 3 MUs, when using filters learned on HDEMG signals with SNR of 10 dB, no matter how much noise was present in the MU filter application phase. However, if there was no or little noise present in the MU filter learning phase then a decrease in precision and an increase in miss rate was observed when MU filter was applied to the HDEMG signals with a lot of noise. The opposite was true when large level of noise was present during the MU filter learning, but no or little noise was present in the MU filter application phase.

# On Visualization and Quantification of Lesion Margin in CT Liver Images

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Cancer is the one of the leading causes of death worldwide, and cancer incidence increases every year. The analysis of lesion margin is quite important to diagnose malignant and benign masses and to detect the presence and the stage of tumor invasion in case of cancer. Accordingly, the aim of the study is to visualize and quantify margin of lesions in radiological images by means of a digital computer. In this study, computed tomography (CT) images of liver were employed for analysis because the liver has crucial tasks in our body and liver cancer-related deaths is ranked as the forth among the cancer-related deaths. The proposed method consisted of four main steps: image cropping and smoothing, specification of target lesion, the boundary detection of target lesion, and visualization and quantification of margin. First, the images were converted to gray scale. The blank regions surrounding the liver in CT images were removed before specification of target lesion, and further were smoothed with a bilateral filter. Next, the target region was specified roughly by drawing it manually. The boundary of lesion was more precisely determined with the active contour method employing the sketched borderline as the initial curve. Next, the properties of the target region: the centroid, major axis length, and the orientation values were computed. The intensities along a line passing through the center of the tumor were obtained for eighteen different rotation angles. A pulse model was fit to each of the intensity signal corresponding to a rotation. Then, the intensity change, margin sharpness and width were acquired from the pulse approximation associated to each rotation angle. The level difference provided the intensity change, the slope of edges gave the margin sharpness, and distance between the start and end points of the pulse edge represented margin width. Besides, the inner (core) and outer diameter with respect to angle were also displayed.

# Open Source Robust Machine Learning Software for Medical Patients Data Analysis and Cloud Storage

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Big data and artificial intelligence-based researches in the health care arena have radically changed the sector with better preventive health care, early diagnosis of diseases, and advanced assistive technology along with numerous other areas. Health care facilities, academic research centers, and industries are collaborating in developed countries on such researches in the field of health care. At the same time developing and underdeveloped countries have lacked behind in this field of research due to infirm health and e-health infrastructure, insufficient technical manpower, low physicians to patient ratio along with a great many other limitations. Our research focuses on developing an open-source and easy to use Machine Learning Software System that should uplift Big Data and data science researches focusing on health care in the developing and underdeveloped countries amid such obstacles. Apart from medical data analysis, it could serve as an efficient platform for storing patient data in hospitals of lower-income localities. Along with that, our research group hopes academicians, professionals, and physicians around the globe will be aided by such robust data analysis software, as it facilitates automated preprocessing of data, building of prediction models, comparison of different prediction models, cloud storage of data and implements numerous advanced data visualization techniques.

# Optical projection tomography for particle counting and morphology analysis

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Optical projection tomography (OPT) is a powerful technique for imaging in developmental biology. It is similar to X-ray computed tomography where shadowgrams of rays transmitted through sample are recorded and, based on these shadowgrams, the internal structure of the sample is reconstructed. In OPT however, light is used instead of X-rays, and hence the effect to the sample is practically negligible in many cases. OPT can also be used in fluorescent mode, where emission of the excited fluorescent markers is imaged. The optical instrumentation, consequently, imposes blurring into sample details outside the focal plane of the imaging objective. To increase the quality of the tomographic reconstructions, we incorporated light beam model into the reconstruction process, both in transmission brightfield and in fluorescent emission modes. In this work, we quantitatively compare the performance the new models with that of conventional filtered backprojection. We also provide the related data and codes.

# Optimal positioning of limited number of OPM sensors in MEG

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Standard magnetoencephalographic (MEG) systems are based on a large arrays of SQUIDs (superconducting quantum interference devices) that measure MFMs (magnetic field maps) produced by electrical currents in the brain. These systems need expensive cooling and have fixed sensor locations. As an alternative, OPMs (optically pumped magnetometers) operate on the room temperature and can be placed individually much closer to the head surface. In the standard MEG recordings, we typically encounter the problem of redundancy and uniqueness of signal information contained in a large number of sensors. In this study, we applied the iterative statistical technique (IST) developed by Lux [1] to estimate a transfer matrix that optimally determined measured MFMs from a limited array of measuring channels. This estimator minimizes the RMS error of the estimated map and is based on iteration where on each step the channel that has the highest correlated power with all other channels is selected. We first apply IST on data sets of 14 AEFs (audio evoked fields) measured on 8 healthy volunteers by SQUID MEG system consists of 125 gradiometers measuring only radial component of the magnetic field normal to the head surface. Since we have not had enough OPMs yet to measure full MFMs, we made simulation of OPMs detecting both radial and tangential components of the magnetic field on 80 measuring sites close to the head surface. Simulated OPM MFMs were calculated from MNE (minimum norm estimation) of current distribution of the brain surface calculated from MFMs measured by SQUID MEG system. We have tested IST on various protocols, like taking into account the whole head MFMs or only one side of the head, measuring only one component or combination of both for OPM data, fixing some measuring sites in advance, etc. In all cases we found than most of the information content is in the first 15 to 20 optimally selected channels. The database of our study consisted of measurements and simulations of AEF signals, which have mainly focal origins. The natural extension of this study could include signals that have more complex sources.

[1] R.L. Lux, C.R. Smith, R.F. Wyatt, J.A. Abildskov, IEEE Trans. Biomed. Eng. 25, 270-276 (1978).
[2] Numminen, J., Ahlfors, S., Ilmoniemi, R., Montonen, J., Nenonen, J.: Transformation of multichannel magnetocardiographic signals to standard grid form. IEEE Trans. Biomed. Eng. 42(1), 72–78 (1995).

# Optimization of Phototherapy Machine for advanced Treatment of Neonatal Jaundice

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Neonatal jaundice is a medical condition in which high number of unconjugated bilirubin exists in infant's blood resulting in yellowish color of baby's skin and whites of the eye. It is a very common condition worldwide occurring in up to 60% of term and 80% of preterm newborns in the first week of life. Unconjugated bilirubin is potentially toxic to neural tissue both brain and spinal cord. Even though hospitals use phototherapy machine to treat hyperbilirubinemia, there are a numbers of gaps on the machine related to its effectiveness. Among the gaps long hospitalization time, biological hazards from strong optical radiation and limitation to higher hospitals are the major ones. The main objective of this research work was to optimize phototherapy machine for advanced treatment of neonatal jaundice. Before optimization activities, necessary clinical study was performed and the results from the clinical study are used as an input for optimization work. Among the outcomes the reason phototherapy machine is limited to hospital level is the absence of laboratory test at health center level. Beside this the existing laboratory test at hospital level is invasive and uncomfortable for infants. In addition to this there is no treatment progress indicator and light intensity measurement system on existing devices. The optimization work included integration of non-invasive bilirubin measurement, light intensity measurement, back treatment and different power supply options to overcome the gaps. The actual device using 465 nm light emitting diode was developed and tested against specifications. Non-invasive measurement system avoids invasive bilirubin measurement, comfortable and makes tracking treatment progress easier. Addressing all skin surface of baby by the device improves treatment efficiency and plays vital role in baby to mother bond as it reduces treatment time. Implementation of this technology will solve the existing problem in advanced way.

# Pancreatic Cancer and its Correlation with Embryogenesis: Identification of Biomolecular Markers using Machine Learning Methods

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Pancreatic cancer is a highly lethal disease, projecting to be the second leading cause of cancer-associated deaths. It is considered as one of the most aggressive types of cancer, with one of the major problems reported being the lack of early detection. A patient is diagnosed with pancreatic cancer only in advanced stages, when the possibility of developing a metastasis is high. There is no standard procedure to diagnose high risk patients, since they remain asymptomatic in the cancer's early stages. Based on the accumulated evidence revealing remarkable parallels in key biological signaling pathways that govern embryonic development and cancer, we sought to extract significant genes at the intersection of these two processes, aiming to identify new tumor markers for pancreatic cancer. Specifically, the aim of this work is to apply machine learning methods to identify biomolecular markers that are differentially expressed in pancreatic cancer patients and correlate them with markers from embryogenesis. After extracting such markers, we use them as predictors within different machine learning methods. Our work contributes a "25 gene signature" of biomolecular markers, which are involved in signaling pathways found in both embryogenesis and pancreatic carcinogenesis, obtained via feature extraction and feature selection methods. These markers are used in classifiers for pancreatic cancer classification and two machine learning models are tested, with good results. We finally justify the notion that our "25 gene signature" can play a classification role in discriminating patients with pancreatic cancer from healthy controls.

# PathMiner: An Intelligent Platform for Diagnostic Pathology

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The capacity to distinguish among subclasses of disease affects how patients are treated, which medications are appropriate, and what levels of risk are justified. Unfortunately, inconsistencies often arise during the evaluation process as a result of subjective impressions and inter- and intra-observer variability. Advanced imaging and informatics tools now make it possible to detect and track subtle changes in measurable parameters leading to insight regarding the underlying mechanisms of disease progression and the discovery of novel diagnostic and prognostic clues which are not apparent by human inspection alone. In several recent studies, investigators have reported the use of modern machine-learning methods to automate the process of grading and classifying prostate cancer and colon cancer among other disease states. However, multiple experiments suggest that using a single modality of features (e.g. image signatures) may not offer sufficient discriminatory power for rendering accurate staging of some diseases such as breast cancer. The overarching objective of this work is to develop, evaluate, and maintain the PathMiner hybrid platform including a portable toolset for intelligent archiving, and automated decision support in pathology. To enable the system to automatically circumscribe the boundaries of tumor regions throughout the specimens, we developed a regional segmentation algorithm based on deep convolutional neural network (DCNN)-based machine-learning. The algorithm performs pixel-wise region classification using a sliding window mechanism. The trained DCNN consists of two convolutional layers; two max-pooling layers; one fully connected layer of dimension 64; and one output layer. The current prototype system supports submission of queries to automatically locate and retrieve digitized pathology specimens and correlated genomic studies of those cases from within a well annotated reference library that exhibit spectral and spatial profiles which are consistent with the query. Preliminary feasibility results focused on distinguishing benign from cancerous breast tissue showed that Gentle Boosting using an eight-node CART decision tree as the weak learner provided an overall accuracy of 81% using only 33% of an ensemble of test signatures as the training set. These experiments further showed that maximal margin classifiers, such as boosting, performed significantly better than several other approaches including KNN. By utilizing Kubernetes as the orchestrator for containerized solutions, our team plans to migrate PathMiner workflows seamlessly between on-premises and commercial cloud including the Google Cloud Platform.

# Patient identification workflow for seamless EHR access during patient follow-up

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Patient Generated resources have been proved to be key for the future of the medicine. Thus, the acquisition of these resources must be as smooth and transparent as possible to ensure that patients collaborate on their collection. However, aligning usability with the restricted security and privacy requirements in healthcare information systems might not be an easy task. In this work we propose a two-step authentication and authorization workflow, that relaying on state-of-the-art standards, performs a seamless EHR access to store the data gathered during the patient daily follow-up. It combines a long-term login using strong authentication mechanisms with a just-in-time authentication and authorization that takes advantage of the identifying capabilities of some signals that are usually recorded by patients. A new OAuth grant type has been designed to that end. We finally discuss about the usability and security of the proposed approach and conclude that easing the data collection it is expected to increase patient's implication with the follow-up.

# Patient-friendly speech recognition feedback for aphasia patients

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Prior studies have shown that personalized, tablet-based home practice is effective in the recovery of word finding difficulties in aphasia patients. Currently existing applications for such speech practice rarely include feedback or are not based on a recorded utterance. To improve training motivation, speech recognition might be used for the assessment of naming performance. In order to decrease incorrect feedback a speech recognition-based method is introduced avoiding misstatements, especially in case the spoken word is not determined with full confidence.
A speech recognition model based on Kaldi ASR toolkit was built with a lexicon of 32 standard German words from 162 healthy subjects (2352 audios). It was evaluated with a 10-fold cross-validation. The model-output gives the words back with the Kaldi-probability. To test false-positive and true-negative rates, the results of the cross-validation and 4352 additional audio-recordings of different German words were used.
A third response option "unsure" was introduced in the decision algorithm besides "correct" and "wrong". For the categorization, the best three Kaldi-probabilities are considered. If they contain the searched word and if the corresponding probability is higher than a defined threshold, it is categorized as correct otherwise as unsure.
Thresholds between 0.60 and 0.99 have been investigated with an increment of 0.01. Results were compared to binary classification.
The binary classification resulted in an overall word-error-rate (WER) of 4.39%. For the different thresholds 0.65, 0.80, 0.99 with the ternary classification the WER was 2.49%, 2.39%, 2.03% and the unsure-rate 4.0%, 4.59%, 7.25%. This resulted in a decrease of the WER compared to the binary classification of 43.3%, 45.6%, 53.8%.
Between a threshold of [0.65, 0.74] the number of false-positives moved into the unsure group was constant, while the number of moved true-positives increased. Above a threshold of 0.70, the number of moved false-positives was higher compared to the moved true-positives.

# PCA-based metric reduction for model evaluation in polyp segmentation

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Colorectal cancer is a main death cause worldwide. Early detection of polyps in colonoscopic images can benefit from applying Fully Convolutional Neural networks for semantic segmentation. However, metrics are arbitrarily used to measure performance, precluding methods comparison.

We used a U-Net and transfer learning for polyp segmentation to obtain:

- Model 1 (M1), trained with CVC-EndoSceneStill: 912 images with precise binary mask (547 for training and 183 for validation).

- Model 2 (M2), trained with CVC-VideoClinicDB: polyps approximated with ellipses (10.018 images for training and 1.859 for validation).

- Model 3 (M3), finetune M2 with CVC-EndoSceneStill.

We analysed state-of-art 9 metrics: Intersection over Union (IoU), mean global accuracy (MGA), Dice, precision, recall, specificity, F1-score, F2-score and area under the curve (AuC). Test set of CVC-EndoSceneStill has been used to evaluate all models. A principal component analysis (PCA) was performed on the metrics calculated for each model to identify non-correlated variables, allowing for dimensionality reduction and maximization of the included variance. Resulting components were examined and only those with eigenvalues above 1 were considered.

PCA allows clustering metrics into 2 groups for all models, so we can define:

I1=min{MGA,precision,specificity}

I2=min{recall,F1_score,F2_score,IoU,DICE,AUC}

Conservatively, the minimum was chosen. The 9 metrics do not clearly rank models: M1 performs better in MGA (93.37±9.95), precision (82.96±21.98) and specificity (98.03±4.01); M2 in AuC (95.78±9.63); and M3 in IoU (95.78±9.63), Dice (77.70±25.01), recall (83.14±26.85), F1_score (79.88±21.63) and F2_score (81.80±22.06). Contraryly, the PCA-based indicators clearly show that M3 outstands (best values for I1=78.25±25.19 and I2=69.01±27.43).

I1 and I2 can easily be plotted for visual representation. For model evaluation, the centroid of each model can be calculated: M1=(61.27,51.96); M2=(73.14,60.64); and M3=(77.72,68.51). The closer to (100,100), so perfect overlap, the better the model is.

Performance can be measured with 2 indicators that summarize 9 metrics, facilitating the results interpretation for model evaluation. For many test images, I1 and I2 are similar, so in those cases one metric would suffice. In all cases but one, I1>=I2, as I1 considers background, much larger than the polyp. The PCA-based indicators might serve as unified framework for measuring polyp segmentation algorithms.

# Performance Analysis of Sleep Stages Classification using Multiple Bio-signals

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The sleep is associated with both the central nervous system and autonomic nervous system of the human body. For optimal selection of feature parameter sets used in automated sleep stages classifiers, the multiple bio-signals including EEG (Electroencephalogram), EOG (Electrooculogram), EMG (Electromyogram), PPG (Photoplethysmogram), GSR (Galvanic Skin Resistance) and SKT(Skin Temperature) were analyzed. A total of 11 bio-signal combinations were evaluated using a Bayes' quadratic classifier. The EEG-based bio-signal combinations showed an average of 85% performance for the subject-dependent case and 87% for the subject-independent case, whereas the PPG-GSR-SKT combination among the PPG-based bio-signal combinations showed averages of 80% and 73% respectively for each of these cases. EEG is relatively difficult to measure and is sensitive to external noise in comparison with PPG. Therefore, bio-signal combinations that are based on the results of this study must be selected depending on the goal of examination. In applications requiring accurate sleep stage analysis, EEG-based signal combinations are suitable, whereas applications prioritizing measurement convenience rather than accurate sleep stage analysis like wearable or mobile applications PPG-based PPG/GSR, PPG/SKT, or PPG/GSR/SKT combinations are appropriate.

# Performance of automated melanoma diagnosis by adding lesion information to deep convolutional neural network

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Melanoma is a type of superficial tumor, which is highly malignant that 5-year survival rates decrease by 20% as the lesion becomes 1mm thicker. Early-stage melanoma is difficult to diagnose because it looks like a benign lesion. Even now, dermatologists still diagnose them visually, and their accuracy is reported to be around 80%. Therefore, there is a strong need for developing a quantitative diagnostic method. Many studies have been applied to a deep convolutional neural network (DCNN) to medical images. However, there was little discussion about which parts of the image those networks were focusing their attention on. The network developed in our previous study diagnosed some lesions without paying attention to the lesions. It is expected that the accuracy will be improved by adding a mechanism for our network to focus on lesions.

In this study, we developed an automatic melanoma diagnostic system using the DCNN and used Gradient-weighted Class Activation Mapping (Grad-CAM) to visualize the areas of DCNN's attention. We replaced any one of the three channels of the RGB image with the lesion image to pay attention to the lesion in the DCNN. In the lesion image, the lesion area has a brightness value of 255, and the others have a brightness value of 0. In addition to these, a 4-channel image was created by adding a region image to the RGB image.

1000 melanoma images and 1000 non-melanoma images were randomly extracted from the HAM1000 database. Inception-ResNet-v2 pre-trained with ImageNet was fine-tuned to differentiate melanoma from non-melanoma.

The accuracy of the original images and the images containing the lesion images were 83% and 82%, respectively. There was no significant difference between them. However, the addition of the lesion images improved the probability of Grad-CAM output overlapping the lesion from 53% to 73%. This result is hopeful because it is necessary to focus on the lesion for an accurate diagnosis. We will continue to examine means of paying DCNN's attention to the lesion.

# Pilot study of application of a hybrid transportable system for postural stability measurement in military professions

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Correct posture matters in everyday activities, without it one risks pathological deformities or fall injuries. Military professions consist of wide variety of specific duties, which can have specific impact on physical state. Therefore, it might be useful to monitor each military group for possible occupational disease. This study investigates stabilometric parameters in different groups of military professions with a hybrid transportable system designed and presented in previous study. The system comprises two Microsoft Kinect cameras and two Nintendo Wii Balance Boards, and it is used for evaluation of posture by measuring postural stability parameters, such as mutual position of spine vertebrae, center of gravity and center of pressure. Comparing different military professions, in this study particularly Airborne Troops, Castle Guards and Mechanized Infantry, statistically significant differences were found in center of pressure for anterior-posterior direction and in some of the mutual positions of defined anatomical points.

# Portable Arm Circumference Monitoring Device Design For Breast Cancer-related Lymphedema

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In many areas around the world, breast cancer is the most commonly diagnosed cancer among women. According to the CDC, more than twenty-four thousands new cases of breast cancer were diagnosed in 2016 in United States. Even though prevalence of breast cancer is high, the five-year survival rate of patients with breast cancer is approximately 90?ter appropriate therapy. Breast cancer is currently a well-controlled disease. However, treatment is associated with a series of complications for breast cancer survivors. Breast Cancer Related Lymphedema (BCRL) is one of the most common side effects of breast cancer and its associated treatments. In a systematic review including 30 clinical studies, overall incidence of upper limb lymphedema in breast cancer survivors was 21.4%. That is, more than one in five women who survive breast cancer will develop upper limb lymphedema. Currently, no measures are known with certainty to prevent lymphedema. However, earlier diagnosis and management better could limit the progression of BCRL. It is also a necessity to develop appropriate monitoring methods and devices for establishing comprehensive prevention and treatment strategies.

In this study, we designed one device can provide a faster and easier way to continuously measure the upper limb circumference and compliance for the breast cancer survivors. The device comprises a pull moving module, a longitudinal measurement module and a circumference measurement module. The pull moving module consists of a string encircling around the limb of an individual. The longitudinal recording module along the pull moving module can record the longitudinal axis of the limb and meanwhile the measures the length of the limb. When the first measurement module moving along the limb, the circumference module can record the lengths encircling the limb and thus determine the correlation between the limb length and the limb circumference. By applying a minimal stress, the compliance of limb reflecting the lymphedema can be recorded after careful calibration in a standard module.

The measurement accuracy can reach up to 0.1cm both in length and circumference measurement. The device has been available for in-home use of breast cancer subjects for time-course recording of BCRL. We hypothesize that lymphedema can be detected earlier through the device before the clinical symptoms of BCRL and upper limb dysfunctions develops thus can lead to earlier management and better outcome.

# Potentiation of electrochemotherapy's antitumor effect with peritumoral interleukin-12 gene electrotransfer varies according to tumor immune status

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Electrochemotherapy (ECT) is a well-established ablative therapy in Europe with a 60-90% response rate, depending on the tumor type. Despite high local effectiveness, a systemic antitumor effect (i.e. abscopal effect) of ECT has not yet been observed in clinics. The aim of the study was to test a new combined therapy including ECT with cisplatin, bleomycin or oxaliplatin and gene electrotransfer (GET) of plasmid encoding interleukin-12 (IL-12) in three immunologically different tumors. We hypothesize that in the combination, IL-12 boosts the in situ vaccination effect of ECT by recruiting effector immune cells.

To investigate if the antitumor effect varied according to the tumor immune status, the combined therapy was tested in three immunologically different murine tumor models: malignant melanoma (B16F10), mammary carcinoma (4T1) and colon carcinoma (CT26). Growth of primary treated tumors (B16F10, 4T1, CT26) and of distant untreated tumors in a dual-flank model mimicking systemic disease (B16F10, CT26) was followed. The therapy was performed when tumors reached 40 mm3 in volume. Subsequently, tumor and blood samples were collected for immunohistochemical and cytometric analysis of the tumor microenvironment and detection of IL-12.

In B16F10 melanoma, IL-12 potentiated the antitumor effect of ECT with equally effective low doses of cisplatin, oxaliplatin or bleomycin. However, we observed the most pronounced potentiation after ECT with cisplatin, resulting in 38% of complete responses as well as an abscopal effect. The antitumor effectiveness of this treatment combination could be ascribed to the induction of the local and systemic immune responses. Namely, infiltration of granzyme B positive effector immune cells was observed in both, primary and distant tumors. Furthermore, the combined therapy was also tested in two other immunologically "warmer" tumor models, 4T1 and CT26. The results indicate that the potentiation of peritumoral GET of IL-12 to ECT inversely correlates with the tumor immune status. We observed better responsiveness to ECT in immunologically "hot" tumors, where the addition of GET led to the lowest potentiation.

To conclude, peritumoral GET of IL-12 significantly potentiates ECT in treated melanoma tumors and has some effect on distant untreated tumors, predominantly when cisplatin was used for ECT. Effectiveness of the tested treatment combinations depends on the immunological status of the tumor. ECT was more effective in immunologically "hot" tumors but the contribution of peritumoral GET was higher in "cold" tumors.

# Predicting Dementia onset of Alzheimer's Disease Using Functional Principal Component Analysis of Longitudinal Trajectory Score

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Background: Alzheimer's Disease (AD) is a worldwide prevalent age-related neurodegenerative disease with no available cure yet. Early prognosis is therefore crucial for planning proper clinical intervention. It is especially true for people diagnosed with mild cognitive impairment, to whom the prediction of whether and when the future disease onset would happen is particularly valuable. However, such prognostic prediction has been proven to be challenging, and previous studies have only achieved limited success.
Methods: In this study, we seek to extract the principal component of the longitudinal disease progression trajectory in the early stage of AD, measured as the MRI-derived structural volume, to predict the onset of AD for mild cognitive impaired patients two years ahead. The application of the method is evaluated by measuring the accuracy of predicting the disease onset one and two years in advance in a 5-fold cross-validation framework.
Results: The sign of the FPC curve indicates the direction of variation in the change of the trajectory along time. The first FPC captures more than 95% of the total variation of all the evaluated structures, with each following FPC capturing the largest proportion of the remaining total variation. The AUC for predicting the disease onset is 0.818 for one year towards conversion and 0.802 for two years towards conversion. Using the AD group to train the FPC269model results in a significant improvement in the classification power compared with the model with CN- or MCI- based FPC features. The inclusion of the CN and MCI reference groups on top of the AD data leads to mild improvement.
Conclusion: The functional principal component scores enable us to build functional regression models and apply machine-learning methods for predicting the AD. The results of our study demonstrate the advantageous predictive power of the population-based longitudinal features to predict the disease onset compared with using only cross-sectional data based on volumetric features extracted from a single timepoint.

# Predicting vault size in Implantable Collamer Lenses (ICL) using deep learning

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Implantable collamer lenses (ICL) are a well-known alternative to refractive surgery in many cases, such as correction of astigmatism, myopia or hyperopia. The vault, defined as the distance between the ICL and the anterior crystalline lens surface, remains as a critical parameter to predict the success of the procedure. Our previous work using a central tendency statistical approach shows that there are 5 parameters statistically significant correlated to the vault: the lens size, angle-to-angle (ATA), crystalline lens rise, spherical equivalent and age. This work aims at predicting the vault size based on these set of metrics using deep learning architectures. Threshold for considering a prediction as correct is set at 200µm, as this is the variability between eyes for the same patient.

A database of 360 eyes of 360 patients have been used in this study. Using a 5-fold strategy, networks are trained using 80% of the data, while the remaining 20% is used for validation. Several architectures have been used, varying the number of layers (3 or 4 blocks of dense layer+batch normalization+activation layer+dropout), the activation function (rectified linear unit -ReLU- or hyperbolic tangent -tanh-) and the optimizer (Adam or RMSprop). The networks have been trained for 2000 epochs, with a learning rate of 0.001 and a dropout rate is set at 0.5.

After testing, the best model is composed of 3 blocks, using tanh as activation function and RMSprop as optimizer. In this case, the network correctly predicts the vault in 56.11%±0.02 (range: 58.33%-52.78%). The same network optimized with Adam obtain the same performance with slightly higher variability (56.11%±0.03). It is also important to remark that the worse performance is still higher than 50%. On the other hand, the best model explains 28%±0.1 (range: 42%-18%) of the vault's variability, slightly below other linear regression models.

Based on these results, vault size might be predicted with a certain degree of precision by the deep learning models proposed in this study. As far as the authors know, this is the first work that predict the vault size using deep learning. Further work is still required to obtain more training data or test the trained models in a larger database in order to increase the vault's variability explained by the model.

# Preliminary evaluation of a novel language independent speech-in-noise test for adult hearing screening

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This article presents a preliminary evaluation of a novel language independent Speech-in-Noise test for adult screening in terms of Speech Reception Threshold (SRT) estimates and prediction of hearing sensitivity.
The test is based on multiple-choice recognition of meaningless Vowel-Consonant-Vowel words and was administered to 26 normal hearing young adults and 58 unscreened adults who also underwent pure-tone audiometry. Receiver operating characteristics were built using the World Health Organization criteria for "slight/mild" and "moderate" hearing loss as gold standards and SRTs as test outcome. Both curves showed very good test performance in predicting success/failure in pure-tone audiometry (area under the curve: 0.79 for "slight/mild" and 0.83 for "moderate" hearing loss). A complete generalized linear model including SRT, age, and their interaction showed that the SRT and the interaction between SRT and age were significant predictors of pure-tone audiometry outcomes, whereas age alone was not a significant predictor of the degree of hearing loss. Moreover, preliminary results from test-retest data showed that the test was reliable in repeat-ed measures (Spearman's rank-order correlation coefficient = 0.72; Cohen's kappa = 0.83 for "slight/mild" and 0.64 for "moderate" hearing loss). Further research is needed to fully assess test performance in a larger sample of participants, also including subjects with higher degrees of hearing loss (e.g. "severe" and "profound").

# Preliminary Results of a Numerical Model to Predict Heart Rate Variability Changes Following Cardiac Denervation and Later Reinnervation in Heart Transplant Patients

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Introduction: Heart transplantation (HTx) inevitably leads to cardiac denervation, which typically manifests in increased resting heart rates (HRs) and reduced heart rate variability (HRV). Although there is evidence for cardiac reinnervation, it is hard to be reliably assessed. HRV is often used as a non-invasive physiological marker to determine cardiac reinnervation. However, still, the underlying mechanisms giving rise to HRV in heart transplant recipients (HTxR) and the correlation with cardiac reinnervation are not fully understood yet.
Methods: To establish a quantitative relationship between cardiac reinnervation and HRV measures, we modified a numerical model of HTxR that we had previously developed, which integrates intrinsic and autonomic cardiac control into a closed-loop human cardiovascular system model. This model implements autonomic cardiac control governed by arterial baroreflex and pulmonary stretch reflex as proposed by Ursino and Magosso (Ursino et al., Am J Physiol Heart Circ Physiol, 2003), while the intrinsic HR control is realized as a Hodgkin-Huxley-type single-cell human sinoatrial node model (Fabbri et al., J Physiol, 2017). The model parameters of autonomic cardiac and intrinsic HR control were adjusted based on published clinical data, to reproduce temporal and spectral HRV measures of HTxR and a healthy control cohort at rest.
Results: The simulation results for both, HTxR and a healthy control group are in good accordance with the literature. Simulations of HTxR predict notably reduced SDNN of 4.3 vs 46.1 ms (literature, 5.8 ± 2.2 vs 50 ± 16 ms) and significantly diminished LF- and HF-power of 0.5 vs 740.3 $ms^2$ (literature, 0.5 ± 0.4 vs 519 ± 291 $ms^2$) and 11.1 vs 539 $ms^2$ (literature, 10.8 ±8.1 vs 657 ± 777 $ms^2$) respectively.
Discussion: The simulations predict substantial, yet not fully diminished HRV which is consistent with the findings in literature. The model suggests that the present LF-peak is a sign of sympathetic reinnervation, while for the presence of the HF-peak no clear conclusion could be drawn. Varying the degree of cardiac innervation in the model while observing the changes in spectral HRV measures may allow us to establish a relationship to quantify sympathetic and vagal cardiac reinnervation. Ultimately, this could aid clinicians to better assess cardiac reinnervation based on HRV obtained from patient electrocardiogram recordings.
Conclusions: The present model can predict denervation induced changes in temporal and spectral HRV measures and forms the foundation for future investigations that aim to assess the degree of cardiac reinnervation through progressive changes in HRV

# Prevention of musculo-skeletal disorders during work by use of active exoskeletons

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Nowadays so-called exoskeletons (also known as wearable robotics, exosuits or power suits) gain more and more importance in working environments, to support tasks with heavy loads for workers. This is a fortiori relevant for tasks with high content of static postures coupled with heavy loads to lift (overhead) as well as for elderly or workers with limitations.
Due to high costs and several severe problems in certification of active systems, it is current state that only passive exoskeleton systems find widespread application in working tasks, mostly in companies in automotive engineering. Esp. SME or their workers could not currently participate on benefits of exoskeleton systems.
To bridge this gap between requirement for active systems to support concerned workers and a seemingly missing economic potential, quite new design concepts are necessary for the development of active exoskeletons. One possibility to solve this problem is to use the principle of modularization, by which it is possible to have one exoskeleton system, which is adaptable to different workers (with different shapes, conditions, requirements) and to different working tasks. Additionally, the use of bio-sensory concepts like sEMG to detect the current user's state regarding to muscular fatigue or prediction of wanted motions is promising.
We shall show the concept of an exoskeleton system for upper extremities that fulfils those above-mentioned requirements. Starting with an comprehensive overview of existing systems and a systematic to classify them, and a biomechanical analysis of upper extremity system from hand to limb, we show creation and layout of this exoskeleton system with sEMG biosensors and inertial measurement units (IMUs) for control of that system. The whole design process strictly follows the biomechatronic design process. We shall illustrate the control strategy with special focus on the use of sEMG data for prediction of planned motion and occurring muscular fatigue, and the use of IMUs to improve precision and give safety redundancy. We conclude with an overview of preventive possibilities of such a system, but also with pointing to problems and limits.

# Protocol stack for bidirectional communications in networks of wireless implants powered by volume conduction

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We are proposing the use of volume conduction to power wireless active implantable medical devices (AIMDs) deployed deeply within tissues using an external unit that delivers high-frequency (HF) currents through skin electrodes. The implants, which can be shaped as thin and flexible devices for percutaneous injection, pick up these currents and rectify them to power their electronics.

The safety standards with respect to human exposure to radiofrequency electromagnetic fields identify two risks of delivering alternating currents through the body: thermal damage (indicated as a limitation to the specific absorption rate (SAR)), and unwanted electrostimulation. For the former, it is proposed to deliver the HF currents in the form of bursts. For the latter, frequencies above 5 MHz are proposed, as from this frequency only SAR limitations apply. We have recently demonstrated that thin (diameter $< 1$ mm) and short (length $< 20$ mm) devices can obtain dc powers above 1 mW using HF current bursts that comply with the standards (IEEE Access 2020;8(1):37808-37820).

In addition to power transfer, the external unit can also send information to the wireless devices to control their behavior and receive information from them, as that required for closed-loop control. Since this information is transferred by means of volume conduction using the HF current bursts, ad hoc communication protocols are required to comply with the safety standards. In this context, we present a protocol stack intended for volume-conduction-based bidirectional communications. The layered architecture of the proposed protocol stack is based on the Open System Interconnection (OSI) model. In particular, four layers are defined.

L1 corresponds to the physical layer and encompasses the network topology and the signal transmission method. Its data unit is the bit stream.

L2 is the data link layer and is in charge of several tasks such as encoding, error detection and frame management. Its data unit is the frame.

L3 corresponds to the network and transport layer, and is responsible for addressing the implants (unicast, multicast and broadcast). Its data unit is the packet.

L4 is the application layer and encompasses the functional tasks of the implants (e.g., configuration, stimulation or test). Its data unit is the data (payload).

Regarding the bit-level encoding, each layer has its own headers for data encapsulation of the immediate higher layer.

We have tested the proposed protocol stack, both in vitro (using agar phantoms) and in vivo (with anesthetized rabbits), by performing bidirectional communications at 256 kbps.

# Prototype Hat as a Biofeedback System to Address Vestibular Balance Impairment

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Loss of vestibular feedback is considered a significant disabling factor among older adults. Studies show that prosthetic vestibular feedback in the forms of electro- and vibrotactile mechanisms expedite the treatment and recovery of vestibular feedback loss. We propose an alternative vibrotactile system in a hat that provides vestibular feedback to the skull based on signals from an accelerometer mounted on the hat. This work presents a proof of concept of our proposed wearable system and evaluates the balance performance of two healthy volunteers before and after wearing the hat. The balance performance evaluations were based on the Sensory Organization Test (SOT) protocol. Qualitative comparisons of balance performance show that our proposed system changes balance performance after wearing the hat for a short training session.

# Pulmonary Crackle Detection using the Hilbert Energy Envelope

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This paper presents a method for automatic pulmonary crackle detection based on the Hilbert energy envelope (HEE). Automatic detection of crackles in lung sounds offers a non-invasive way of monitoring or diagnosing cardiopulmonary diseases. The algorithm is divided into four main steps: (a) preprocessing, (b) estimation of HEE, (c) thresholding, and (d) applying time width conditions based on crackle two-cycle deflection and initial deflection width. Its performance is tested using a publicly available lung sound dataset of fine and coarse crackles and evaluated by the sensitivity (95.7%), positive predictive value (89.5%), and F-score (91.7%) for crackle detection. The good detection performance indicates the potential of the HEE-based algorithm as an automatic method for crackle detection in lung sound recordings.

# Pulsed current saturation as an indicator of tumor permeabilization

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Electroporation is a phenomenon of reversible or irreversible permeabilization of biological cells, which is triggered by cell polarization in pulsed electric fields (PEF). One of the most established applications of electroporation is the treatment of cancer. In this work, we have used microsecond (1.4 kV/cm x 100 µs x 8) and nanosecond (3.5 kV/cm x 800 ns x 1000) non-thermal PEF (<10 J) for electrochemotherapy of Sp2/0 tumors with doxorubicin and evaluated the feasibility of pulsed current measurement as a real-time marker of tumor permeabilization. The changes in pulsed current amplitude during the in vivo experiments were compared to the changes of the permeabilization rate of the cells in vitro. It was shown that the permeabilization rate follows the same pattern as current increase in the tumor when non-thermal protocols are applied (the pulses were delivered with delays to prevent any influence of Joule heating). The tendency was detectable both for microsecond and nanosecond range treatments, while both electrochemotherapy protocols resulted in a significant delay of tumor growth. Nevertheless, electroporation can be accompanied by thermal effects if other protocols are used. In case of higher energy density protocols (accompanied by rise of temperature) compensation/calibration models should be developed, which is a matter of our future works.
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# Quantification of Arm Tremor

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Tremor is considered to be the most common movement disorder. The qualitative assessment of tremor is widely used for diagnosing patients with neural diseases. Tests are available to determine the dominant frequency and amplitude of tremor. These tests usually require special equipment and trained operator.

The aim of the research is to provide a simple and cheap method for the objective and quantitative assessment of arm tremor. The arm tremor of the participants was assessed using a 3-D acceleration meter x-IMU attached to the wrist with a rubber ribbon. x-IMU is lightweight (59 g) and its size is equivalent to a matchbox. It integrates an accelerometer, a gyroscope and a magnetometer. The former two have 16-bit resolution and max. 512 Hz sampling frequency, for the magnetometer these are 12-bit and max. 160 Hz.

Four stroke patients' rehabilitation was followed for five weeks in the National Institute for Medical Rehabilitation, Budapest, Hungary. Four healthy subjects were tested in the Biomedical Engineering Laboratory of Budapest University of Technology and Economics both at rest and also following mild physical exercise: twenty stair-steps down and up.

Five movement patterns were performed by stroke patients and healthy subjects: arm resting on the table, arm resting on the thigh while sitting, arms outstretched forward in parallel, touching the nose four times with eyes closed and lifting a phone handset. Two parameters were used to characterize each movement: the energy and the frequency spectrum of tremor.

The group of tests reveals the reduced movement ability of stroke patients. Two dimensional presentation of arm tremor (energy vs. dominancy in frequency spectrum) depicts well the changes in stroke patients' actual state during rehabilitation. For them the lowered tremor is not always a favorable condition, it also indicates the partial blockade of the motor control. The results of healthy subjects show that a mild physical exercise does not necessarily increase arm tremor.

The evaluation algorithms based on measurements with x-IMU give a useful assessment of stroke patients' actual arm tremor. Therapists and medical doctors get a valuable feedback on the efficacy of rehabilitation.

# Quantification of Effects of Aging and Disease on Gait using Normalized Corrected Shannon Entropy

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The effects of aging and disease on gait have been extensively reported. These include, for example, a reduction in gait speed and an increase in gait variability in older adults and the exaggerated impact of cognitive function and dual tasking abilities on gait quality, variability, asymmetry and fall risk in diseased and older adults. Parkinson disease is usually associated with aging and advancing age is considered as the biggest risk factor of this disease. In this study we have examined the effect of aging on Parkinson disease. Normalized Corrected Shannon entropy (NCSE) based on threshold oriented symbolic entropy is used to measure the effect of aging and disease on human gait. NCSE is selected because of its robustness and low computationally complex. To quantify this, a gait time series corresponding to stride interval is first converted into certain symbols (usually binary 1 & 0) to construct a uniform symbol series. NCSE is then quantified by making symbolic sequences of the symbol series. Wilcoxon- rank-sum test (Mann–Whitney–Wilcoxon (MWW) test) was used to check the significant difference between the subjects. The degree of separation between groups at different threshold values was quantified by using the p-values (significance level: p=0.05). The data sets representing the stride interval time series was obtained from obtained from open access gait database provided by Physionet.

The quantification of NCSE showed a significant difference between normal adults and Parkinson disease subjects as well as between aged subjects and those with Parkinson disease at a range of threshold values. We have found out that advanced aging is not the only the biggest risk factor associated with Parkinson disease. P-values smaller than 0.05 were obtained while comparing NCSE values of old and Parkinson disease subjects which indicates that the hypothesis: both data sets belong to same group of data is not valid. However, while comparing young and elderly healthy subjects we did not get significant degree of separation between these two groups. The current study indicates that the correlation of aging and Parkinson disease is not as much strong as it is considered. There may be other strong factors causing Parkinson disease and should be considered while doing research. Future studies will confirm these findings in a larger sample of persons with Parkinson disease.

# Quantifying Chronic Cognitive Stress Using EEG and a Wearable Smart Ring

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Chronic stress is a risk factor for cardiovascular diseases, diabetes, cancer and depression. Continuous monitoring of stress can help people make better lifestyle choices and help in prevention of chronic diseases. In this study, electroencephalogram (EEG) and a smart ring were used to measure relaxation levels and stress responses in the central and autonomic nervous systems from healthy volunteers ($N = 10$; age 23 – 26). The smart ring is capable of optical heart rate (HR) and heart rate variability (HRV), as well as peripheral temperature and hand motion measurement. In the protocol, there was a cognitive stress phase induced by a mathematical task, and relaxation phase induced by a voice-guided meditation exercise. In the results of this study, beta band EEG (12 – 25 Hz) showed higher activity in the cognitive stress phase, compared to relaxation ($p < 0.03$). Autonomic response to the cognitive stress task showed increased heart rate ($p < 0.001$), decreased root-mean-square-of-successive-differences (RMSSD) of HRV ($p = 0.05$) and decreased peripheral temperature ($p < 0.02$). Results show that the changes in autonomic nervous system responses acquired with the smart ring correlate with the changes in central nervous system responses acquired by EEG. This suggests that a smart ring could be used in measurement of stress, perhaps as an indirect measure of cognitive stress. Follow-up studies with larger sample sizes are planned to confirm the findings of this study and to determine the most suitable features for representation of human stress level for prevention of chronic disease.

# Regional Segmentation of Biomedical Image Data using OTSU method

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Improving health applications for the detection of pathological tissues is a logical step in today's world of computing technology and use of artificial intelligence to everyday routine. Accurate detection plays an essential role in the planning of surgical procedures and the associated post-operative condition. Moreover for right segmentation is fundamental to perform as efficiently as possible. Therefore, experts are constantly focused on the accuracy of segmentation procedures. This paper deals with this issue, specifically regional segmentation. The essence of this work is a comparative analysis of regional segmentation methods based on hard thresholding. Paper deals with comparison of conventional OTSU method with various segmentation levels. The value of this work are segmentation analyzes depending on the dynamic effect of noise intensity. For analysis purposes, image dataset from computed tomography and magnetic resonance were selected. The main goal of this paper is in-depth comparative analysis of the Otsu segmentation method based on hard thresholding. The results show that using OTSU method is better for a smaller number of segmentation regions.

# Reliability of Muscle Tendon Junction Detection with Deep Learning

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Individual contributions of muscles and tendons to the behaviour of the whole muscle and tendon unit during locomotion are versatile. Therefore, movements of distinct landmarks such as the muscle tendon junction are recorded and tracked to investigate internal dynamics of the whole muscle and tendon complex. A time demanding and mostly manually or semi-automatically done tracking procedure in clinical gait analysis and research. We propose a time efficient, automatic method to track the muscle tendon junction based on deep learning. Our neural network is built upon an attention mechanism to focus on relevant regions in ultrasound images. We initially trained our network with a large and diverse data set of 7200 hand annotated video frames generated from 107 healthy and impaired individuals. The probands performed passive range of motion and maximum voluntary contractions during recordings. To evaluate the generalization of our approach to new subjects we extended the training set data step-wise with new individuals. Moreover, we estimated the performance for each training-iteration on an independent test set composed of unrelated individuals. We benchmarked our model to other open source tracking algorithms. We proof that our approach is reliably detecting the muscle tendon junction in new individuals with a mean euclidean distance between ground truth label and prediction of $2.55 \pm 1.00$ mm at a calculation time of 0.75 s/100 frames.

# Reliability of Pigs Gait Inertial Signals: A Pilot Study

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Gait is an essential movement and has been shown to be a relevant measure for differentiating gait pathologies and neurological conditions in the humans as well as in the animals. Inertial measurement units have been suggested as a promising tool for gait analysis. Gait analysis performed in the pre-clinical animal models can improve translational reliability of preclinical research. Large animal models can confirm and augment results achieved in rodents prior to translation into humans. Because pigs are of similar body size to humans and their brains are more similar to human than rodent brain, pigs are a more direct assessment of dosing in a preclinical model. Pig gait analysis is used to characterise pathologies of motor control and to evaluate the effectiveness of treatments prior performed in clinical settings. Nowadays, there is no information on the reliability of large animal model gait signals, namely pig gait signals. This paper presents the pilot analysis of gait angular velocity and acceleration provided by inertial sensors placed on the front shoulders and tests them for intra-individual reliability. Intra-class correlation was employed to analyse inertial sensors signals from three healthy pigs. Most of tested pigs performed with good reliability of a roll and pitch angular velocity, and vertical and medio-lateral acceleration. Therefore, we can recommend these signals as the signals served as basis in the continuous signal analysis.

# Resolution Resampling of Ultrasound Images in Placenta Previa Patients: Influence on Radiomics Data Reliability and Usefulness for Machine Learning

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Placenta previa (PP) and Placenta Accreta Spectrum (PAS) are obstetric patholo-gies whose early detection is fundamental for an appropriate patient management. In this paper, ultrasonography (US) is performed on 53 patients and from the im-ages a texture analysis feature extraction is performed through PyRadiomics. The US images were acquired with 3 different resampling resolutions: 1x1, 2x2 and 3x3. The features extracted from the images at each resolution were used to in-vestigate which one is the best to make the correct diagnosis by employing ma-chine learning techniques. Knime analytics platform was employed to implement decision tree, k nearest neighbor and naïve Bayes. Synthetic minority over-sampling technique was used to balance the dataset and some evaluation metrics were computed after a leave one out cross-validation. Averaging all the metrics among all the algorithms, 1x1 resolution achieved the best mean accuracy, sensi-tivity, specificity and Area Under the Curve Receiver Operating Characteristics. Despite using also artificial data to balance the dataset (less than 30% of total ana-lysed sample), this study provides researchers with the idea that employing a 1x1 resolution could be the best option when analysing images with machine learning algorithms on texture analysis features US-derived.

# Resonance Raman and stimulated Raman scattering for biomedical applications

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Since the discovery of Raman spectroscopy in 1928 the technique has been used to study biological samples. The development of time resolved lasers, fast detectors and advanced signal analysis including deep learning has pushed this weak inelastic light scattering technique towards biomedical applications. In our lab we perform resonance Raman spectroscopy to study the mitochondrial action in pulmonary arterial smooth muscle cells (PASMCs) during oxygen deprivation and to distinguish different grades of cancer tumors. Furthermore, near infrared (NIR) Raman spectroscopy is used for prostate cancer detection directly after operation to ensure that all cancerous tissue has been removed and to check if nerve-sparing techniques can be applied. Promising results have been achieved, but, continuous wave Raman spectroscopy is time consuming; both in terms of measurements and signal analysis. Further, Raman spectroscopy suffers from other types of light scattering like fluorescence or ambient light. In our lab we develop a new imaging technique that combines stimulated Raman spectroscopy (SRS) with interferometric imaging. Time resolved SRS has proven to be a valuable imaging technique that does not suffer from these drawbacks. SRS depends on two lasers, i.e. the pump and the Stokes laser, respectively. One of them is wavelength tunable whereas the other one is fixed. When the energy difference between the two lasers corresponds to a specific Raman shift of interest a stimulated Raman effect is created, where the pump laser - in contrary to the Stokes - laser loses energy. This loss or gain of signal can be measured and imaged by a sensitive fast camera. By further splitting the Stokes laser into two arms, a reference wave can be created that allows for the recording of interferometric or holographic images. The reference wave reaches the camera directly, while the other wave first interferes with the sample. The phase difference between the two waves can be used to analyze density, shape and movements of the sample. In other words, not only the biomolecular content and action of the sample can be studied in real time, but also the movement and density of the sample. This talk will give the latest results of our Raman studies on cancer detection and grading directly after brain surgery as well as preliminary results of direct SRS imaging on Cytochrome c in single cells. The results show the potential of Raman imaging in biomedical applications.

# Responses of individuals with an amputation to anteroposterior platform perturbations during walking: influence of a microprocessor-controlled prosthetic knee

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66% of individuals with a transfemoral amputation falls at least once a year. It is therefore of clinical importance to understand how interventions can decrease the number of falls. One potential intervention is the use of microprocessor-controlled prosthetic knees (MPK) which has been associated with a reduced number of self-reported falls and stumbles. A biomechanical explanation for this finding, however, is lacking.
The aim of this study was to compare the use of a non-microprocessor-controlled prosthetic knee (NMPK) and an MPK (the Rheo Knee II) on responses to anteroposterior platform perturbations during walking.
Participants were measured twice: once with their own NMPK and once with the Rheo Knee II. Data were collected using a CAREN system. We measured perturbed and non-perturbed walking. A control group was included for reference purposes. Anteroposterior platform perturbations (magnitude 0.2m, speed 0.2 m/s) were applied during the single stance phase on the prosthetic leg and during the end of the swing phase of the prosthetic leg. The primary outcome measure was the backward margin of stability (BMoS), which is the distance between the extrapolated center of mass and the anteroposterior base of support.
MPK vs NMPK condition: The BMoS of the steps after the stance phase perturbations in the Rheo Knee II condition was significantly increased when compared to NMPK condition. This is explained by a smaller foot forward placement and step length in the Rheo Knee II condition when compared to the NMPK condition. For the BMoS of the steps after the swing phase perturbations no differences were found.
Perturbed vs non-perturbed condition: In the Rheo Knee II condition, the BMoS of the steps after the stance phase perturbation was significantly increased when compared to non-perturbed walking. This was also seen in the controls. In the NMPK condition, the BMoS of perturbed walking was comparable to the BMoS of non-perturbed walking. In the Rheo Knee II condition participants decreased the step length and foot forward placement when compared to non-perturbed walking. Similar strategies were also used by controls.
The Rheo Knee II enabled the use of strategies that are also used by non-amputees where this was not the case for the NMPK condition. This study provides initial findings that might explain the decrease of self-reported falls and stumble while walking with an MPK.

# Review of Artificial Neural Networks for QSAR predictions

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Quantitative Structure Activity Relationship (QSARs) are used in pharmaceutical industry to predict drug activity. These are simple regression models which can be combined with Artificial Neural Networks (ANNs) to create robust predictions. These systems are useful because they are able to find rules for drug discovery based on numerical representation of molecule structures. They involve analysis of structural activity data, gene prediction, position of protein-encoding regions in DNA sequences, 3D alignment of structure, pharmacophore perception as well as analysis of docking of ligands to receptors and automated generation of receptors. Recently, various applications for drug property and behavior prediction have emerged reporting different accuracy of predictive models based on different architecture of ANNs. This review is based on research papers that have been published in the previous year, and that were available in databases Medline and PubMed Central. The comparison of papers was done based on neural network architecture, performance and input parameters used. The aim of the review is to assess the current state of the art of using ANNs in QSAR predictions.

# Role of Standards and Guidelines in the assessment of Medical devices

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In general, every medical device that it is put on the market and/or in use shall meet the relevant legal requirements. When appropriately implemented, regulation ensures public health benefit and the safety of patients, health care workers and the community.

In the European marketplace to keep up with advances in science and technology the new Medical Device Regulation 745/2017 (MDR) is replacing the existing directives on medical devices. Manufacturers of currently approved medical devices will have a transition time of four years until May 26th 2021 to meet the requirements of the regulation.

Sometimes the laws and regulations are written very rigidly and extra interpretation and explanation is needed. Therefore, the European Commission provides a range of guidance documents to assist stakeholders in implementing the medical devices regulations.

Legally non-binding guidance documents, adopted by the medical device coordination group (MDCG) in accordance with Article 105 of MDR, pursue the objective of ensuring uniform application of the relevant provisions of the regulations within the EU. The guidance documents cover different topics from the MDR.

Furthermore, the keystone for establishing conformity with the MDR is to fulfil the requirements with the 'General Safety and Performance Requirements' (GSPR), Annex I in MDR. The most common way to demonstrate compliance with the GSPRs is to consider a harmonised standard. Standards are documents, adopted by regional bodies or international standardization committees, to document the "state of the art". The harmonized standards are identified and published in EU Official Journal. The harmonized standards are important since, they can then be used to derive a presumption of conformity with the GSPR of the MDR. Meaning that manufacturers, other economic operators or conformity assessment bodies can use harmonised standards to demonstrate that products, services or processes comply with relevant EU legislation.

Standard-setting activities include the development of performance characteristics, characterization and testing methodologies, manufacturing practices, product standards, scientific protocols, compliance criteria, ingredient specifications, labelling, or other technical or policy criteria. For example, for the active medical devices the EN 60601 family of standards is of major importance for demonstrating compliance with the GSPR of the MDR. The family comprises over 70 separate particular standards. The "Part 1" standard, EN 60601-1 covers basic safety and essential performance for all Medical Electrical Equipment and the "Part 2" or "Particular" standards cover requirements for specific product groups.

Clearly, the suitability of a device (safety and efficiency) must also be proven by compliance with other MDR requirements, which are not standardized (Technical file, clinical evaluation, etc.).

# Rule extraction in the assessment of alzheimer's disease based on brain mri imaging

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Motivation and Objective: Although a plethora of machine learning and deep learning methods were used for the assessment of Alzheimer Disease (AD) MRI structural changes, the main drawback of these models is that they are regarded as black-box models and even though the results obtained are highly satisfactory, they lack an explicit declarative knowledge representation, and thus we have difficulty in generating the underlying explanatory imaging structures. The objective of this study was to investigate the usefulness of rule extraction in the assessment of AD using decision trees and random forests algorithms. Material and Methods: The decision trees and random forests algorithms were applied on brain MRI images acquired from normal controls (NC) (N=114), Mild Cognitive Impairment (MCI) (N=129) and AD (N=69). These images were downloaded from the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset. All the subjects had a standardized protocol on 1.5-T MRI units (typically 1.25×1.25×1.25mm3 voxels) according to an ADNI protocol. Regions of interest (ROI) segmentation was performed using the Freesurfer v6.0 software. The following MRI brain features were extracted when a subject was diagnosed from the hippocampus: volume (HipVol) and texture features (Angular Second Moment, Contrast, Correlation, Sum Average, Entropy and Cluster Shade). The KNIME analytics platform was used to compute the decision trees. Results: The overall accuracy achieved for the NC versus AD models was in the region of 90%, whereas the overall accuracy achieved for the NC versus MCI models was in the region of 65%. Sample rules generated for the NC versus AD models were the following: (R1) If Age>70 AND HipVol>2782mm3 AND HipsSumAverage>35.5 AND HipsSumAverage<=36 Then NC; (R2) If HipVol<=2782 mm3 Then AD. Sample rules generated for the NC versus MCI models were the following: (R1) If Gender=Female AND Age>70 AND HipVol>2649mm3 AND HipVol<=3188mm3 AND HipsSumAverage>39 Then NC; (R2) If Age>72 AND HipVol<=3301mm3 AND HipsSumAverage<=39 AND HipContrast<=189 Then MCI. Discussion: The overall performance achieved in this study is in agreement with other studies. Concluding Remarks: This study demonstrated the usefulness of rule extraction in the assessment of AD based on MRI features. Future work will further investigate explainability by integrating symbolic reasoning applied on more cases and more structures.

# Scientic machine learning for biomechanics

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After several Artificial Intelligence (AI) ”winters”—periods of lack of interest and funding—, it is currently believed that we live in an AI ”spring” motivated, among other causes, by the success in many applications of deep learning algorithms. In general, machine learning methodologies are able to construct black box models, provided enough data is available.
However, there is also a growing interest in developing white box, or interpretable, machine learning methods. These are understood as the use of machine-learning models for the extraction of relevant knowledge about domain relationships contained in data. More precisely, model-based interpretability refers to the construction of models that provide insight into the relationships they learn [1].
Thus, merging non-mechanistic machine learning with centuries of knowledge about mechanistic modeling has given rise to the emergence of a new discipline coined as scientific machine learning. This paves the way towards the development of techniques able to unveil scientific laws, with less data, good at extrapolation and that preserve the well-known structure of the phenomena at hand.
There remains, however, many aspects that have not been fully understood yet. For instance, how learn multiscale models, or the need for phenomenological internal variables—something related, in turn, to the appropriate scale at which a phenomenon should be described—. These aspects will be analyzed during our presentation and examples will be provided for constitutive modeling of biological soft tissues, or biological flows, for instance. Particular attention will be paid to the development of techniques able to satisfy by construction the laws of thermodynamics [2,3].

References:
1. Murdoch, W. James, et al. Interpretable machine learning: definitions, methods, and applications.” arXiv preprint arXiv:1901.04592 (2019).
2. Gonzalez, David, Francisco Chinesta, and Elias Cueto. Thermodynamically consistent data-driven computational mechanics.” Continuum Mechanics and Thermodynamics 31.1 (2019): 239-253.
3. Chinesta, Francisco, et al. Learning Physics from Data: a Thermodynamic Interpretation.” arXiv preprint arXiv:1909.01074(2019).

# Selection of Health Apps and EU perspective

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Mobile health apps hold great promise to accelerate the transition to the new paradigm of patient centric health care. A large number of health apps are available today, and this number is growing rapidly because mobile apps can be created and deployed relatively easily. While some apps serve critical medical purposes and fall under medical device regulations, the majority are non-medical. Many of those aim to improve the user's health, e.g., by encouraging lifestyle changes. Since health apps commonly collect personal data from the user and then provide information thereupon, they must be medically safe and ensure the user's privacy and security. Here, the need for regulation appears evident. However, no generally accepted mechanism for quality control and certification exists to date.

One obstacle for regulation is defining assessment criteria of health apps. Important assessment domains are privacy, safety, technical stability, medical efficacy, and usability. However, recent efforts have shown that the multiple stakeholders, i.e., patients, healthcare professionals, payers, and app developers, differ considerably in their definition of the exact criteria and scope due to their different objectives.

To aid the adoption of mobile health technology, many international governing bodies and national authorities have issued guidelines. The European Commission's Digital Single Market strategy, for example, recognizes the great potential of mobile health technology to address the serious challenges that Europe's health care systems are facing, e.g., an aging population, and shortage of trained health care professionals. It is therefore driving the process standardization and regulation in the mobile health sector.

# Sensitivity study of electrode position on the effectiveness of electroporation-based treatment

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Interventional oncology is a fast-growing field for the treatment of subcutaneous cancer due to its minimally invasive procedures. One of the subfields of this cancer intervention is electroporation-based treatment, which includes Irreversible Electroporation (IRE) and Electrochemotherapy (ECT). Both methods deliver a specific voltage directly to the tumor through electrodes, but the former kills the tumor irreversibly while the latter leverages reversible electroporation to introduce chemicals into the tumor volume. Hence, in both cases, the accurate positioning of the electrodes is extremely important in reducing the operation time and the degree of invasiveness (i.e., reducing the number of insertions, decreasing the healthy tissue ablation, etc.).

However, identifying the optimal location of the electrodes and placing them at those exact locations are two complex challenges. Though there exists prior research to find the optimal electrode positions, the identification still needs an accurate (and efficient) model, as well as a fast optimization algorithm to enable real-time calculations. The difficulties in the placement include the absence of a precise guiding tool, the lack of continuous intra-operative image guidance and the presence of other structures (e.g., lipid tissues, vascular network). It is therefore crucial to understand how positioning will affect the treatment planning of electroporation-based processes. This work is a primary step towards that goal, by performing a sensitivity analysis (SA) of the electrode position (and other geometric features like tumor shape) on the tumor ablation.

We model the electroporation-based treatment in liver tissue with an expandable electrode, spheroid-shaped tumor, simplified vascular geometry, and homogeneous tissue properties. The voltage and pulse duration values for the simulations are taken from the operating range of the state-of-the-art pulse generators. Material properties of liver tissue, tumor and blood vessels are obtained from clinical datasets and literature surveys. The quantity of interest for the SA represents the relative amount of tumor ablation as compared to the original tumor volume. We see this as a measure for the treatment effectiveness.

The results of the SA show the relative significance of the electrode position and tumor shape on the treatment planning. The effect of electrode misplacement on the "required" ablated volume is clearly shown. This should eventually lead towards a more efficient and optimal electrode placement in the treatment planning of electroporation-based processes.

# Silencing of enhanced green fluorescent protein in a murine B16F10 melanoma after siRNA electrotransfer mediated by a high intensity pulsed electromagnetic field

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Gene electrotransfer represents a promising non-viral gene therapy approach in the treatment of cancer. A high intensity pulsed electromagnetic field (HI-PEMF) can induce electroporation and have been shown effective in gene electrotransfer. Because the efficiency, stability, long term expression, integrity and safety issues, are the most important aspects in a delivery system, we performed in vivo experiments to explore the feasibility of HI-PEMF induced electroporation for delivery of siRNA molecules against the enhanced green fluorescent protein (EGFP) in B16F10 melanoma stably expressing EGFP. Electrotransfer of siRNA by HI-PEMF was performed in subcutaneous tumors and was compared to conventional electrotransfer. HI-PEMF was applied by a custom-made magnetic field pulse generator connected to an applicator consisting of a round coil with 68 turns. The pulse sequence of the electric current delivered to the applicator consisted of 400 bipolar electric pulses of 345 µs duration and 370 A amplitude at the frequency of 33 Hz. The conventional siRNA electrotransfer (GET) was performed by application of eight 5 ms long square wave electric pulses at 600 V/cm voltage to distance ratio delivered at 1 Hz. Electroporation of tumors was performed every second day three times (on days 0, 2 and 4). The silencing effect of EGFP was evaluated at mRNA level using qPCR, at the protein level by flow cytometry and with noninvasive fluorescence stereomicroscope by monitoring tumors once per day. Cell proliferation, apoptosis, necrosis, and immune cell infiltration were evaluated histologically. Efficient silencing of EGFP after electrotransfer was demonstrated by HI-PEMF and conventional GET, but more pronounced with conventional GET. The level of EGFP at mRNA and protein was reduced for up to 41?ter electrotransfer by HI-PEMF and for up to 63% by conventional GET two days after the third electrotransfer. Similarly, in vivo imaging demonstrated a significant silencing of EGFP 8 h after each HI-PEMF electrotransfer (~40% smaller fluorescent tumor area), however more pronounced after conventional GET (by 77%). Furthermore, the electrotransfer by HI-PEMF induced less morphological changes (decrease in proliferation, increase in apoptosis) and approximately the same immune cell infiltration (9.1% in EGFP+HI-PEMF group and 10.1% in EGFP+GET group) in tumors than the electrotransfer by conventional GET. Obtained results in a mouse melanoma demonstrated that simple and contactless application of HI-PEMF could represent an alternative approach to conventional electroporation. Still, further studies are warranted to improve the equipment and optimize the protocol of genetic material delivery to normal and tumor tissues.

# SILICOFCM: In Silico clinical trials for cardiovascular disease

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In silico clinical trial represents a new paradigm for development of new drug and medical device. In SILICOFCM project Familial Cardiomyopathy disease was modelled with comprehensive list of patient specific features such as genetic, biological, pharmacologic, clinical, imaging. Transport through biological barriers as vessel walls, or cell and organelle membranes, depends on the transport properties of these barriers, as hydraulic or diffusion coefficients, and also on the size of the surface which separates the continuum domains. In electrophysiology, the goal is to determine the electrophysiological properties of all compartments and signal propagation characteristics within the body. A coupled model which includes multiscale modelling of realistic sarcomeric system, genetics patient profile, electrophysiology, realistic directions of muscle fibers, solid-fluid interaction coupled to electrophysiology of the heart was implemented.Initial results give influence of left ventricle deformations on deformations of mitral valve, and on general blood flow in heart. Also drug distribution in the heart and effects of different drugs are tested for cardiomyopathy disease. SILICOFCM project will connect basic experimental research with clinical study and bioinformatics, data mining and image processing tools using very advanced computer models drug, and patient database and regulative in order to reduce animal and clinical studies.

# Simulation of selective nerve branch stimulation in the vestibular system considering tissue permittivity

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Our sense of balance and spatial orientation rely on the vestibular system. The sensory epithelia in the ampullae of the three semi-circular canals (SCCs) are responsible for sensing rotation, whereas the two otolith organs sense horizontal and vertical acceleration. A loss of functionality of these organs due to disease or injury reduces the quality of life. Recent studies have shown it is possible to restore, even though just in part, the function of the vestibular system by means of a vestibular implants.

Electrical modeling is a valuable tool in assisting the development of these implants by investigating and predicting the stimulation effects. For this purpose, a semi-automatic modular workflow was developed to transform segmented anatomy of human vestibular systems using high-resolution µCT scans to realistic electrical computer models. A 3D tetrahedral mesh was generated from those segmentations. The labeled components are embedded in a bone sphere with radius of 25 mm, surrounded by a saline layer of 10 mm thickness. We present an approach to consider the capacitive effects of the electrode/tissue interface and the reactive component of tissue impedance in the model.

The Fourier finite element method was implemented to calculate the potential distribution of a defined electrode configuration using the Poisson equation with respect to its frequency components. Dielectric properties were assigned to each volume element according to its underlying material. A spherical active electrode with a diameter of 200 µm was positioned close to the ampulla of the posterior SCC. The reference electrode was defined as the outer boundary of the model. The scar tissue around the electrode has a radius of 500 µm and a constant contact encapsulation conductivity, whereas the capacitor reactance between electrode and tissue is frequency dependent.

A cathodic-phase-first charge balanced biphasic current stimulus waveform was applied to the active electrode. The resulting potential waveforms obtained at the active electrode and central points of the sensory epithelia of the posterior, anterior and utricle nerve have shown how the different waveforms are influenced by the dielectric properties: rise time and decay time are increased by considering the capacitive effects included in the model.

The reactive component of impedance and the electrode/tissue interface were taken into account in the model and an influence on resulting potential waveforms during stimulation was demonstrated. In future work, optimized stimulation waveforms and electrode configurations will be determined based on patient specific anatomy.

# Simultaneous Raman spectroscopy and Imaging for investigations of dynamic cell behavior; a case study using Red Blood Cells

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Pulmonary arteries constrict upon oxygen deprivation, Hypoxic pulmonary vasoconstriction (HPV), to redirect blood flow to areas of the lung where more oxygen is available. HPV is generally a reversible but can become irreversible in patients who has been exposed to prolonged hypoxia or is subjected to a lung disease, such as chronic obstructive pulmonary disease (COPD). Irreversible HPV results in, pulmonary hypertension (PH), elevated pressure in connection to the lungs. Symptoms of PH include fatigue and shortness of breath. The strain from PH on the heart eventually leads to heart failure. Advances have been made in the treatment of PH, but it is generally considered an incurable disease.

HPV is the result of pulmonary arterial smooth muscle cells (PASMCs) that constrict in unition. The biochemical process in PASMCs used to sense hypoxia and open the ion-channels is unknown. Deciphering how oxygen sensing takes place is crucial for the development of new therapies to PH.

We have developed a gas-tight microfluidic system that is compatible with measurements using the Patch Clamp technique, Raman spectroscopy and imaging. The fluidic system can be used to trigger HPV in PASMCs. The Patch Clamp technique can be used to measure the dynamical behavior of the ion-channels and Raman spectroscopy can be used to measure the molecular composition of PASMCs. In order to confirm that the mechanical changes of HPV have occurred it is desirable to image the cells with simultaneous Raman spectroscopy and Patch Clamp.

We show that simultaneous Raman spectroscopy and imaging can be acquired through illumination with an incoherent light source of distinct different wavelength than the laser used for probing the Raman effect. The signal acquisition is possible with dichroic optics, which can separate the Raman spectrum, image and laser light. Measurements on free-flowing red blood cells (RBCs) was used as a test case. The motion of the RBCs was traced using image correlation.

The gas-tight microfluidic system contaminates the Raman spectrum with a background signal. It has been have shown that a deep convolutional neural network can be used to process Raman spectra from samples by removing background signal, fluorescence, noise and cosmic rays in a single step. As far as we are aware, the spectrum from RBCs is the first biological measurement that has been processed using this technique.

# Simultaneous Skull Conductivity and Focal Source Imaging from EEG Recordings with the help of Bayesian Uncertainty Modelling

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The electroencephalography (EEG) source imaging problem is very sensitive to the electrical modelling of the skull of the patient under examination. Unfortunately, the currently available EEG devices and their embedded software do not take this into account; instead, it is common to use a literature-based skull conductivity parameter. In this paper, we propose a statistical method based on the Bayesian approximation error approach to compensate for source imaging errors due to the unknown skull conductivity and, simultaneously, to compute a low-order estimate for the actual skull conductivity value. By using simulated EEG data that corresponds to focal source activity, we demonstrate the potential of the method to reconstruct the underlying focal sources and low-order errors induced by the unknown skull conductivity. Subsequently, the estimated errors are used to approximate the skull conductivity. The results indicate clear improvements in the source localization accuracy and feasible skull conductivity estimates.

# Six Sigma approach for a first evaluation of a pharma-cological therapy in tongue cancer

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Tongue cancers are among the most frequent malignancies in the population and their influence can be affected by many risk factors. Patients undergoing tongue surgery face different complications and can experience a long length of hospital stay (LOS). The aim of this paper is to compare two pharmacological therapies in order to understand which one makes the LOS decrease. At the University hospi-tal of Naples "Federico II" two antibiotics were employed: Cefazolin plus Clindamycin and Ceftriaxone. Six Sigma methodology was employed to analyse two group of patients treated with these two different antibiotics: 55 patients treated with the antibiotic Cefazolin plus Clindamycin and 66 patients with the an-tibiotic Ceftriaxone. The results obtained show clearly and with a statistical evi-dence that patients treated with Ceftriaxone experienced a lower LOS. Reducing the LOS for patients limits the number of complications and, therefore, reduces the hospitalization costs. It would be valuable for both hospital and patients.

# Six Sigma Process Optimization of Healthcare Services - The Radiotherapy Case

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Nowadays, there is an intense debate on issues related to hospital management of which emerges the quality and efficiency of services provided by health units. The radiotherapy has been taking a place of extreme importance when it comes to cancer therapy and therefore an increasing demand for this service requires the new demands for assistance and quality. This fact makes this service a target for optimization. The optimization is performed by applying the methodology Six-Sigma, which is based on five pillars (Define, Measure, Analyses, Implement and Control): 1) Problem definition; 2) Measurement of variables could change the process; 3) Analyses the variables impact in the process performance; 4) Solutions implementations; 5) Implemented solutions control to ensure its success. From the stage of defining, is showing the importance of workflow mapping, providing a tool either in the systematization of such flows, both in reality perception and even in the ideal situation perception. Some considerations were still made based on protocols, guidelines and directives in order to achieve continuous improvement, always taking primarily aim at increasing the efficiency and effectiveness of a health care provider.

# Smart Textiles for Healthcare: Preliminary Design and Development of an Outreaching Neonatal Phototherapy Vest using Embedded Fibre Optics and Integrated Diagnostics

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This talk will present a project aiming to design, test and develop a prototype vest, with embedded fibre optics and sensors, to be a means of delivering complete and effective phototherapy treatment to jaundiced neonates in low-resourced settings (LRSs). Particular innovations of the design being researched are: garmented treatment, accessibility in LRSs and integrated diagnostics for a closed loop control. The scope will hopefully facilitate treatment outside of healthcare facilities (i.e. domestic treatment) in an effort to fulfil the global unmet need for phototherapy, typically occurring in rural and LRSs. Design considerations involve planning and testing for resiliency using military standards (where possible), which will be an adjacent pivotal process to encompass and fully realise the scope.

The relevance of this project can be described by the prevalence of the condition being treated itself. Worldwide, jaundice occurs in 60% of all neonates, whereby 10.5% all neonates require phototherapy. Where this demand is unmet primarily falls within the regions of Africa, South America and South Asia, hence the focus on LRS. With preventable symptoms of untreated neonatal jaundice ranging from hearing loss and cerebral palsy all the way to death, it should be deemed imperative to work towards the simple process of phototherapy being made accessible for all. If successful in application, this project will contribute towards the United Nations' Sustainable Development Goal 3.2.2 – lowering the global neonatal mortality rate.

# Smartphone-based image diagnosis without use of tabletop microscopes

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Introduction: Generally, in the educational and clinical fields, cytological judgment is made by a tabletop microscope with stained specimen. Whereas, the performance and functions of smartphone cameras have been drastically improved and evolved in recent years, which has a high potential for handy and reliable histopathological image diagnosis. Therefore, we investigated whether or not it is possible to do cytological diagnosis by a smartphone camera without the use of an optical microscope in the present experiment.
Methods: Smartphone camera:H&E-stained specimens were set on a microscope slide, and an eyepiece adapter was attached to the camera lens of a smartphone . The adapter was set closely to the specimens, with a magnification power as one hundred (100x). The magnification of smartphone eyepiece was adjusted to the actual size (x1). The pictures of specimen were taken by the smartphone camera focusing onto the specimen by the adapter.
Results: H&E stained specimens. Although acinar cells, ducts, islets of Langerhans, and epithelial cells of pancreatic ducts were discernible in a low-power field, the image was grainy on the left side, making it difficult to perform a cytological diagnosis . In a high-power field, there was no blurry part, and it was possible to distinguish acinar cells, ducts, islets of Langerhans, and epithelial cells of pancreatic ducts . The structural view of the epithelial cells of each pancreatic duct was slightly unclear when the photo was enlarged and scrolled
Discussion: Since smartphone is equipped with identical functions as those of personal computers, such as generating images, sending and receiving emails and photos, and viewing and accessing websites, with necessities for our daily life. In the present study, it was possible to make cytological diagnosis in pancreas based on the pictures of stained specimens. This suggests that a smartphone-based imaging technology can be applied not only to pancreases, but also to other organs and tissues3). Because the thickness of H&E-stained specimen was 2-3 $\mu$m, which makes its structure from three-dimensional to planar view, the smartphone camera can focus accurately on these very thin sliced sections. However, regarding the Pap staining samples, specimens' cellular structure was remained as three-dimensional with alcohol based fixative, and that was the major cause why it makes arduous to focus the specimen.
Conclusion: Since the needs for smartphone-based image is increased, our current study gives an idea and example of the usage.

# Some significant steps to vitrification of mesenchymal stromal cells in tissue-engineered constructs

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Development of tissue engineered constructs (TECs) with mesenchymal stromal cells (MSCs) for regenerative medicine is a promising strategy. An efficient method for long-term storage of ready-to-use TECs is required for their implementation in clinical practice. Conventional cryopreservation protocols based on slow rate freezing are accompanied with ice crystals formation which may lead to cell death and carrier destruction. Vitrification is achieved without ice formation and so it is an encouraging alternative to conventional cryopreservation.
Objective: To evaluate significant steps for successful vitrification of mesenchymal stromal cells within alginate microspheres and macroporous scaffolds.
Materials and Methods: To design the vitrification solution, compositions of dimethyl sulfoxide (DMSO), ethylene glycol (EG), 1.2-propanediol (1.2-PD), sucrose (called DEPS) in various concentrations were used. Polyvinyl alcohol (PVA), polyethylene glycols (PEG-400, PEG-8000) were used as ice blockers. Human dermal MSCs in suspension, entrapped in alginate microspheres or seeded into alginate-gelatin macroporous cryogel scaffolds disks were used. Glass-forming properties of multicomponent solutions were studied by visual analysis and differential scanning calorimetry (DSC). Viability, metabolic activity, adhesion and differential potential of cells were assessed both after exposure with vitrification solutions and following rapid cooling-warming in standard cryovials.
Results: The minimal concentrations of cryoprotectants in solution, which allowed avoiding ice formation during rapid cooling and rewarming comprised 10 % DMSO, 20 % EG, 20 % 1.2-PD and 0.5 M sucrose. After vitrification in this solution both MSCs suspension and MSCs within alginate microspheres retained the viability, metabolic activity and capacity to osteogenic and adipogenic differentiation. However, the usage of this solution was not successful for vitrification of cell within macroporous scaffolds. We studied a number of solution modifications and found out that increasing the concentration of DMSO to 15% and adding 1% PVA prevented the development of crystallization during carrier rapid cooling-thawing. Then, based on thermal characteristics of the solution obtained by DSC, we developed a two-step cooling and thawing modes, which prevented vitreous phase cracking. The modified vitrification protocol provided high viability rate of MSC in suspension, but should be further improved for vitrification of MSCs in macroporous scaffolds.
Conclusion: Obtained results are feasible for further development of vitrification protocol for TECs preservation.

# Spatiotemporal measurements of visually evoked fields using quantum magnetometers

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Magnetoencephalography is a widely-used neuroimaging technique with numerous clinical applications. New technological developments combined with the traditional notions of MEG have brought a more precise and flexible neuroimaging system. Instead of superconducting quantum interference devices (SQUIDs), OPM-MEG uses optically-pumped magnetometers (OPMs) to measure cortical brain signals. Due to the reduced sensor-standoff, OPMs offer higher signal-to-noise- ratios (SNR) and better spatial resolution than in SQUID-MEG [1]. With a focus on the visual cortex, this research compares OPM-MEG to SQUID-MEG using two well-established visual stimuli; the flash stimulus (FS) and the pattern reversal stimulus (PR). In this work, two OPMs were placed at designated regions over the occipital lobe, one at the primary visual cortex (Oz) and one at the associative visual cortex (POz), using the 10-20 system. OPM-MEG visually evoked response (VER) has higher signal to noise ratio (SNR) and a greater resemblance to the well-characterized VER compared to SQUID-MEG VER. Also, the OPM-MEG measurements showed a difference in the signal timing, with an early activation at POz followed by the Oz activation at the main and late components (P2/P100 and P3). This phenomenon is present across subjects and stimuli. Although the SQUID-MEG signal demonstrates the time delay, the low SNR and the low spatiotemporal resolution make the results unclear, and extra evaluation methods are needed. OPM-MEG system detects the same signal from the two neighbouring regions with a significant onset difference. Hence, OPM-MEG could be a reliable neuroimaging method to identify the activation patterns of close cortical regions in response to a specific stimulus.

References:
[1] Boto, E., Meyer,S.S., Shah V., Alem O., Knappe S, Kruger P., T. Fromhold M., Lim, M., Glover, P., Morris, P., Bowtell, R., Barnes, G., Brookes, M. J. (2017). A new generation of magnetoencephalography: Room temperature measurements using optically-pumped magnetometers, NeuroImage, 149, 404-414, ISSN 1053-8119

# Spectral Analysis of EEG Signals of Imagined Hand Twisting for Post-Stroke Rehabilitation

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Stroke is a leading cause of death and remains a major healthcare burden world-wide. Effective rehabilitation strategy is required to improve motor impairment and functional status of stroke survivors. The imagination of movement is one of the methods that can be used in the therapy of stroke survivors at home to gain full recovery. This paper describes the spectral analysis and 2D topography of EEG signals obtained during actual and imagined of hand twisting for stroke re-habilitation. The EEG signals were recorded from thirty-two channels, processed and filtered to remove the unwanted signals. The signal features were then ex-tracted using power spectral density and analysed through EEG 2D topography. The results showed that monitoring the status of brain region during actual and imagined twisting could be performed using eight electrodes. The EEG topogra-phy revealed the suitable frequency range to monitor the status of brain activation area for both cases.

# Split electrodes for electrical-conductivity-based tissue discrimination

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This work presents a method to minimize the inadvertent cutting of tissues in surgeries involving bone drilling. We present electrical impedance measurements as an assistive technology to image-guided surgery to achieve online guidance. Proposed concept is to identify and localize the landmarks via impedance measurements and then use this information to superimpose the estimated drilling trajectory on the offline maps obtained by pre-operative imaging. To this end, we propose an asymmetric electrode geometry, split electrodes, capable of distinguishing impedance variations as a function of rotation angle. The feasibility of the proposed approach is verified with numerical analysis. A probe with stainless steel electrodes has been fabricated and tested with a technical phantom. Although the results are impacted by a non-ideality in the phantom, we could show that the variation of impedance as a function of rotation angle can be used to localize the regions with different impedivities.

# Statistical re-evaluation of material properties of human cerebral arteries

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A statistical re-evaluation of an earlier series of measurements on healthy and diseased (aneurysm) brain arteries was performed. Several researcher deal with the simulation of brain aneurysms, which makes it important to learn the modified properties of such adverse vessel sections. Naturally, to make a comparison, for this purpose we have to know the material properties of the healthy vessels as control data. Our goal is to determine material properties of both the adverse and the healthy vessels, which can be applied to computational models. We made statistical investigation and we determined material properties too. In order to reach this goal, laboratory measurements have been undertaken for several years in the Institute of Human Physiology and Clinical Experimental Research of the Semmelweis University in Budapest. We have taken the specimens of the vessel wall from patients under operations, and from brain vessels extracted from cadavers, and then we have measured the stress-strain curves of the material of the vessel wall in uniaxial and biaxial tensile tests. We have evaluated the measurements on the 12 specimens of arteria carotis interna and determined the properties of elasticity. During these measurements we have calculated material properties of lengthwise, circumferential, and square-shaped (for the biaxial tests) specimens for all artery sections, therefore we were able to evaluate a total of 46 valid measurement data. By calculating the material properties we did not purely aim to provide data for our own research, but to make the foundations of a database which can be utilized by both medical doctors and engineers, and expanded in the future, too. Precisely for this purpose we have separately evaluated each specimen, and then tried to generalize the results. In the case of measurements on arteria carotis interna used as a control group, we found the biaxial results particularly valuable. Following our measurements on the walls of healthy arteries we dealt with the examination of aneurysms. On stripes cut out of the aneurysms parallel to the imaginary axis (meridional) and perpendicular ring-like direction (circumferential) for the uniaxial tests we have performed the procedure shown for the arteria carotis interna now for the total of 91 uniaxial measurement results, too. We formed a total of 9 groups possessing identifiable characteristics. Curves obtained from them are clearly distinguishable: all together, males and females separately, circumferential (perpendicular to the main axis of the aneurysm) and meridional (approximately in the main axis of the aneurysm) separately, and also the cases of circumferential female, circumferential male, meridional female, and meridional male.

# Stimulation Electrodes Which do not Generate Reactive Oxygen Species do not Permeabilize Cells

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Electric pulses applied by metal electrodes to biological environments initiate electrochemical processes at the interface. These reactions can lead to the formation of gas, change in pH and the generation of reactive oxygen species which affects the electroporation efficiency.[1][2] Although some effects have been studied, there is need to better understand the impact of these electrochemical events. In this study, we compare the performance of bare metal electrodes to electrodes coated with the conducting polymer PEDOT:PSS. The polymer coating changes the electrochemistry at the interface which has remarkable effects on cell permeabilization.
Comparison of both types of electrodes is performed with single, unipolar, 100µs, 1-30V pulses with an electrode spacing of 50µm. Electrochemical characterization with the metal electrodes confirms Faradaic currents, changes in pH and the generation of reactive oxygen species. In comparison, coated electrodes show capacitive currents, limited change in pH and almost no generation of reactive oxygen species. U87 glioblastoma cell response show similar dose-responses for Fluo4-AM which indicates the stimulation of voltage-gated calcium channels. However, the propidium iodide dose-response reveals that the coated electrodes do not permeabilize cells for voltages up to 30V.
These results suggest that the electrochemical processes at the electrode interface are not merely a side effect; they play an essential role in the mechanism of cell permeabilization.

[1] Y. Li et al., "Electroporation on microchips: The harmful effects of pH changes and scaling down," Sci. Rep., vol. 5, pp. 1–11, 2015.
[2] P. Ruzgys et al., "Influence of the electrode material on ROS generation and electroporation efficiency in low and high frequency nanosecond pulse range," Bioelectrochemistry, vol. 127, pp. 87–93, 2019.

# Subject-specific Head Models using Conductivity Tensor Imaging (CTI) for Evaluating Brain Stimulation

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Brain stimulation, such as transcranial direct current stimulation (tDCS), has been used for treatments of neuropsychiatric diseases and neurological disorders. When treatment planning in tDCS using the computational modeling approach, however, includes uncertainties caused by unknown conductivity distributions inside the brain. In this study, we present computational modeling results of voltage, electric field and current density distributions during tDCS using subject-specific head models with measured conductivity tensor information. Adopting the lately developed conductivity tensor imaging (CTI) technique, we reconstructed absolute conductivity tensor images of the human brain and incorporated the images in the finite element model as material property values. Distributions of voltage, electric field and current density inside the heads of two human subjects were calculated using the subject-specific head models with reconstructed conductivity tensor images. The current density distributions using the reconstructed conductivity tensor images were significantly different from those using the isotropic literature values with the average relative L2 errors of 73 and 71% for the first and second subjects, respectively. Adopting the C3-FP2 and F4-F3 electrode montages, the current density distributions using the reconstructed conductivity tensor images were more localized especially in the anisotropic white matter regions. The directions of the current densities in the white matter regions were mostly in parallel with the fiber directions. The isotropic gray matter regions tended to convey larger amounts of current densities. We suggest adopting the CTI technique to build a subject-specific head model of an individual subject for personalized treatment planning of brain stimulation.

# Surface-based cryopreservation of stem cell products for diagnostic and therapeutic approaches

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Basic cryotechnology has been an integral part of biomedical research and applications for decades and still is. For instance, any laboratory working with cells and tissues keep frozen stocks of their research objects. The necessary infrastructure for this stock keeping, like disposables, tailored storage racks, and accordant cryogenic tanks, is readily established. Cryopreservation routines for such purposes usually apply the so-called slow freezing protocols. According to these protocols, the biological material is either mechanically or enzymatically detached and subsequently dissociated into a suspension of single cells or small cell aggregates. Cryoprotective agents like DMSO are then added to the suspension and the temperature is decreased with relatively slow cooling rates of about 1 °C/min until 80 °C minimum. Thus, nucleation is induced within the sample that can be tolerated by suspended cells or aggregates. When it comes to cells exhibiting cell-matrix or cell-cell contacts like adherent cells or tissues, the occurring nucleation in these slow freezing protocols causes severe damaging effects followed by loss of function or even cell death. Most often mature cell systems like neurons that have been differentiated for up to months, or tissues lose their functionality upon this harsh treatment. However, these adherent and multicellular states are the interesting ones for biomedical research on diagnostics and therapeutics as they mimic the native, three-dimensional structure and function. Hence, the development of application-oriented cryopreservation procedures for such sophisticated cell systems is crucial and focus needs to be placed on. We here demonstrate strategies to enable application-oriented cryopreservation of human stem cells and their derivates by the application of a second cryopreservation regime that avoids nucleation by ultra-fast cooling rates (vitrification) as well as by the application of flexible growth surfaces that modulate cell's cytoskeleton in order to enhance their tolerance against nucleation during slow freezing regimes.
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# Surgical Tool Detection in Laparoscopic Videos by Modeling Temporal Dependencies Between Adjacent Frames

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Video-based surgical tool detection is an important yet challenging problem for developing context-aware systems (CASs) in the operating theatre. In this paper, we address tool presence detection in laparoscopic videos using a combination of convolutional neural network (CNN) and Long-short term memory (LSTM) network. Firstly, a pre-trained CNN model was fine-tuned to learn visual features from laparoscopic images. Since the data is sparsely labelled, an LSTM network was then employed to learn temporal dependencies from short sequences of adjacent frames. Several experiments have been conducted with the Cholec80 dataset to validate the proposed framework and investigate the effect of the video clip length on tool prediction performance. Results demonstrate the advantage of employing temporal information to the tool detection task and show the most notable improvement is achieved when sequences of previous and next frames were employed.

# Swallowing onset detection: comparison of endoscopy- and accelerometry-based estimations

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The swallowing process involves the coordinated activation of several muscles to ensure the transfer of nutrients from the mouth to the stomach. A proper segmentation of swallowing into its constituent phases is relevant to obtain a quantitative biomechanical and electrophysiological description of this sensorimotor task. An experimental study on five healthy subjects was performed to compare the accelerometer-based swallowing segmentation with that obtained through the Fiberoptic Endoscopic Examination of Swallowing (FEES), considered as clinical gold standard. The comparison was performed in terms of: (i) swallowing onset detection and (ii) event-related symmetry indexes computed on surface electromyograms (sEMG) during the oropharyngeal phase. Results from different swallowing tasks showed that the swallowing onset identified through the accelerometer preceded that identified by FEES of 204±192 ms (mean and standard deviation), regardless of the type or volume of bolus. Despite the bias in onset estimation, sEMG symmetry indexes computed within a 1.5s epoch from the accelerometer- and FEES-based onset, exhibited comparable values. This result suggests that the observed underestimation was not relevant in order to study symmetry differences in swallowing muscular activation. These preliminary results suggest that acceleration measurement can provide a possible non-invasive alternative to the FEES-based segmentation for the extraction of event-related symmetry indexes during the oropharyngeal phase of swallowing.

# SWEET-Shirt: an Innovative Wearable Health Monitoring System

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SWEET-Shirt is a new wearable system that allows the acquisition and transmission of body biosignals with purposes related to remote health care monitoring. The system looks like a simple t-shirt, inside which sensors and electronic connections are integrated. Electrocardiogram, electromyography and accelerometer signal are the physiological variables collected and monitored from the proposed device. An electronic board must be connected to the textile platform, programmed to transmit the acquired signals to any mobile device through BLE protocol. In order to receive the data flow from the wearable sys-tem, a custom-made mobile application, named SWEET App, was developed. It also allows to store signals in a .csv file and load it on a cloud platform where further digital signal processing actions are made by a custom made Matlab GUI software. The purpose of this work is to illustrate the design and development of the device, showing its characteristics and possible scenarios of use.

# Tanzanian District hospitals - the gap between governmental vision and reality

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In strategic plan 2014–2019 the Tanzanian Ministry of Health and Social Welfare identified "Human Resource for Health" to be the key component for "delivery of quality health and social welfare services, with the ultimate goal of having effective health services in a dispensary at every village, a health center at every ward and a district hospital at every district". Another five year development plan from 2016 announced the construction of 67 new health facilities, in part improving existing district hospitals. In 2019 the government gave notice to end the public private partnership (PPP) with faith based (district) hospitals (at least 13% of Tanzanian hospitals). - District hospitals are supposed to have a minimal total staff 200 persons with a low number of (biomedical) technologists. The lack of human resources for health, particularly doctors, is nothing new. Therefore, district hospitals hardly can find the recommended number of doctors: 75% of the Tanzanian population lives in rural areas, 26% of doctors serve in rural areas. This situation mirrors in respect to clinical and hospital engineers: in 2017 the Tanzanian minister of education reported a shortage of 7000 biomedical engineers. A substantial relief is hardly to be expected in the near future: the gap between the governmental efforts and reality appears evident. In respect to biomedical engineering, extensive knowledge transfer, supervision and training to increase the provider‘s skills will become more important than financially supporting the installment of technologically most advanced medical equipment in an inadequate infrastructure of district hospitals.

# The atomic sensors in preliminary study of MCG and MEG signals

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The new generation of atomic magnetic sensors with sensitivity of 10 pT/rtHz provides new tool for the assessment of magnetocardiography (MCG) and magnetoencephalography (MEG). The method needs the passive attenuation of the magnetic field of the Earth and magnetic noises by shielded magnetically room (MSR). Additionally, for the improvement of the sensitivity of the sensor the active compensation of Earth's magnetic field to near zero level is necessary. Such conditions can be provided by three dimensional systems of compensation coils incorporated in an MSR. Author, with coworkers, has designed, based on Vacuumschmelze MSR, a laboratory for atomic sensors' measurements with compensation coils system zeroing magnetic field of the Earth within whole area inside shielded cabin. The laboratory consists of two stands: for MCG and MEG signals' assessment. The MCG stand is composed of a wooden table and a universal holder for sensors printed in 3D technique. The MEG stand consists of a wooden chair and a universal helm holder, also printed in 3D technique. For both stands the two atomic sensors of SERF type were used. Five healthy volunteers, two women and three men, were incorporated in a preliminary study. In all volunteers the MCG and Visual Evoked magnetic signals were recorded. In order to achieve a clinically useful MCG, the averaging technique has to be applied. The sufficient improvement of the signal to noise ratio was seen after 8-16 averaged cycles. The Visual Evoked MEG was induced by the photostimulator signal. In that study the averaging technique was also necessary. The best results were achieved after at least 20-30 cycles. The visual evoked magnetic signals were definitely recognized. However, the noise level was still fairly high. To conclude, the novel magnetic sensors seem to be the promising diagnostic tools for MCG and MEG studies. The method should provide the opportunity to open new diagnostic areas such as the diagnosis of the disturbances of the cardiac rhythm in a fetal or to define more precisely the locations of the MEG signal's sources.

# The correlation between the clinical and immune response after the combined treatment of electrochemotherapy and interleukin 12 gene electrotransfer in dogs with oral and mast cell tumors

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Preclinical studies in companion dogs with spontaneous tumors present a valuable tool in translation of novel treatments into human oncology. Cancer is a prevalent disease in dogs, specifically skin and oral tumors, which are the most common solid tumors in canine population. In veterinary oncology, electrochemotherapy (ECT) and gene electrotransfer of interleukin 12 (IL-12 GET) proved to be safe and effective in treating different types of tumors in dogs. However, several questions remain unanswered, especially those regarding the immune response to treatment and selection of appropriate dogs. Therefore, the aim of this study was to evaluate the systemic immune response and the expression of the programmed death receptor and its ligand (PD-1 and PD-L1) in the tumors to define the immune response to ECT and IL-12 GET and possible predictive factors for the treatment response.

Fourteen dogs, with mast cell tumors (MCT) and nine dogs with oral malignant melanoma (OMM) were included in the study where combined treatment of ECT and IL-12 GET was used. Samples of blood were drawn before the treatment and after the treatment (1, 2, 4 weeks after the treatment and at the end of observation period). The subpopulation of T lymphocytes: CD4+ (helper T cells), CD8+ (cytotoxic T cells) and Foxp3+ (regulatory T cells) were determined using flow cytometry. Additionally, before treatment, tumor biopsies of 30 treated dogs (21 MCT and 9 OMM) were collected and evaluated for the expression of PD-1 and PD-L1 using immunohistochemistry.

The results show that the percentage of regulatory T cells gradually decreased during treatment/follow up period and was the lowest at the end of observation period ($p<0.05$). The treatment did not have any influence on the amount of circulating helper and cytotoxic T cells before and after the treatment. Immunohistochemical staining of the samples taken before the treatment showed higher expression of PD-1 and PD-L1 in dogs with OMM compared to those with MCT. Moreover, expression of PD-1 and PD-L1 was higher in the patients with shorter overall survival and progression free survival ($p<0.05$) and lower in those with longer survival and progression free survival.

To conclude, a systemic immune response to the treatment was observed. The PD-1 and PD-L1 expression in the tumors taken before the treatment could be used as a prognostic marker in ECT and IL-12 GET treatment.

# The effect of anisotropy on the impedance and electric field distribution in deep brain stimulation

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Deep brain stimulation (DBS) is an intervention used for several neurological conditions such as Parkinson's disease. To evaluate the clinical response in relation to anatomical location, computer-aided electric field simulation is commonly used. The models presented in different studies are varying in complexity and this study aims to evaluate the effect of including anisotropy in the tissue model using homogenous tissue with varying level of anisotropy both parallel and perpendicular to the DBS lead. As a benchmark, data from one patient was included and simulations was performed in zona incerta (Zi) and the internal capsule (IC). The parameters investigated were impedance, volume within the 0.2 V/mm isosurface, radial and longitudinal expansion as well as visual representation of the isosurface. The investigations show that both the impedance and volume are increasing with increasing anisotropy together with the electric field isosurface in the principal direction of the anisotropy. When comparing different stimulation modes, current control (CC) stimulation had a steeper increase with increasing anisotropy for all parameters compared to voltage control (VC) stimulation. This could be due to a joint effect of the anisotropy and the increasing impedance. The result from the patient simulations are in the anisotropy range where simulations from the homogenous models starts to have a higher slope for all parameters. This indicates that including anisotropy in computer models will be of importance in areas of high anisotropy.

# The effect of cryopreservation protocol on kinetic characteristics of semen from saanen and alpine goats

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Using of cryopreserved sperm for artificial insemination, in vitro embryo production and embryo transfers may lead to more efficient goat reproduction on farms. Therefore, freezing media should be easy to prepare and the cryopreservation protocol should be easy to use in farm conditions. The objective of this study was to investigate the effect of different cryopreservation protocols with glycerol freezing media on the motility after the freeze-thaw process of Saanen and Alpine goat semen. A total number of 60 ejaculates were collected using artificial vagina and goat in estrus twice a week during breeding season (September-November). Immediately after collection sperm volume, total concentration of spermatozoa and total motility was calculated. Each ejaculate was split into 3 equal aliquots and diluted with HEPES based extenders supplemented with 10% glycerol. Extended semen from each goat breed was loaded in straws and cryopreserved with 3 different protocols: 1 – 2 min at 30°C, 20 min at room temperature (25°C), 15 min 15 cm above liquid nitrogen, liquid nitrogen; 2 - 5 min at room temperature (25°C), 5 min at 5°C, 10 min 15 cm above liquid nitrogen, liquid nitrogen; 3 - 15 min at room temperature (25°C), 15 min 15 cm above liquid nitrogen, liquid nitrogen. Sperm motility was evaluated 0 and 1 h after thawing on water bath at 37°C and removing cryoprotectants by centrifugation manually using Makler‘s chamber. Cryopreservation process affected motility of spermatozoa by reducing this parameter, however, the effect of cryopreservation protocols was different. The results indicate that total sperm motility was significantly ($P<0.05$) higher in protocol 2 for both goat breeds compared to protocol 1 and 3. We can conclude that cryopreservation protocol with 3 steps (25°C, 5°C, vapor liquid nitrogen) has better cryopreservation effect on kinetic characteristics of Saanen and Alpine goat.

# The Effect of Force Sensor Arrays Integration into Textile for a Novel Head-Foot Wheelchair Steering System

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In this paper a novel head-foot wheelchair steering system based on force sensor arrays (FSAs) for people diagnosed with dyskinetic cerebral palsy (DCP) is introduced. The user applies pressure on FSAs placed on the head, and foot supports of the electrically powered wheelchair (EPW), based on his/her intention to accelerate, brake, steer right or left. The microcontroller-based electronics of the system acquire and translate the mean voltage generated by the applied force into wheelchair control signals. In such a system, FSAs are integrated into the head support of the wheelchair using support materials and textiles for the comfort of the user, having an effect on the sensor readings. This work aims to explore the effect of integrating FSAs into the head support of the wheelchair using support material and textiles. Four different sensor integration approaches were examined and compared to baseline readings of a non-integrated FSA. It was found that when a maximum force of 80 N is applied to a single sensing element (sensel) the support material decreases the mean voltage by approximately 70%, and the sensor integration into textile has shown increases between 5.2 and 14.9% compared to the support material. Furthermore, when force is applied over multiple sensels, the support material accounts for a reduce in the mean voltage ranging from approximately 3 to 32%. The addition of textile has exhibited peak decrease in the mean voltage up to roughly 41% for the tested integrations.

# The Effect of Passive Exoskeleton on Shoulder Muscles Activity during Different Static Tasks

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In this study we used the bipolar surface electromyography to investigate whether a passive exoskeleton reduces the degree of activity of four shoulder muscles during four different static postures: (P1) shoulder abducted at 90°, elbow flexed at 90°, elbow pronated at 90°; (P2) shoulder flexed at 90°, elbow flexed at 90°, elbow pronated at 90°; (P3) shoulder flexed at 90°, elbow pronated at 90°; (P4) shoulder abducted at 90°, elbow pronated at 90°. Our main statistical results showed a significant ($p<0.05$) attenuation effect of exoskeleton on the RMS amplitude computed for all muscles evaluated, though not for all postures. For the anterior, medial deltoids and upper trapezius a lower level of activity was observed in all postures with than without exoskeleton, while for posterior deltoid only for P2-P3 and P1-P4 respectively. These findings suggest the passive exoskeleton evaluated in this study attenuates the shoulder muscles' effort during static work-related tasks, with implications on the prevention of musculoskeletal disorders.

# The future of healthcare - the clinician engineer

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For decades medical doctors reached a diagnosis and commenced treatment based on undertaking a history and performing a physical examination. However this in itself is subjective. History taking relies on patients understanding the questions asked and being transparent with their symptoms. A physical examination has also proven to be a subjective process. Currently doctors in healthcare are relying on engineering solutions to guide management, be it CT scans, dialysis machines, endoscopes, ventilators, cardiac stents... the list is endless. However clinicians have limited knowledge of how engineering platforms work. Surely as frontline health care providers being equipped with advanced engineering knowledge can help to build more advanced solutions and overcome limitations of current innovations. The clinician engineer hub is the first international platform aimed at educating early career doctors in the field of engineering. We will share the steps taken to launch such a venture, our work so far and future plans.

# The Human Body and Weightlessness: Mass-Inertial Characteristics in One of the Basic Positions Selected by NASA via 3D Mathematical Modelling

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Among all possible postures of the human body, NASA selected eight of principle importance for space exploration. The aim of the current article is to determine the mass-inertial characteristics of the human body of the average Bulgarian male in one of these positions – the so-called relaxed, or weightless position. We determine the corresponding characteristics of the centre of mass and principal moments of inertia using a 16-segmental biomechanical mathematical model that is generated within the SolidWorks environment. We verify the model by comparing the analytical results for each of the body segments with the results obtained using the computer model. The geometric data needed for the construction of the 3D model are taken to be in correspondence with experimentally available anthropometric data for about 2500 Bulgarian men. One their basis one determines the characteristics of the average Bulgarian men. Then, using the CAD realization of the model the inertial parameters of this "average" male in different body positions can be determined. The comparison made be-tween our model results described in this article and the data reported in the literature, where available, gives us confidence that the suggested model can be used to calculate the properties in question at any postures of the body of interest. In principle, our approach can be also used to calculate the corresponding mass inertial data for any individual provided that the anthropometric set of parameters for that individual are measured. The model we used is suitable when one needs such parameters in problems appearing not only in space exploration with the participation of male astronauts but also in rehabilitation, sport, criminology, robotics, etc.

# The Impedance Cardiography in clinical, noninvasive assessment of hemodynamic parameters

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The plethysmography based on the rheological measurements is widely applied in assessment of hemodynamic parameters of the heart and the circulatory system. The first clinical method of calculation of cardiac output (CO) and stroke volume (SV) of the left ventricle of the heart based on the cylinder model of the torso was introduced by prof. W. Kubicek from University of Minnesota. The Kubicek model was modified by prof. S. Sramek by introducing of truncated cone model in the place of cylinder which better fits to the shape of the human torso. The both methods were realized in many technical constructions around of the world. The all constructions of electric plethysmography utilized tetrapolar current mode of work with fix frequency in the range 20-100 kHz and fix current in the range 1-5 mA. The method named later as an Impedance Cardiography (IC) became the standard in noninvasive assessment of SV, CO and other parameters describing of the hemodynamic activity of the heart. For some clinical applications, as for instance parallel assessment of aortic and pulmonary flow, the unit consists of two independent channels with different sets of parameters for each channel, were designed. Now a day, the most important areas of it clinical application are: pharmaceutical tests of the impact of new drugs on the human circulation, head up tilt tests in the syncope diagnosis procedure, follow up and adjustment of parameters in cardiac pacing patients. The IC was also tested by authors in maximal stress tests performed for assessment of sportsmen's physical performance ability and reserve, but in the peak of stress the method were fund as non acceptable due to pervasive artifacts related to border line exhaust of tested subjects. The method has shown its prevalence in authors comparative study with also noninvasive measurements system based on the Penaz method. The statistic analysis of results, assessed in the same patient at the same time, didn't show any statistically significant differences between two tested methods but the IC was found as more convenient in the clinical use due to its simplicity and lack of any impact on the circulation of the subject of the study.

# The Recurrent Neural Networks for Muscle Stress Prediction in Finite Element Analysis

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Muscle models can be classified as phenomenological, often called Hill-type, and biophysical, often called Huxley-type. Phenomenological models oversimplify many structural and functional properties but are computationally cheap. On the other hand, biophysical models are based on the underlying physiology of the system but are computationally expensive. Parameters of the Hill-type models are not directly related to the characteristics of muscle proteins. The influence of muscle protein characteristics on muscle contractions can be better examined using biophysical models. In order to efficiently use biophysical muscle models in finite element analysis, we create neural networks that mimic these models. The neural network used is the bidirectional gated recurrent unit with the self-attention mechanism. During finite element analysis, the network receives values of muscle fiber stretch and activation in current and previous time steps and values of stress and stress derivative in previous time steps. Based on these inputs, the network predicts stress and stress derivative values in the current time step, which are further used in finite element simulation. We achieved highly accurate predictions and the network behaves very similarly to the original Huxley-type model. Since the network is computationally more efficient than the original model, it can be used in very large finite element models, such as heart model.

# The Rhinodiagnost Project - Concept and Implementation of a Nasal Airflow Simulator

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"Internationally recognized research centers and market-leading medical technology companies are cooperating via the RHINODIAGNOST project in order to establish a coordinated morphological and functional diagnostics for ENT (Ear – Nose – Throat) physicians. The RHINODIAGNOST services shall be organized in a rapid network providing new, additional decision aids, such as 3D models and flow simulations, for ENT physicians and radiologists" (taken from: http://www.rhinodiagnost.eu ). The Austrian coordinator of the Rhinodiagnost Project, AIT – Applied Information Technique Research Inc., developed an experimental station which allows the simulation of airflow in the nasal cavities using a 3D printed model. The system was designed as low cost system which doesn't need great financial efforts and fits on a DIN-A-4 sized area of a desk. It consists of: 1) a Control Unit which hosts a Raspberry Pi 3 Model B+ microcomputer, a Sensor Box which contains twelve air pressure sensors controlled by two Arduino Nano V3 microcomputers and motor drivers for the pump and valve, 2) a Pump driven by a DC motor and generating the necessary airflow using a Francis-Turbine, 3) a Cross Valve which switches the airflow between inspiration and expiration, 4) a Flow Meter measuring the volume stream of the air flow bevor it enters the 5) 3D printed model of a nasal cavity. The 3D model is connected to up to ten sensors of the Sensor Box via small hoses. Pump, Valve, Flow Meter and 3D Model are inter connected via standard breathing tubes. The Raspberry Pi comes with a MySQL (MariaDB) database system which stores the values delivered by the sensors in a relational data base located at the experimental station itself. Measurements (pressures at specific points at the wall of the nasal cavity) taken by the experimental station - in vitro - can be compared to the results of a CFD (Computational Fluid Dynamics) simulation - in silico - using same boundary conditions (model, volume stream, etc). Since the experimental station can be connected to a computer network infrastructure of a research lab, "in vitro results" immediately can be compared to "in silico results". The station is used to compare the experimental results of a bigger amount of patient data (up to 100) to the outcome of CFD simulations.

# The rotational center on the ulnar head during forearm rotation

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Background: The center of rotation on the ulnar head during forearm rotation has not been identified.
Methods: Three-dimensional bone models reconstructed from 21 set wrist CT images taken with supination and pronation were investigated. Numerous points were set on the surface of the ulnar head. The same points were matched on pronated image and supinated image. The pronated image and the supinated image were overlapped so that the radii were in the same position. Rotation center (RC) was defined as the point which had the least distance between the point in pronated ulna and the point in supinated ulna. The distance between RC in pronation and RC in supination was measured. Correlations between parameters were analyzed.
Results: The distance between RC in pronation and RC in supination was 0.7 $\pm$ 0.6 mm (range, 0.11-2.41 mm). The position of RC in radio-ulnar direction had significant correlation with translation of the ulnar head (TUH) (Pearson's correlation coefficient = 0.775, $p < 0.001$). The RC was located more ulnarly when the TUH was greater. The position of RC in radio-ulnar direction also had significant correlation with the amount of forearm rotation (Pearson's correlation coefficient = 0.454, $p = 0.039$). The RC was located more ulnarly when the amount of forearm rotation was greater.
Conclusions: There was no isometric point on the ulnar head during forearm rotation. The center of rotation on the ulnar head during forearm rotation moves ulnarly with increased amount of radio-ulnar translation and forearm rotation.

# The state of art in nasal airway function tests , the development of 4-phase-rhinomanometry and the aim of future diagnostics

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Nasal airway obstruction is a trivial problem. In the daily practice of an ENT-specialist the causing morbidities are belonging to the most frequent ones with a huge social and financial impact worldwide. While in inflammatory or neoplastic diseases the optical information by inspection or endoscopy, CT and MRI are determining the indication of a treatment, in all cases with intended surgical treatment the respiratory function should be analyzed before irreversible operations changing form and function of the nose. Because of the enormous costs of nasal surgery for governments or assurances and an outcome of estimated 30-40% non-successful operations the tendency to introduce reliable functional diagnostic is steadily growing. One example is the German-Austrian “Rhinodiagnost” project with here presented results. The basic information about the nasal air stream is the nasal flux and the differential pressure between the nares and the nasopharynx. The non-linear quotient between these parameters is the nasal resistance. Its measurement is for about 100 years conventionally called “rhinomanometry”. The introduction into the clinical practice started in the 1970th by COTTLE and MASING, analogue measurement devices using capacitive pressure sensors and analogue xy-recorders followed in the 80th. The resistance was measured by determining the flow at 150 Pa. By introducing personal computers in 1990 (VOGT et al.) the entire averaged breathing curve was evaluated. In the following years the graphs showed open loops during inspiration, releasing a long-lasting discussion about their background. After exclusion of technical errors by hysteresis of the transducers the loops could be explained as a follow-up of Bernouilli-effects by the aspiration of the lateral nasal wall (“Starling”- resistor). The term “4-phase-rhinomanometry (4PR)” was introduced with the parameters Effective Resistance as the root mean square (RMS) of pressure and flux and the Logarithmic Effective Resistance ( log(10*Reff)). In 36,500 measurements, we could show the first time a significant correlation between the logarithmic transformed resistances to the sensing of obstruction on a VAS, thus following the basics of psychophysics of Weber and Fechner 150 years ago. In addition, the influence of elasticity can be estimated from the depicted graphs. In 2016 4PR was confirmed as the new standard of physical investigations of thee nasal air stream. 4-phase-rhinomanometry determines the air stream energetic of one nasal cavity. It should be followed by Computational Fluid Dynamics.

# The use of SCORE and GRACE risk tools to assess the Length of Stay in a Cardiac Intensive Care Unit

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The possibility of using simple and effective models to estimate the patient's length of stay in intensive care units is decisive to support the clinical professional decisions. These models can help professionals in the stratification process and, particularly, in the identification of the necessary intervention plan to improve the patient's health condition. In clinical practice specific prognostic scores are available and validated in the cardiovascular context. These risk tools address the primary prevention domain, as well as the secondary prevention domain, usually involving long-term (years) and short-term (months) prediction periods, respectively.
The aim of this study is to investigate the capacity of available prognosis risk tools, in particular SCORE (primary tool) and GRACE (secondary tool), to estimate the length of stay in a cardiac intensive care unit. For validation purposes a dataset collected by the Centro Hospitalar Universitário de Coimbra was used, consisting of approximately 1400 patients that have been admitted into the cardiology intensive care unit. The obtained results suggested that SCORE and GRACE models are not sufficiently accurate to estimate the actual length of stay. Moreover, GRACE presents better results than SCORE, which can be justified by the employed risk factors, more specific for short-term prediction periods.

# The use of Six Sigma to assess two prostheses for immediate breast reconstruction

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Breast reconstruction is fundamental and urgent for patients in order to avoid future psychological and physical issues. That's why immediate breast reconstruction has been requested increasingly in the last years. In this study two prostheses with different structures and properties were compared according the aesthetic appearance (BREAST-Q© was employed) and five complications (seroma, hematoma, infections, dehiscence and red breast syndrome). The overall population was composed by 56 patients: 24 received a Tutomesh prosthesis and 32 received a Surgimend prosthesis. The DMAIC (define, measure, analyse, improve and control) cycle was implemented as a problem-solving strategy of the Six Sigma to compare the prostheses. While statistically significant difference between of the two groups was found neither according to the overall BREAST-Q© scores nor according to the complications, the number of complications of the two groups resulted statistically different (p-value of chi-square test less than 0.001). Although it is not possible to understand from this study the reasons of the differences between the complications, this research proved that Surgimend and Tutomesh prostheses can be both implanted safely for immediate breast reconstruction since the higher costs of Surgimend could be neutralized with its lower hospitalization compared to Tutomesh.

# Therapeutic ultrasound transducers conformal to medical needs

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The use of ultrasound for therapy has seen a growing interest since the nineties and the development of endorectal transducers for ablating thermally prostatic tissues. Different devices are currently under clinical evaluation for the treatment of many disorders. Numerical modelling plays a significant role in these developments. For each clinical need, it allows defining the geometry of the transducer and the exposure conditions. The technology for manufacturing the transducer is chosen according to the required acoustic output, density of elements, frequency bandwidth and medical use (endocavitary, disposable, implantable…). The imaging modality for treatment monitoring is also critical and should be considered in the design process.
The goal of this presentation will be to list the various challenges faced during the design of a therapeutic transducer, discuss some solutions that were proposed and illustrate the process with two examples: 1- a disposable ultrasonic device for performing cyclo-coagulation and treating glaucoma and 2- an ultrasonic implant for opening the blood brain barrier, facilitate the diffusion of chemotherapy and treat glioblastomas.

# Thermographic Evaluation Of Dental Implants Inser-tion With Different Diameters: In Vitro Comparison Be-tween Regular And Narrow Implants

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Caries and periodontal disease are considered a primary cause of tooth loss and extraction. Implant dentistry has improved the rehabilitation of edentulous pa-tients providing a 10-year success rates of over 97%. However, the insertion torque, the superficial characteristics of the implants, and the heat generated dur-ing implant site preparation could represents a critical factor for early implant fail-ure. Hence, monitoring the temperature during the insertion could be fundamental to predict the probability of success of the prothesis. Although several studies investigated the thermal effects of drilling and fixture placement, a comparative study between the thermal outcome of the insertion of implants with different di-ameter is missing. The objective of the study was to compare thermal changes, evaluated through infrared thermal imaging, induced by the insertion of narrow (3.0mm x 10.0mm) and regular (4.5mm x 10.0 mm) implants in an animal bone model (swine ribs). An increase of the bone temperature was found for both nar-row and regular implants. Moreover, a higher thermal effect was found for the narrow with respect to regular implants ($p<0.05$), but always lower than the tem-perature limits of the bone necrosis. Although preliminary, these results con-firmed that narrow implants are thermally and clinically safe.

# Three-dimensional Reconstruction of Carotid Arteries using Computed Tomography Angiography

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Carotid artery disease is the pathological disease of carotid arteries and is consid-ered as a principal cause of stroke. Therefore, early diagnosis of carotid artery disease is of high clinical importance. This study aims to present an overall methodology for the accurate identification of the inner wall, outer wall and the atherosclerotic plaques (calcified and non-calcified) of the carotid arteries. The proposed methodology is based on a level set based approach, which is fully adapted in each computed tomography acquisition protocol. Briefly, the method-ology includes the following steps: (i) the estimation of intensity membership functions for the inner wall, the outer wall and CP, (ii) the carotid artery center-line extraction, (iii) the inner wall, outer wall and calcified plaques segmentation, (iv) the noncalcified plaques segmentation and finally (v) the 3D models con-struction. The segmentation accuracy of the proposed methodology has been val-idated against manual expert's annotations in 4 patients, and more specifically in 300 computed tomography angiography slices for the inner wall segmentation and in 30 slices as far as the atherosclerotic plaques is concerned. The utilized evaluation metrics were the Dice coefficient and the Hausdorff Distance and our very first results are promising for the accurate and automated segmentation of carotid arteries.

# Towards a finite element simulation of minimally-invasive tissue ablation employing electrolytic electroporation (E2)

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The combination of electroporation and electrolysis, short E2, is an ablation technique which can be utilized to remove tissue in a minimally invasive approach. It is often applied in the shape of low-energy exponential decay pulses, where the short high voltage phase of the pulse induces reversible electroporation, and the longer low voltage phase produces electrolysis species. As both processes are intended to occur simultaneously, their effects are likely to interact with each other. Whether this can potentially initiate a new set of phenomena that only occur in this combination is not yet understood. It is hypothesized that the electrolysis species can enter the cells in high concentrations after cell membrane permeabilization, and kill the cells by triggering intracellular mechanisms with a delay of a few hours after the application. In order to understand the principle lethal mechanisms of action of an E2 application, mathematical modeling is being applied. The presented work demonstrates the electrochemical effects of a set of E2 pulses in a 2D model, where the tissue is considered a sodium chloride solution containing a bicarbonate buffer system. Nernst-Planck transport equations are used to consider ion transport within the electrolyte. The equations are solved with the finite element-based COMSOL Multiphysics software. The main outputs of the model are concentration profiles of different species and pH distribution as functions of time and space. The model validity is investigated by comparing simulated with experimentally obtained pH profiles. This work indicates that a simple mathematical model can potentially provide a qualitative description of the electrochemical processes of an E2 application. Mathematical models which are capable of predicting pH fronts in treatments with an electrochemical component are a useful tool to predict the spatial and temporal movements of ion concentrations and pH within the treatment area. The obtained information can help optimize treatment parameters of electroporation-based treatments.

# Towards a smart smoking cessation app: a 1D-CNN model of predicting smoking events

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Smoking is considered the cause of many health problems, with about 78,000 deaths per annum in England. While most smokers wish to quit smoking, many relapse; this may be reduced via personalised messaging on mobile devices. To support efficient and timely delivery of intervention, it is important to be able to model the smoker's behaviour. This research describes the creation of a hybrid model which learns the smoker's daily routine and predict smoking events. This combines a Control Theory model, describing the homeostatic maintenance of the smoker's nicotine level across a range of temporal scales, and a One Dimensional Convolutional Neural Network (1D-CNN) classifier, which describes the external conditions associated with smoking.
Data was collected from 5 long-term smokers, over 14-day periods. An Android phone-app collected the occurrence of smoking (via self-report), and the time, location via GPS (longitude, latitude and altitude) and phone accelerometer readings (on X, Y and Z axes) once per minute. Separate models were trained for each participant, capturing individual differences in behaviour. 1D-CNNs were built on each measured channel with 64 filters, before concatenation into a 30-unit dense layer connected to the smoking record. Mean accuracy for smoking vs. non-smoking for the 1D-CNN classifier was 87 across participants; this significantly out-performed other classifiers (SVM 80%, Decision Tree 81%).
The values generated by the 1D-CNN were passed to the control theory model, combining with endogenous nicotine and craving levels to determine instances of predicted smoking. Normalised RMS Error was found on changes in nicotine level between that derived from smoking self-reports alone and with input from the 1D-CNN. Weekdays had mean errors of 0.19 and weekends 0.17; although some smoking events were missed, the model in general reliably predicts the smoking behaviour. While accuracy of prediction is negatively affected by un-reported instances in some participants, overall it remains high, with an ROC area under curve of 0.65 for 30 minute prediction intervals and 0.74 for 60 minute intervals.
Overall, the combination of 1D-CNN with the control theory model of smoking gives promising results, although the accuracy is limited by participant compliance. Separate work is underway to detect smoking from hand movements, and also to add extra geographical information concerning the addresses of the participant's home, work and socialising locations.

# Towards certification of clinical electroporators following the Medical Device Regulation (MDR) 2017/745

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Developing a device can be sometimes easy, but doing it in accordance with the standards and regulations, i.e. assuring safety, quality and efficiency, can be quite challenging. Getting approval for selling the device on the market (CE marking) and having a post-market surveillance takes additional effort. This is especially demanding for manufacturers when developing and manufacturing a medical device where patient's safety comes first. Before placing a medical device on the European market, manufacturers need to present technical documentation (TD) providing evidence of conformity with the relevant legislation. As of May 26 2020, the TD needs to comply with the Medical Device Regulation (MDR) - European Union (EU) Regulation 2017/745. The preparation of the TD in compliance with Annexes II and III from the MDR is manufacturer's responsibility and according to Article 10 of the MDR: 'technical documentation shall be such as to allow the conformity of the device with the requirements of the regulation to be assessed'.

For successful application of electroporation, we need an electronic device – electroporator and electrodes. Electroporators are able to generate high voltage pulses of specific shape, different amplitudes, number of pulses, duration and pulse repetition rate. Generated pulses create an electric field around the electrodes which intensity is controlled by the pulse amplitude. Depending on the application, electroporators are divided in several groups of which clinical electroporators are medical devices used for medical treatment in clinics. They are considered to be active, therapeutic and high-voltage medical devices which are classified as class IIb medical devices by Annex VIII of the MDR. The pulses are delivered to the tissue via electrodes as a necessary but separate medical device.

From a clinical electroporator's perspective in order to get a CE mark, TD during the design and development process in compliance with the new MDR has to be prepared. The aim of the presentation will be to overview the EU regulatory process, to present the necessary documents that we need to prepare within the TD for a clinical electroporator and introduce the safety requirements that have to be met. Furthermore, the standards to be followed will be presented and how the design and development process should be conducted will be explained.

# Towards magnetic tracking for Deep Brain Stimulation

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Deep Brain Stimulation (DBS) is a treatment for movement disorders like Parkinson disease. The therapy consists in delivering electrical stimulation through electrodes implanted in brain structures responsible for movements regulation. Targeted anatomical structures have millimeters sizes. Minor errors in the targeting can lead to massive differences in the treatment efficacy.
One solution used to track the electrode in relation to pre-operative imaging is using electrophysiology recordings to identify anatomy-specific patterns. This however requires the patient to be awake and comes with increased risks of complications. A second option is to use intraoperative imaging which is rarely available. In addition, imaging of DBS electrodes causes artefacts introducing uncertainties in the detection of their position. During the treatment as well, the electrode may move substantially, impacting the symptoms, due to his intentional flexibility. Despite the importance of the placement of the electrode in the brain, currently available solutions to non-invasively determine it are complex, costly and cause inconvenience to the patient. In this context, a magnetic tracking system is proposed. Magnetic tracking is the most promising solution because unlike optical tracking no line of sight is required. Three-dimensional magnetometers, in wafer-level packages, have been integrated in a probe mimicking a DBS electrode. This combined with a dedicated three coils magnetic source and a trilateration algorithm allows tracking the position precisely during the surgery. Our approach, based on a magnetic field mapping, uses a magnetic field camera making the system more adaptable and robust. Constant magnetic perturbations are rejected by the system.
Tracking is possible within a mapped volume of 16.8 x 11.2 x 12.2cm3. This volume of interest can be increased using a larger map in the tracking algorithm. The tracking accuracy is close to 1 mm, i.e. smaller than the electrode diameter. The position refreshes every 60 s, which is short compared to the implantation duration. The present algorithm performs averaging in order to increase accuracy instead of making real time tracking.
These present work has demonstrated the feasibility of a magnetic tracking directly integrated in a DBS electrode. This magnetic tracking system has been developed to make a link with the preoperative imaging during the surgery, in order to increase surgeon's control on the implantation trajectory. Future investigations will also evaluate a continuous monitoring after implantation in patient's brain reusing sensors inside electrode. Such a monitoring could be performed in the specialist's medical cabinet equipped with a dedicated magnetic source.

# Towards quantitative MR-based imaging: the European project QUIERO

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Standard MRI (magnetic resonance imaging) results mostly have a qualitative nature that limits their objectivity and comparability. Although a significant effort has been put in the development of MR-based quantitative techniques (having the potential to improve the diagnostic capabilities, the reliability of follow-up analyses and the effectiveness of subject-specific therapy design), a comprehensive characterization of these innovative procedures, required to bring them into clinics, is still lacking.

The research project "Quantitative MR-based imaging of physical biomarkers" (identified as QUIERO, i.e. QUantitative Imaging Enables Reproducible Outcomes), funded by the European Metrology Programme for Innovation and Research, started in June 2019, is working to overcome this problem. The project involves six national metrology institutes, two clinical centres and three universities, and it is intended to evaluate the suitability of two MR-based emerging techniques, Electric Properties Tomography (EPT) and Magnetic Resonance Fingerprinting (MRF), to become clinical tools. Within the realm of quantitative MRI, EPT and MRF have been chosen because they are promising techniques, which could find a synergistic use. Indeed, the parameters measured through EPT (dielectric permittivity and conductivity) and MRF (relaxation times of magnetization) can be considered as biomarkers in one single multiparametric analysis. In addition, the possibility to exploit MRF as an efficient technique to provide the input required by EPT is under investigation.

During the project lifetime, EPT and MRF will undergo a full metrological characterization, to provide the clinical community with a quantification of their reliability. Currently, EPT and MRF algorithms are being implemented and their intrinsic performances checked in silico, against artificially produced theoretical data. The experimental activity involving clinical MRI scanners, will soon start on reference phantoms (including 3D–printed heterogeneous and anthropomorphic structures), to identify the uncertainty contributions coming from the real measurement process, under controlled conditions. Finally, two clinical studies, one focused on brain and the other on cardiac MRI (where specific attention is given to motion-compensation techniques, to maximize the quality of the acquisitions in the presence of breathing and heartbeat), will be performed on human subjects. The collected clinical data will be processed to explore the possibility to detect pathological anomalies in the produced quantitative maps of the biomarkers, without mistaking them for the physiological variability of parameters. Besides traditional approaches, artificial intelligence methods will be used, together with the knowledge coming from the previous characterization activities, to train models for diagnostic decision support systems.

# Transmembrane Voltage on Realistic Models of Suspended and Adhered Cells Induced by Electroporation

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The transmembrane voltage induced by reversible electroporation protocols in cell suspensions and adhered cells is reported in this work for five cancerous cell lines and one non-cancerous cell line. For this purpose, cell-specific morphology and realistic three-dimensional models of adhered cells reconstructed from confocal microscopy images were used. Induced transmembrane voltage (ITV) analytically determined for cell suspensions resulted in much higher values in comparison to the values numeri-cally determined for adhered cells. Analytical and numerical values are in good agreement only for cells showing a spheroidal shape when adhered. In general, the ITV numerically determined for all adhered cells, ranged between 200 mV and 800 mV. Specifically, the ITV resulted to be dependent on the cell type and the pathophys-iological state of cells since ITV is much higher in non-transformed cells than in can-cerous cells. These higher values may be attributed to the high endogenous membrane potential compared to the low cell membrane potentials that malignant cells exhibit. Determination of cell-specific reversible electroporation thresholds influence on an accurate approximation to the ITV which should not be unnecessarily high in order to not lead to intracellular signaling to the cytoskeleton of non-target cells and influence a metastatic process.

# Ultra-wideband Localization of Pulmonary Nodules During Thoracoscopic Surgery

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Lung cancer is one of the most common causes of cancer-related death worldwide. It is usually detected by CT or MRI and removed through thoracoscopic surgery. However, during the surgery, the lung collapses and a new determination of the position of the pulmonary nodule is necessary which is particularly challenging in the case of minimally invasive surgeries when palpation is not possible.
In this contribution, ultra-wideband (UWB) radio technology is proposed for the localization of lung cancer. This was investigated through numerical simulations mimicking the frequencies range between 0.5 and 5 GHz and a nodule depth of 1 to 6 cm.
A confocal map was reconstructed by positioning a monostatic antenna on a 5 x 5 grid distribution on top of the lung tissue. The results show that the cancer localization was possible in the frequency between 0.5 and 1 GHz and nodules depth between 4 and 6 cm, while at lower depths artifacts appeared and at higher frequencies the electromagnetic attenuation given by the lung tissue was too high to detect the pulmonary nodule.

# Ultrasound Shear-Wave Elastography of the Tongue in Adults with Obstructive Sleep Apnea

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Obstructive sleep apnea is a chronic breathing disorder characterized by intermittent sleep state-dependent upper airway collapse. The tongue comprises the primary upper airway dilator muscle and plays an essential role in the pathogenesis of obstructive sleep apnea. We examined whether tongue stiffness measurement using ultrasound shear-wave elastography is useful for predicting the existence of obstructive sleep apnea. Forty-six participants (twenty healthy controls and twenty-six patients with obstructive sleep apnea) underwent transcutaneous submental shear-wave elastography using an ultrasound system. Quantification with a shear modulus of 0–200kPa was recorded during normal breathing and the Müller maneuver. Polysomnography was used as the reference standard. Mid-sagittal tongue stiffness was significantly higher in awake patients with obstructive sleep apnea than in controls during normal breathing and the Müller maneuver ($P < .0001$). The posterior third of the tongue in patients with obstructive sleep apnea had the highest value of shear modulus during the Müller maneuver ($P < .001$). With cutoffs of 27.6 and 35.2kPa for the whole tongue and posterior third during the Müller maneuver, respectively, the sensitivity obtained was 69.2% and 76.9%, and specificity was 85% and 95% respectively, for detecting obstructive sleep apnea. The corresponding areas under the receiver operating characteristic curve were 0.82 and 0.88, respectively. Ultrasound shear-wave elastography may have the potential for noninvasive tongue stiffness measurement in obstructive sleep apnea. Future application of the technique may involve ultrasonographic measurement of tongue stiffness during sedative or natural sleep, which will help to define the pathophysiology for an individual patient with obstructive sleep apnea and to verify treatment results for those procedures targeting the tongue.

# Use of Histology in Interpreting Dielectric Measurements of Heterogeneous Tissues: Challenges and Limitations

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The dielectric properties of biological tissues are key parameters in the design, development, and clinical implementation of microwave medical technologies. Typically, dielectric properties of tissues are measured using an open-ended coaxial probe connected to a network analyzer. This method is intended for the measurement of homogeneous materials; however, tissues can be complex heterogeneous structures.

Histological analysis of tissue samples may be conducted to support the dielectric measurement, and the interpretation of the dielectric properties, of heterogeneous samples. Performing histology enables the identification of the individual tissue types that a heterogeneous sample is composed of, as well as their relative volumes and distributions. However, histological analysis protocols were not designed with dielectric measurements in mind, and several adjustments to the protocols must be made to achieve accurate dielectric data.

This presentation will first review the histological processes, including tissue fixation, embedding, slicing, and imaging. Then, the current state-of-the-art in dielectric studies using histology will be discussed. Finally, the challenges with using histological analysis for dielectric properties, which have gone under-examined in the literature to date, will be examined in detail. Through quantification of the errors introduced in the interpretation of the dielectric data, at each of the steps of the histological process, we can conclude that that errors in the histology process are likely causing significant errors in the interpretation of dielectric data of key tissues. Therefore, the dielectric properties that medical microwave technologies are based upon may have higher uncertainties than previously thought.

# Using Artificial Intelligence in Ultrasound Image of the Long Head of Biceps Tendon to Grade the Severity of Inflammation

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Inflammation of the long head of the biceps tendon is a common cause of shoulder pain. Bicipital peritendinous effusion (BPE) is the most common biceps tendon abnormality and is related to various shoulder injuries. Physicians usually use ultrasound imaging to grade the inflammation severity of the long head of the biceps tendon. However, obtaining a clear and accurate ultrasound image is difficult for inexperienced attending physicians. To reduce physicians' workload and avoid errors, an automated BPE recognition system will be developed in this study for classifying inflammation into the following categories—normal and mild, moderate, and severe. An ultrasound image serves as the input in the proposed system; the system determines whether the ultrasound image contains biceps. If the image depicts biceps, then the system predicts BPE severity. In this study, two crucial methods will be used for solving problems associated with computer-aided detection. First, the faster regions with convolutional neural network (faster R-CNN) used to extract the region of interest (ROI) area identification to evaluate the influence of dataset scale and spatial image context on performance. Second, various CNN architectures will be evaluated and explored. Model performance will be analyzed by using various network configurations, parameters, and training sample sizes. The system will provide the severity of BPE with the optimal settings after the evaluation. The predicted severity of BPE can be regarded as a reference and used to assist the inexperienced physicians to diagnose the patients' severity of BPE more accurately.

# Vertebra Segmentation for Clinic CT Image using Mask R-CNN

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Spine disease is a growing problem in modern society and has been debilitating for every age-group. Researches have shown that more than 266 million people are facing degenerative spine disease and low back pain. CT scanning is a fast, painless, non-invasive diagnostic imaging modality that provides high spatial accuracy in obtaining the 3D structure of the vertebral. However, in real-life scenario, the clinic CT image might not cover the whole spine and the field of view might be hard to determine. Henceforth, this project aims to create and validate an automatic method that can detect, locate, and classify each vertebra from the partial field of view using deep learning. We used Mask R-CNN, a deep neural network aimed to solve the instance segmentation problem in machine learning or computer vision, and produce features such as bounding boxes, classes, and masks to identify each vertebra. This auto-detection method was validated on a open source dataset which has been used on Computational Spine Imaging (CSI 2014). The dataset was physically chosen by a radiologist with an eight-year-long time of involvement based on thoracic and lumbar spine column scans, and the data of twenty patients were collected using CT protocol. The accuracy of the vertebra mask on 210 test images has been increased up to 99.9% DICE Coefficient in Mask R-CNN compare with 69.2% Dice Coefficient in another Deep-learning-based semantic segmentation framework U-Net.

# Wearable Graphene Smart Textile Electronics for Monitoring and Processing of Biopotential Signals

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In the past decade, ordinary textiles have witnessed a paradigm shift from their traditional role in clothing towards being enablers of soft and smart platforms for wearable electronics particularly in health monitoring, healthy living and assistive technology applications. Along these lines, we report our pioneering efforts on the synthesis and application of graphene-coated functional textile platforms with peripheral electronics; otherwise referred to as smart garments, towards the development of wearable sensors for acquisition, routine monitoring and processing of biopotential signals in personalized healthcare and human-computer interaction applications. Low-cost and scalable techniques were used to achieve functionalization of ordinary fabrics (e.g. nylon, cotton) with graphene, where textiles were dipped in graphene oxide (GO) solution, followed by thermal treatment and chemical reduction to allow cladding of graphene around fibers. Upon preparation, graphene textiles were sewed directly into elastic bands for seamless measurement of surface biopotentials. To achieve IoT-compatible and portable operation, battery-powered electronic readout circuitry was built and attached onto clothing, which provided remote transmission of sensor readings to a graphical user interface (GUI) and facilitated truly wearable and mobile use. The functionality of the graphene textile embedded wearable systems were demonstrated by non-invasive measurement of cardiac (ECG), ocular (EOG) and muscular (EMG) biopotentials. Excellent cross correlation of up to 97% was achieved between signals measured with wearable graphene e-textile garments and that of commercial silver/silver-chloride (Ag/AgCl) “wet” electrodes.

# Wearable sensor based real-time gait detection

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Real-time gait analysis is key to the development of gait rehabilitation techniques. In contrast to reliable, yet expensive laboratory equipment used in gait analysis, recent advancements in technology enabled affordable, reliable and wearable sensors for gait analysis, often also enabling it to be used outside of laboratory environments. Here we present the results of a systematic review and meta-analysis carried out to identify various wearable sensing options and real-time gait analysis techniques (focusing on intra-stride temporal gait features) reported in scientific literature. It was observed from the review that toe off and heel strike are the most sought-after gait events while foot is the most preferred location for placement of Inertial Measurement Unit (IMU), closely followed by shank. Insole pressure sensor is the most widely used and only wearable sensor to be used for ground truth validation. A comprehensive list of real-time wearable sensor-based gait detection techniques were identified from the literature. Rule-based techniques relying on threshold or peak detection are the most widely used gait analysis techniques with nearly 60% of the studies using it. Although the above methods couldn't be compared under the same scale quantitatively due to differences in reporting methods among other factors, it was noted that machine learning techniques reported highest accuracy (>95%) compared to other methods. Although many of the studies expressed optimism that the proposed methods would work on pathological gait, only less than one-third of the studies validated with some form of impaired/pathological gait data. Since many of the gait detection algorithms used processed pitch angle information instead of raw data from IMU (linear acceleration and angular velocity), we will also discuss results of a benchmarking study carried out by us, comparing major orientation estimation algorithms and also discuss the choice of Euler angle conventions with respect to IMU placement orientation, to extract pitch angle from quaternions.

# Which biocompatibility issues are overlooked by medical device manufacturers?

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Biocompatibility is a word, for which there have been offered many definitions. The most widely cited is: “Biocompatibility is the ability of a material to perform with an appropriate host response in a specific application” and updated definition is: “Biocompatibility refers to the ability of a biomaterial to perform its desired function with respect to a medical therapy, without eliciting any undesirable local or systemic effects in the recipient or beneficiary of that therapy, but generating the most appropriate beneficial cellular or tissue response in that specific situation, and optimising the clinically relevant performance of that therapy [1].”
For a medical device, which comes into direct or indirect contact with patient’s body, a biocompatibility is one of important requirements. Manufacturers shall evaluate the biological compatibility of materials and final product, at which is optimal to follow standard ISO 10993-Part 1 [2]. The last, fifth edition was issued in August 2018 and in Table A.1 defines extended aspects of biological assessment based on body contact type and contact duration. Biological evaluation may upon material chemical and physical characterization rely on either biological testing or may consider already published data about biological compatibility of materials and/or final medical device. Standard emphasizes the importance of consideration the manufacturing conditions effects (e.g. process contaminants, disinfection/sterilization agents etc.) and primary packaging impact on biological safety, which are often overlooked by medical device manufacturers. Ultimately, a toxicological risk assessment must be carried out and overall conclusion in evaluation shall show overweighed benefit vs. risk [3].
One of the things, which is often not properly understood is that there is no such thing as a biocompatible material, but the most crucial is to show compatibility between the system: material and biological host. Therefore, manufacturer shall justify the biocompatibility not only with laboratory tests and data, but also with clinical studies of materials/final devices [4].

References:

1. Ratner, BD.: The biocompatibility manifesto: biocompatibility for the twenty-first century. Journal of Cardiovascular Translational Research, 4(5): 523-527 (2011).
2. ISO 10993-1:2018 Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process
3. Anderson JM.: Future challenges in the in vitro and in vivo evaluation of biomaterial biocompatibility. Regenerative Biomaterials, 3(2): 73-77 (2016)
4. Williams DF.: There is no such thing as a biocompatible material. Biomaterials, 35(38): 10009-14 (2014).

# Whole-Night Simultaneous Ultrasonographic and Polysomnographic Study for Tongue Obstruction in Adults with Obstructive Sleep Apnea

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Obstructive sleep apnea (OSA) is a respiratory disorder characterized by partial or total obstruction of the pharyngeal airway during sleep. Polysomnography (PSG) is the gold standard method used to diagnose OSA. Although PSG measures valuable physiologic characteristics of a patient with OSA during whole-night sleep, it fails to provide information regarding the form/function of the upper airway. Because the tongue comprises the essential upper airway dilator muscle, namely genioglossus muscle, recognizing the prevalence and patterns of tongue obstruction during sleep will provide insights into treatment decisions for OSA patients. However, it is currently impracticable to quantify tongue deformation during whole-night sleep in clinical settings.

We innovated an ultrasound system with PSG to simultaneously record changes in tongue depth (TD) during a whole night's sleep. Our ultrasound system included a custom-designed curvilinear transducer. The center frequency of the probe was 3 MHz, and it had 16 channels. We placed the probe in the submental midline sagittal plane. We designed a dedicated ultrasound device to automatically detect maximum TD at a recording rate of 1 Hz. The device synchronizes with the PSG and transmits the measured data to a computer for storage. The system receives an A-line signal from each channel, determines the depth of the air–mucosal interface, and then registers the maximum TD and its channel number. We generated a "SonoPSG" report for each patient, reporting on the mean maximum TD and the distribution of the registered channels in various sleep stages as well as during various respiratory events.

Among the 60 participants, the majority of OSA patients (88.4%) exhibited a significant increase in the maximum ultrasonographic TD during hypopnea or apnea. The proportion of these changes increased with disease severity. A mixed-model analysis of variance demonstrated that compared with patients with primary snoring or mild OSA, those with moderate-to-severe OSA have significantly higher maximum ultrasonographic TD during respiratory events (P=.0047). We identified three different patterns of tongue obstruction, namely en-bloc, tongue body, and tongue base. Approximately 82% (27/33) of patients with moderate-to-severe OSA demonstrated an en-bloc tongue obstruction. By contrast, 70% (19/27) of primary snorers or patients with mild OSA showed a tongue body obstruction. Identifying changes in TD and patterns of tongue obstruction through simultaneous ultrasonography and PSG may help to develop an individualized surgical plan for each patient with OSA.

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